European Society of Endocrinology

EJE European Journal of Endocrinology

Clinical and translational endocrinology from around the globe

Volume 195, Supplement 1
August 2026

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

28th European Congress of Endocrinology 2026 Abstract Book

European Society of Endocrinology

ECE 2026

28th European Congress of Endocrinology

9–12 May 2026

Prague, Czech Republic

OXFORD UNIVERSITY PRESS

European Journal of Endocrinology
Volume 195, Supplement 1, August 2026

28th European Congress of Endocrinology (ECE 2026), 9-12 May 2026, Prague, Czech Republic, Abstract Book

Editors

Abstracts were marked by the Abstract Marking Panel and selected by the Programme Organising Committee.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

European Journal of Endocrinology

Volume 195, Supplement 1, August 2026

CONTENTS

iv **ECE 2026 Programme Organising Committee (POC)**

v **Abstract Marking Panel**

vii **Sponsors**

Abstracts

i1	Prize Lectures	AW1–AW7
i1	Plenary Lectures	PL1–PL8
i4	Symposia	S1.1–S16.3
i14	Joint Sessions	JS1.1–JS6.3
i18	ESE EYES Symposium	EYS1.1–EYS1.5
i19	EUWIN Symposium	EW1.1–EW1.2
i19	New Scientific Approaches	NSA1–NSA3
i20	Debate Sessions	D1.1–D1.4, D2.1–D2.4
i21	Meet the Expert Sessions	MTE1–MTE12
i21	Meet the Expert Basic Scientist Sessions	MTEBS1–MTEBS4
i22	Pre-Congress Events	PCC1.1–PCC7.2
i28	Nurse Sessions	N1.1–N3.4

Oral Communications

i30	Oral Communications 1: Thyroid	OC1.1–OC1.6
i33	Oral Communications 2: Diabetes, Obesity, Metabolism and Nutrition Part 1	OC2.1–OC2.6
i36	Oral Communications 3: Pituitary and Neuroendocrinology Part 1	OC3.1–OC3.6
i39	Oral Communications 4: Reproductive and Developmental Endocrinology	OC4.1–OC4.6
i42	Oral Communications 5: Pituitary and Neuroendocrinology Part 2	OC5.1–OC5.6
i45	Oral Communications 6: Adrenal and Cardiovascular Endocrinology Part 1	OC6.1–OC6.6
i49	Oral Communications 7: Endocrine-related Cancer	OC7.1–OC7.6
i53	Oral Communications 8: Environmental Endocrinology	OC8.1–OC8.6
i55	Oral Communications 9: Adrenal and Cardiovascular Endocrinology Part 2	OC9.1–OC9.6
i58	Oral Communications 10: Calcium and Bone	OC10.1–OC10.6
i61	Oral Communications 11: Diabetes, Obesity, Metabolism and Nutrition Part 2	OC11.1–OC11.6
i64	Oral Communications 12: Late Breaking	OC12.1–OC12.5

Rapid Communications

i67	Rapid Communications 1: Thyroid	RC1.1–RC1.6
i70	Rapid Communications 2: Diabetes, Obesity, Metabolism and Nutrition Part 1	RC2.1–RC2.6
i73	Rapid Communications 3: Pituitary and Neuroendocrinology Part 1	RC3.2–RC3.6
i76	Rapid Communications 4: Reproductive and Developmental Endocrinology	RC4.1–RC4.6
i79	Rapid Communications 5: Pituitary and Neuroendocrinology Part 2	RC5.1–RC5.6
i82	Rapid Communications 6: Adrenal and Cardiovascular Endocrinology Part 1	RC6.1–RC6.6
i86	Rapid Communications 7: Endocrine-related Cancer	RC7.1–RC7.6
i88	Rapid Communications 8: Environmental Endocrinology	RC8.1–RC8.6
i91	Rapid Communications 9: Adrenal and Cardiovascular Endocrinology Part 2	RC9.1–RC9.6

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

i94	Rapid Communications 10: Calcium and Bone	RC10.1–RC10.6
i97	Rapid Communications 11: Diabetes, Obesity, Metabolism and Nutrition Part 2	RC11.1–RC11.6
i100	Rapid Communications 12: Late Breaking	RC12.2–RC12.6
	Poster Presentations	
i102	Adrenal and Cardiovascular Endocrinology	P1–P68
i133	Calcium and Bone	P69–P121
i156	Diabetes, Obesity, Metabolism and Nutrition	P123–P208
i186	Endocrine-related Cancer	P210–P228
i194	Environmental Endocrinology	P230–P241
i198	Pituitary and Neuroendocrinology	P242–P317
i233	Reproductive and Developmental Endocrinology	P320–P372
i256	Thyroid	P373–P437
i280	Late Breaking	P440–P509
	ePoster Presentations	
i309	Adrenal and Cardiovascular Endocrinology	EP1–EP208, EP1675, EP1677, EP1683
i389	Calcium and Bone	EP209–EP368
i442	Diabetes, Obesity, Metabolism and Nutrition	EP369–EP890, EP1673, EP1678, EP1680
i585	Endocrine-related Cancer	EP891–EP978, EP1672
i619	Environmental Endocrinology	EP983–EP987, EP1674
i622	Pituitary and Neuroendocrinology	EP989–EP1301, EP1676, EP1684, EP1909
i750	Reproductive and Developmental Endocrinology	EP1304–EP1446, EP1905–EP1908
i799	Thyroid	EP1449–EP1679
i865	Late Breaking	EP1700–EP1903
i926	**Author Index**	

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

ECE 2026 Programme Organising Committee (POC)

Programme Organising Committee (POC)
Cynthia Andoniadou (UK) Congress Committee Chair
Peter Igaz (Hungary) Joint Chair Clinical
Sander Kooijman (The Netherlands) Joint Chair Basic-science
Michal Krše (Czech Republic) LOC

Adrenal and Cardiovascular Endocrinology
Nicole Reisch (Germany)
Andreas Schedl (France)

Calcium and Bone
Peter Kamenicky (France/Slovakia)
Annegreet Vlug (The Netherlands)

Diabetes, Obesity, Metabolism and Nutrition
Kostis Michalakis (Greece)
Lora Heisler (UK)

Environmental Endocrinology
Jorma Toppari (Finland)
Pauliina Damdimopoulou (Sweden)

Endocrine-related Cancer
Beata Kos-Kudla (Poland)
Rodrigo Toledo (Spain)

Pituitary and Neuroendocrinology
Cristina Capatina (Romania)
Kim Jonas (UK)

Reproductive and Developmental Endocrinology
Andrea Isidori (Italy)
Vincent Prevot (France)

Thyroid
Rosella Elisei (Italy)
Edward Visser (The Netherlands)

Clara Lazzaretti (Italy) **EYES representative**
Kirsten Davidse (The Netherlands) **Nurse representative**

Ex-Officio
Wiebke Arlt (UK) ESE President
Mirjam Christ-Crain (Switzerland) ESE President-Elect
Sebastian Neggers (The Netherlands) ESE Treasurer
João Sérgio Neves (Portugal) ECAS representative
Elena Valassi (Spain) Chair of Rare Disease Committee
Peter Kühnen (Germany) ESPE representative

Local Organising Committee
Michal Kršek (Czech Republic) Chair
Běla Bendlová (Czech Republic)
Filip Gabalec (Czech Republic)
Jan Jiskra (Czech Republic)
Michal Krčma (Czech Republic)
Jan Lebl (Czech Republic)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract Marking Panel

Adamski, Jerzy
Aimaretti, Gianluca
Alexandraki, Krystallenia
Alonso-Magdalena, Paloma
Alvarez, Clara V
Ambroziak, Urszula
Amrein, Karin
Anastasilakis, Athanasios
Andersson, Anna-Maria
Andoniadou, Cynthia
Appelman-Dijkstra, Natasha
Arlt, Wiebke
Ayuk, John
Badiu, Corin
Bancos, Irina
Baranowska-Bik, Agnieszka
Barbu, Carmen Gabriela
Bargiota, Alexandra
Barlier, Anne
Basham, Katie
Bednarczuk, Tomasz
Belaya, Zhanna
Benrick, Anna
Bertherat, Jérôme
Beuschlein, Felix
Bevan, Charlotte
Bidlingmaier, Martin
Biermasz, Nienke
Bislev, Lise Sofie
Bodor, Miklós
Boelaert, Kristien
Boelen, Anita
Boguszewski, Cesar Luiz
Bollerslev, Jens
Bouillon, Roger
Bourguet, William
Boutzios, Georgios
Brandi, Maria Luisa
Broglio, Fabio
Brue, Thierry
Brunetti, Giacomina
Buchanan, Charles
Buffet, Alexandre
Buffet, Camille
Buha Dordevic, Aleksandra
Burman, Pia
Butz, Henriett
Calissendorff, Jan
Campbell, Rebecca
Campi, Irene
Cannavò, Salvatore
Cap, Jan
Capatina, Cristina
Caputo, Marina
Cariboni, Anna
Carmeliet, Geert
Caron, Philippe
Castaño, Justo P.
Castinetti, Frederic
Censi, Simona
Chanson, Philippe
Charmandari, Evangelia
Cherradi, Nadia
Chiloiro, Sabrina
Chowen, Julie
Chrisoulidou, Alexandra
Christ-Crain, Mirjam
Christoforidis, Athanasios
Cohen-Solal, Martine
Criseno, Sherwin
Crona, Joakim
Czupryniak, Leszek
Dahlqvist, Per
Daly, Adrian
Damdimopoulou, Pauliina
Daousi, Christina
Dattani, Mehul
Dayan, Colin
de Herder, Wouter Willem
Delemer, Brigitte
Derakhshan, Arash
Dhillo, Waljit
Dieguez, Carlos
Dischinger, Ulrich
Duntas, Leonidas
Effraimidis, Grigoris
Eisenhofer, Graeme
Elian, Viviana
Elisei, Rossella
Esposito, Katherine
Falhammar, Henrik
Fassnacht, Martin
Favier, Judith
Feelders, Richard
Fekete, Csaba
Feldt-Ramussen, Ulla
Fernandes-Rosa, Fabio
Ferraù, Francesco
Fini, Jean-Baptiste
Flück, Christa
Follin, Cecilia
Fowkes, Rob
Franks, Stephen
Frara, Stefano
Froidevaux, Marie-Stephanie
Frystyk, Jan
Fugazzola, Laura
Fuss, Carmina Teresa
Gabalec, Filip
Gaberšček, Simona
Gahete, Manuel D.
Gärtner, Roland
Gatto, Federico
Gawel, Damian
Gennari, Luigi
Gheorghiu, Monica Livia
Gherlan, Iuliana
Gibson, Douglas
Gilis-Januszewska, Aleksandra
Gittoes, Neil
Godlewska, Marlena
Goulis, Dimitrios
Granata, Riccarda
Gravholt, Claus H.
Grineva, Elena
Groop, Per-Henrik
Grossman, Ashley B.
Groussin, Lionel
Grozinsky-Glasberg, Simona
Gruden, Gabriella
Guasti, Leonardo
Hana, Vaclav
Hannan, Fadil
Heck, Ansgar
Heisler, Lora
Hofland, Leo
Höflich, Andreas
Högler, Wolfgang
Howard, Sasha
Höybye, Charlotte
Hubalewska-Dydejczyk, Alicja
Hubina, Erika
Husebye, Eystein Sverre
Ibañez-Costa, Alejandro
Igaz, Peter
Ilias, Ioannis
Iotova, Violeta
Isenovic, Esma R.
Isgaard, Jörgen
Isidori, Andrea
Jääskeläinen, Jarmo
Jácome de Castro, João
Jaffrain-Rea, Marie-Lise
Jessen, Niels
Jezova, Daniela
Johannsson, Gudmundur
Jørgensen, Anders
Jørgensen, Jens Otto
Juhlin, C Christofer
Kalsbeek, Andries
Kaltsas, Gregory
Kanaka-Gantenbein, Christina
Kanakis, Georgios
Kandaraki, Eleni
Karavitaki, Niki
Kaser, Susanne
Kastelan, Darko
Kaufman, Jean-Marc
Keil, Meg
Kelestimur, Fahrettin
Kelk, Eve
Kero, Jukka
Kineman, Rhonda
Kocjan, Tomaz
Köhrle, Josef
Konrade, Ilze
Kooijman, Sander
Korbonits, Marta
Korevaar, Tim
Krajewska, Jolanta
Krarup Hansen, Troels
Kroiß, Matthias
Krsek, Michal

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Kühnen, Peter
Kurylowicz, Alina
Kyle, Catriona
Lalli, Enzo
Langdahl, Bente
Lapauw, Bruno
Laven, Joop
Lavery, Gareth
Lazúrová, Ivica
Le Tissier, Paul
Lefebvre, Hervé
Lips, Paul
Livingstone, Dawn
Llahana, Sofia
Loli, Paola
Luger, Anton
Luque, Raul M
Lyssenko, Valeriya
MacKenzie, Scott
Macut, Djuro
Makras, Polyzois
Mannucci, Edoardo
Mantovani, Giovanna
Marina, Ljiljana
Martinez, Antoine
Marzullo, Paolo
Matikainen, Niina
McCabe, Christopher
Meier, Christian
Meijer, Onno
Mellanby, Richard
Messina, Andrea
Metherell, Louise
Metso, Saara
Mezosi, Emese
Michalaki, Marina
Michalakis, Konstantinos
Miettinen, Paivi
Mittag, Jens
Møller, Niels
Morin-Papunen, Laure
Mukherjee, Abir
Musat, Madalina
Neggers, Sebastian
Newey, Paul
Niculescu, Dan Alexandru
Niedziela, Marek
Nogueiras, Rubén
Obermayer-Pietsch, Barbara
Olarescu, Nicoleta Cristina
Oliveira, Pedro F.
Olsson, Daniel S
Opitz, Robert
Pagotto, Uberto
Papanas, Nikolaos
Papanastasiou, Labrini
Parent, Anne Simone
Peeters, Robin
Pekic Djurdjevic, Sandra
Perez-Rivas, Luis Gustavo
Persani, Luca
Perseghin, Gianluca
Petakov, Milan
Piekiełko-Witkowska, Agnieszka
Pilz, Stefan
Poiana, Catalina
Poladian, Raffi
Polyzos, Stergios
Poplawski, Piotr
Popovic, Vera
Poutanen, Matti
Power, Deborah
Prevot, Vincent
Prodam, Flavia
Radian, Serban
Ragnarsson, Oskar
Rahman, Nafis
Rajpert-De Meyts, Ewa
Ramhøj, Louise
Rapizzi, Elena
Rauner, Martina
Raverot, Gerald
Reincke, Martin
Rejnmark, Lars
Rice, Suman
Rizzoti, Karine
Robledo, Mercedes
Rodien, Patrice
Romijn, Hans
Ruchala, Marek
Rutten, Elisabeth
Sachs, Laurent
Santi, Daniele
Saponaro, Federica
Schalin-Jantti, Camilla
Schopohl, Jochen
Schulte, Dominik
Schwarz, Peter
Sherlock, Mark
Shestakova, Marina
Shimon, Ilan
Siggelkow, Heide
Simoni, Manuela
Skrha, Jan
Soares, Paula
Söderlund, Sanni
Solini, Anna
Sourij, Harald
Spyroglou, Ariadni
Stalla, Günter Karl
Steenblock, Charlotte
Stener-Victorin, Elisabet
Stimson, Roland
Storbeck, Karl
Strasburger, Christian
Sykiotis, Gerasimos
Tabarin, Antoine
Tamagno, Gianluca
Tankova, Tsvetalina
Tena-Sempere, Manuel
Tentolouris, Nikolaos
Terzolo, Massimo
Theodoropoulou, Marily
Tigas, Stelios
Timmers, Henricus Johannes Louis Maria
Tőke, Judit
Toledo, Rodrigo
Tomlinson, Jeremy
Toppari, Jorma
Tóth, Miklós
Touraine, Philippe
Trifanescu, Raluca
Trummer, Christian
Tsagarakis, Stylianos
Tsourdi, Elena
Tzanela, Marinella
Underbjerg, Line
Valassi, Elena
van den Akker, Erica
van der Eerden, Bram
Van der Lely, AJ
van Hul, Wim
Vantyghem, Marie Christine
Vassiliadi, Dimitra Argyro
Verkauskiene, Rasa
Vila, Greisa
Visser, Edward
Volke, Vallo
Widimsky, Jiri
Wiersinga, Wilmar
Wilding, John
Wilkinson, Ian
Williams, Tracy
Winter, Elizabeth M.
Wirth, Eva
Xekouki, Paraskevi
Yavropoulou, Maria
Yedinak, Christine
Yildiz, Bulent
Zabuliene, Lina
Zandee, Wouter
Zarkovic, Milos
Zatelli, Maria Chiara
Zennaro, Maria-Christina
Zilaitiene, Birute
Zillikens, Carola

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Sponsors

The **28th European Congress of Endocrinology** would like to thank the following industry partners for their support of the 2026 Congress in Prague.

Gold Sponsors
Alexion, AstraZeneca Rare Disease
Ascendis Pharma

Silver Sponsors
Amgen
BridgeBio
Crinetics Pharmaceuticals
Esteve
Rhythm Pharmaceuticals
Soleno Therapeutics

Bronze Sponsors
Camurus
Corcept Therapeutics
Immedica Pharma
Immunovant
Kyowa Kirin International
Neurocrine Biosciences
Novo Nordisk Healthcare Ag
Recordati Rare Diseases
Uni-Pharma

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstracts

Prize Lectures

AW1 - Genetics of thyroid function and disease: past, present and future

Abstract Unavailable

AW2 - Harnessing heterogeneity to deliver precision medicine for diabetes

Abstract Unavailable

AW3 - Genetic mechanisms of aldosterone related disorders—towards precision medicine in hypertension

Abstract Unavailable

AW4 - From bench to bedside: primary aldosteronism revisited

Abstract Unavailable

AW5 - Cushing's syndrome: new ways of personalized medicine

Abstract Unavailable

Abstract citation ID: lvag096.001

AW6 - Basic science—molecular memory—how the liver remembers fasting

Ido Goldstein
The Hebrew University, Jerusalem, Israel

Mammals withstand frequent and prolonged fasting periods due to hepatic production of ketone bodies. Because the hepatic fasting response is tightly regulated transcriptionally, we asked whether transcription factor and enhancer activity impose a transcriptional program during repeated fasting and whether this generates effects distinct from a single fasting bout.

We found that mice undergoing alternate-day fasting respond profoundly differently to a following fasting bout compared to mice first experiencing fasting. Hundreds of genes enabling ketogenesis were "sensitized", meaning that while their level was reduced back to basal levels upon refeeding, their induction became stronger in the next fasting bout. The activity of thousands of enhancers was also sensitized. Enhancer sensitization was governed by the transcription factor PPARα: sensitized enhancers harbored increased binding of PPARα and gene sensitization was abolished in hepatocyte-specific PPARα-deficient mice. As a result of sensitization, repeated fasting led to augmented ketogenesis compared to a single fasting bout; an effect which was absent in hepatocyte-specific PPARα-deficient mice.

In summary, we found a transcriptional memory mechanism where past fasting events are "remembered" in hepatocytes, sensitizing their enhancers to the next fasting bout and increase ketogenesis via amplified gene induction. Our findings reveal a new adaptation mechanism to repeated environmental signals: transcription factor-mediated sensitization of enhancers resulting in an amplified transcriptional response.

AW7 - Clinical—extreme insulin resistance syndromes: from pathophysiology to therapeutic management, national and European expertise

Abstract Unavailable

Plenary Lectures

PL1 - The work on the discovery of leptin

Abstract Unavailable

Abstract citation ID: lvag096.002

PL2 - Hormones for life: the enigma of LH and HCG

Manuela Simoni
Department of Biomedical, Metabolic and Neural Sciences; Unit of Endocrinology—OCSAE, University of Modena and Reggio Emilia, Modena, Italy

The reason why two hormones acting on the same receptor, ie LH and hCG acting on LHCGR, are necessary for reproduction remain enigmatic. The beta subunit gene of hCG (CGB) evolved from the *LHB* gene from a frame shift mutation and successive, multiple gene duplications, so that one *LHB* and six *CGB* genes exist in the species *Homo*. Such a complication is justified by a progressive specialization of hCG function, which should be differentiated from that of LH. Yet the two hormones have been traditionally thought to be equivalent and our textbook knowledge about "LH action" derives form experiments in rodents (which do not have hCG) using hCG instead of LH. *In vitro* experiments demonstrate that the two hormones have different activity on signal transduction, being hCG mainly steroidogenic (via cAMP) and LH acting as a growth and anti-apoptotic factor (via ERK and AKT signaling). The LHCGR discriminates between the two ligands through exon 10, encoding the hinge region. *In vivo*, deletion of exon 10 results in lack of LH action with hypergonadotropic hypogonadism in the presence of normal androgenization, suggesting that hCG can act on the deleted receptor while LH cannot.

The main actions of hCG are: 1) maintenance of pregnancy via stimulation of progesterone by the corpus luteum; 2) embryo implantation; 3) development of the fetal testis; 4) development of the fetal thyroid (through TSH receptor); 5) virilization of the external genitalia via the backdoor steroidogenic pathway. Therefore, hCG is essential for male fetal development and androgenization. The main action of LH is evident in females: LH is essential for follicular maturation, ovulation and luteinization of granulosa cells.

© The Author(s) 2026. Published by Oxford University Press on behalf of European Society of Endocrinology. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (https://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

In theca cells LH stimulates progesterone and androgen production via expression of StAR and steroidogenic enzymes. In the male, the action of LH is less clear. Preliminary results suggest that, in men with hypogonadotropic hypogonadism, LH alone is unable to stimulate testosterone production, which probably requires FSH action as well.

In conclusion, hCG is essential for primate pregnancy but has developed a number of other functions, while the function of LH is only partly understood. The enigma continues …

Abstract citation ID: lvag096.003

PL3 - Human exposure to microplastics and implications for health

Majorie van Duursen
Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

The increasing production and use of plastics poses a serious threat to human endocrine health. Chemicals can leach from plastics that are know to interact with our endocrine system and have been associated with endocrine-related diseases and disorders, including subfertility and changes in age of pubertal onset. More recently, scientific and societal attention has been been directed towards micro- and nanoplastics (MNPs); small plastic particles resulting of plastic degradation. While MNPs are found everywhere in the environment, and increasing number of studies report on the occurrence in humans as well, the health impact they may have on humans remains unclear. Studies addressing human health impact generally suffer from poor exposure assessment and limited number of participants. This talk will address the current state of science, including the scientific challenges we are facing in the complex field of plastics research.

Abstract citation ID: lvag096.004

PL4 - Cellular diversity of the hypothalamus

Tibor Harkany
Medical University of Vienna

The hypothalamus is the central site where neurendocrine modules cocluster in the brain. During evolution, cellular diversification rather than progeny expansion had taken place to increase the specificity, precision, and adaptive potential of neuroendocrine output pathways. This is why the hypothalamus became a brain region with a unique constellation of cell types, including exceptional numbers of phase- and state transitions to allow for maximal flexibility. Here, I will discuss developmental principles that underpin the organization of neuroendocrine command centers for brain-body communication, and integrate them with extrahypothalamic neurocircuits that offer upstream control. Thereafter, I will showcase novel understanding on neuron-glia communication and circuit-specific interactions to control bodily metabolism. A central role for neuropeptides, which are commonly co-released with fast neurotransmitters, will be made in defining cell states, labile neurocircuit output, and disease vulnerabilities. These topics will be presented and discussed by combining single-cell techniques with optical and chemical manipulations to experimentally modulate, disrupt or even attempt to repair neuroendocrine cell contingents of the hypothalamus.

Abstract citation ID: lvag096.005

PL5 - Shining light in the darkness of pheochromocytoma

Karel Pacak
AKESO, Prague, Czech Republic

Pheochromocytomas and paragangliomas (PPGLs) remain among the most genetically complex and clinically unpredictable endocrine tumors, associated with substantial morbidity and metastatic potential. Yet what was once a field defined by uncertainty is rapidly becoming a model of precision oncology. Over the past decade, comprehensive genomic discovery has unveiled more than 25 susceptibility genes and seven biologically distinct molecular clusters, redefining PPGL as a family of molecularly stratified diseases. Genotype now informs biochemical phenotype, metastatic risk, imaging strategy, and therapeutic vulnerability. Contemporary international guidelines embed this taxonomy into daily practice, ensuring that precision is no longer theoretical, but operational. Newly established international consensuses and evidence-based guidelines now formally incorporate this molecular taxonomy into screening protocols for *SDHx* mutation carriers, imaging selection algorithms, metastatic management strategies, and lifelong surveillance frameworks, ensuring that precision is no longer theoretical, but operational. Functional imaging has evolved from a “one tracer fits all” philosophy to cluster-specific precision selection. The emerging “precision imaging card” concept links molecular background with radiopharmaceutical choice, enabling biologically informed detection and treatment planning. Theranostics, integrating ^{68}Ga-DOTATATE imaging with ^{177}Lu-DOTATATE or ^{225}Ac-DOTATATE therapy, demonstrates that diagnosis and treatment are no longer separate acts, but a continuous, biologically guided strategy. Prospective clinical data confirm durable disease control, while HIF-2α inhibition and anti-angiogenic tyrosine kinase inhibitors expand systemic options for advanced disease. Beyond tumor cells, the microenvironment, angiogenesis, immune architecture, macrophage predominance, emerges as both signal and therapeutic target. Multi-omic integration and international data sharing are reshaping how we define aggressiveness, recurrence, and therapeutic response. Artificial intelligence now stands at the horizon. Predictive models integrating molecular, biochemical, imaging, and clinical variables are beginning to identify metastatic potential at diagnosis and anticipate therapeutic efficacy. Generative AI may soon assist in designing personalized therapeutic strategies for resistant disease. Together, these advances shine unprecedented light into the biological darkness of PPGL with molecular clarity and predictive precision, transforming a once enigmatic endocrine tumor into a model of globally collaborative, data-driven precision medicine.

Abstract citation ID: lvag096.006

PL6 - Thyroid hormone action in bone

Graham Richard Williams
Department of Medicine, Imperial College London, Molecular Endocrinology Laboratory, Room 10N5, Commonwealth Building, London, United Kingdom

Introduction: Thyroid hormone (T3) has critical roles during skeletal development, growth, and adult bone maintenance.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Hypothyroidism delays bone development and linear growth, whereas thyrotoxicosis accelerates skeletal maturation and is an important risk factor for osteoporosis in adulthood. Even sub-clinical hyperthyroidism is associated with fracture, and treatment with thyroxine at doses that suppress TSH increases bone turnover and decreases bone mineral density. Skeletal phenotypes resulting from abnormal T3 action in genetically modified mice faithfully reproduce genetic disorders in humans and reveal complex physiological relationships between centrally regulated thyroid status and peripheral T3 actions.

Methods: We generated mutant mice with cell-specific thyroid hormone deficiency in each of the major skeletal cell lineages. Skeletal tissues were analysed at birth, weaning, during rapid growth and in adulthood by whole mount staining of the skeleton, X-ray microradiography, back-scattered electron scanning-electron microscopy, histology and histomorphometry. We established primary cultures of cartilage-forming chondrocytes, bone-forming osteoblasts and co-cultures of osteoblasts and bone-resorbing osteoclasts from T3 receptor (TR) deficient mice for analysis of T3-target gene expression by RNAseq.

Results: T3 actions during skeletal development were mediated by TRα in chondrocytes via target genes involved in gene transcription, membrane transport and signalling, hypertrophic chondrocyte differentiation, bone morphology, extracellular matrix organisation, and cellular and extracellular matrix interactions. T3 actions in adults were mediated by TRα in osteoblasts via target genes involved in bone formation, osteoclastic bone resorption, glycolysis and oxidative phosphorylation, and endocrine, paracrine and cytokine signalling. T3 actions in osteocytes modulated skeletal responses to oestrogen deficiency. By contrast, osteoclasts responded indirectly via TRα-mediated T3-actions in osteoblasts.

Conclusions: The skeleton is exquisitely sensitive to thyroid hormones throughout life and T3 actions are mediated by TRα in chondrocytes and cells of the osteoblast lineage.

Abstract citation ID: lvag096.007

PL7 - The bone rebound phenomenon: understanding bone loss mechanisms after Denosumab withdrawal

Bente Langdahl
Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus, Denmark

Denosumab (DMAB) is a human monoclonal antibody that binds to the receptor activator of nuclear factor κB ligand (RANKL) and inhibits the binding of RANKL to RANK, an interaction responsible for osteoclast formation, function, and survival. Treatment with DMAB reduces bone resorption, leading to rapid and significant increases in BMD and decreases the risk of both vertebral and non-vertebral fractures.

If DMAB is discontinued, bone turnover not only returns to pre-treatment levels but increases above, a phenomenon known as bone turnover overshoot. This overshoot lasts for 6-12 months before slowly normalizing toward pre-treatment level and is associated with loss of the BMD gained during DMAB therapy as well as an increased risk of multiple vertebral fractures.

The bone turnover overshoot after DMAB discontinuation distinguish DMAB from bisphosphonates, which have residual skeletal binding that provides partial, long-lasting antiresorptive effects even after treatment is stopped. Some aspects of the physiology underlying the overshoot activation of bone resorption upon discontinuation of DMAB are known, but much remains unknown. RANKL accumulates in the bone microenvironment during treatment with DMAB and the OPG response when RANKL is no longer bound to DMAB appears insufficient to counter the rapidly increasing unbound RANKL. Studies in mice have also shown an accumulation of resting pre-osteoclast-type cells, called osteomorphs that can rapidly become active osteoclasts. The mechanostat may also play a role, as bone mass tends to adjust towards an individual's genetically determined pre-treatment level in the absence of drug interference. Clinical observations support some of these mechanisms; several studies have suggested that BMD gain during DMAB and/or the DMAB treatment duration correlates with subsequent BMD loss after discontinuation.

Bisphosphonates offer the best, although incomplete, protection against the overshoot of bone turnover, whereas SERMs, anabolic therapy, and DMAB tapering do not reliably prevent the bone turnover overshoot or fractures. Clinicians should therefore support persistence with DMAB, avoid unplanned discontinuation, and ensure that any planned discontinuation is followed by a timely initiation of a potent bisphosphonate, with consideration of repeated dosing in patients with prolonged DMAB exposure.

DMAB is an effective antiresorptive treatment for osteoporosis, superior to bisphosphonates in improving BMD, but its discontinuation carries clinically significant risks of bone loss and vertebral fractures. Consequently, discontinuing DMAB requires long-term treatment planning, and the timely initiation of appropriate sequential therapy is essential to optimize patient outcomes.

Abstract citation ID: lvag096.008

PL8 - GLP-1 and beyond: next-gen therapies for obesity and metabolic disease

Lotte Bjerre Knudsen
Novo Nordisk, Ringstedt, Denmark

Glucagon-Like Peptide-1 receptor agonists (GLP-1RAs), such as liraglutide and semaglutide, are long-acting pharmacological agents approved for diabetes and obesity management, with additional benefits on cardiovascular, renal, and hepatic systems, and emerging potential in brain-related disorders with significant unmet needs. These fatty acid-acylated molecules bind non-covalently to serum albumin, enhancing pharmacokinetic stability, and signal through a specific GLP-1 receptor expressed on select cell types across various organs. GLP-1RAs mimic the multifaceted physiological roles of GLP-1, a key regulator of post-prandial responses, including glucose homeostasis, appetite regulation, and other biological processes. Peripherally administered GLP-1RAs access specific brain regions via circumventricular organs expressing GLP-1

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

receptors, as shown in rodent whole-brain imaging. The weight loss mechanism is primarily driven by brain GLP-1R activation, reducing energy intake through neuromodulation and potentially altering reward signaling to influence food choice. GLP-1RAs also reduce systemic inflammation by approximately 50%, as measured by C-reactive protein, which, alongside reductions in blood pressure, triglycerides, blood glucose, and body weight, is hypothesized to decrease atherosclerotic burden. Furthermore, the application of omics in clinical trials has elucidated diverse mechanisms underlying GLP-1RA efficacy across diseases, highlighting their broad therapeutic potential and informing drug repurposing approaches. Beyond GLP-1, additional mechanisms come from amylin, GIP and glucagon agonism.

Symposia

S1.1 - Genetics of low/intermediate risk thyroid cancer

Abstract Unavailable

Abstract citation ID: lvag096.009

S1.2 - Treatment of low/intermediate risk thyroid cancer

Emese Mezosi
Ist Department of Internal Medicine, Clinical Center, University Medical School of Pecs, Pécs, Hungary

Differentiated thyroid cancer generally has an excellent prognosis, and treatment strategies increasingly emphasize risk-adapted and individualized management. The 2025 guidelines of the American Thyroid Association recommend a stratified approach based on estimated risk of structural recurrence, categorizing patients into low, low–intermediate, intermediate–high, and high-risk groups. In patients with low or intermediate risk, the primary goal of therapy is to achieve disease control while minimizing treatment-related morbidity through a de-escalated management strategy.

Surgery remains the cornerstone of initial treatment. For selected patients with small, intrathyroidal tumors, thyroid lobectomy may be sufficient, while total thyroidectomy is generally reserved for larger tumors, multifocal disease, or cases with nodal involvement. The updated guidelines place greater emphasis on conservative surgical approaches and, in carefully selected patients with very low-risk tumors, even active surveillance may be considered.

Postoperative radioactive iodine (RAI) therapy is no longer routinely recommended for low-risk patients. Instead, RAI is selectively applied based on clinicopathologic features and recurrence risk. In intermediate-risk disease, RAI may be considered on an individualized basis, particularly in the presence of lymph-node metastases, microscopic extrathyroidal extension, or vascular invasion. Recommended administered activities typically range from 30-100 mCi.

Long-term management includes risk-adapted surveillance with neck ultrasonography, serum thyroglobulin or anti-thyroglobulin antibody monitoring, and dynamic risk stratification to guide the intensity of follow-up. A more conservative approach to thyroid-stimulating hormone (TSH) suppression is also recommended to reduce adverse effects. Overall, the current recommendations highlight personalized care, selective use of adjuvant therapies, and de-escalation of treatment intensity.

Abstract citation ID: lvag096.010

S1.3 - Targeted therapy in radioiodine refractory thyroid cancer

Laura Fugazzola
Università di Milano, Milan, Italy

Radioiodine-refractory thyroid cancer (RAIR-TC) represents a challenging subset of differentiated thyroid cancers characterized by loss of iodine avidity and poor or absent response to conventional radioactive iodine therapy. Over the past decade, advances in molecular biology have significantly improved the understanding of the genetic alterations driving these tumors, leading to the development of targeted therapeutic strategies. Key oncogenic pathways implicated in RAIR-TC include mutations in BRAF, RAS, RET/PTC rearrangements, and alterations in the MAPK and PI3K-AKT signaling pathways.

Targeted therapies, particularly tyrosine kinase inhibitors (TKIs), have emerged as the cornerstone of treatment for patients with progressive RAIR-TC. Agents such as lenvatinib and sorafenib have demonstrated improved progression-free survival by inhibiting multiple kinases involved in tumor proliferation and angiogenesis, including VEGFR, FGFR, and RET. More recently, selective inhibitors targeting specific genetic alterations, such as BRAF and RET inhibitors, have shown promising efficacy with improved safety profiles compared to multikinase inhibitors.

Despite these advances, challenges remain, including the development of resistance, treatment-related toxicities, and variability in patient response. Ongoing research is focused on combination therapies, redifferentiation strategies to restore radioiodine uptake, and the identification of predictive biomarkers to guide personalized treatment.

In conclusion, targeted therapy has transformed the management of RAIR-TC, offering meaningful clinical benefit. Continued investigation into tumor biology and therapeutic optimization is essential to further improve outcomes in this aggressive disease subset.

Abstract citation ID: lvag096.011

S2.1 - Tanycytes at the crosstalk between reproduction and metabolism

Daniela Fernandois
INSERM U1172, Lille, France

Tanycytes are specialized ependymoglial cells that line the walls and floor of the third ventricle, serving as gatekeepers for peripheral blood-borne signals entering hypothalamic circuits that regulate **reproduction** and energy homeostasis. These cells extend processes toward the median eminence and arcuate nucleus, facilitating the transport of metabolic hormones and designed drugs—including leptin and GLP-1 analogs—into the mediobasal hypothalamus. Estrogens, acting via estradiol receptor alpha (ERα), play a crucial role in regulating the hypothalamic–pituitary–gonadal axis and energy balance. However, the mechanisms by which they influence tanycyte function are only beginning to be understood.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Using transgenic mice with tanycyte–selective ERα deletion, ovariectomized models, primary tanycyte cultures, and human post-mortem tissue, we show that estradiol–ERα signaling in tanycytes is crucial for both reproductive and metabolic functions. Female mice with tanycyte–selective ERα deletion become acyclic, display elevated estradiol and LH levels, and require more attempts to achieve successful pregnancy, pointing to impaired fertility. At the cellular and circuit level, tanycytes contact and communicate with NPY neurons, suggesting that tanycytic estrogen/ERα sensing participates in GnRH–NPY communication to fine–tune LH release according to peripheral metabolic cues.

In parallel, estradiol signaling through tanycytic ERα increases leptin uptake and release, and facilitates the entry of leptin and semaglutide into the mediobasal hypothalamus—effects that are especially pronounced in females. Loss of ERα in tanycytes leads to notable structural and morphological alterations, indicating disrupted transport and barrier functions. Furthermore, analysis of human tissue demonstrates that ERα expression in tanycytes during menopause is both sexually dimorphic and sensitive to menopausal status. Together, these results establish tanycytic ERα signaling as a critical integrator of gonadal and metabolic cues within hypothalamic networks, offering a mechanistic explanation for sex- and age-dependent changes in fertility and energy homeostasis, and highlighting tanycytes as promising therapeutic targets for modulating the gonadal–metabolic axis.

Abstract citation ID: lvag096.012

S2.2 - Metabolic impact of PFAS and environmental factors on breast milk and microbiota of mother-infant dyads

Matej Orešič[1,2]
[1]University of Turku, Turku, Finland; [2]Örebro University, Örebto, Sweden

Early-life exposure to environmental chemicals, particularly per- and polyfluoroalkyl substances (PFAS) and related persistent organic pollutants (POPs), is increasingly recognized as a key determinant of metabolic health. In this talk, I will present findings from longitudinal mother–infant cohort studies integrating metabolomics, lipidomics, and microbiome profiling to elucidate how these exposures shape early-life biology.

Our work demonstrates that prenatal and early postnatal exposure to PFAS and POP mixtures is associated with profound alterations in lipid metabolism, including ceramides, phospholipids, and acylcarnitines, as well as disruptions in bile acid and amino acid pathways. These metabolic changes are closely linked to shifts in gut microbiota composition and microbial-derived metabolites, highlighting a coordinated perturbation of host–microbiome interactions. Notably, breast milk emerges as a central interface in this process, acting both as a route of exposure and as a modulator of infant metabolic and microbial development.

We further show that different classes of environmental pollutants exert partially distinct yet overlapping effects: PCBs exhibit strong and consistent associations with lipid and microbiome alterations, while PFAS display broader but more heterogeneous metabolic signatures. Across studies, bile acid metabolism and gut–liver axis signaling emerge as key pathways linking environmental exposures to systemic metabolic outcomes.

These findings challenge traditional toxicological paradigms by demonstrating that environmentally relevant exposures reprogram metabolic networks early in life through microbiome-mediated mechanisms. A systems-level, multi-omics perspective is therefore essential to understand how the exposome shapes developmental trajectories and long-term disease risk.

Abstract citation ID: lvag096.013

S2.3 - Anti-Mullerian hormone (AMH) role in programming PCOS

Paolo Giacobini[1,2]
[1]INSERM U1172, Univ. Lille, Inserm, CHU Lille, U1172 -LilNCog(JPARC) –Lille Neurosciences & Cognition, Lille, France; [2]Lille Neuroscience and Cognition, Lille, France

Polycystic ovary syndrome (PCOS) is the most prevalent reproductive and metabolic disorder, affecting up to 13% of women worldwide. Although initially characterized as a reproductive condition and the leading cause of anovulatory infertility, PCOS is now recognized as a systemic disorder associated with long-term comorbidities, including obesity, type 2 diabetes, cardiovascular disease, and an increased risk of neuropsychiatric disorders. Despite its substantial impact on women's health, there is currently no cure for PCOS, underscoring the urgent need for improved therapeutic strategies.

Hyperandrogenism and elevated circulating anti-Müllerian hormone (AMH) levels are hallmark features of PCOS. Recent studies using animal models demonstrate that prenatal and/or postnatal exposure to excess AMH predisposes female offspring to develop reproductive and metabolic abnormalities that closely resemble the human condition. These studies highlight an unexpected role for AMH in the development of PCOS, beyond its classically described ovarian function.

By leveraging a PCOS-like mouse model with pharmacological preclinical interventions and clinical investigations, we have identified key neuronal populations involved in PCOS pathophysiology. These findings reveal a central neuroendocrine contribution to disease etiology and highlight novel therapeutic avenues for the treatment of PCOS.

Abstract citation ID: lvag096.014

S2.4 - GLP1 induced weight loss and pregnancy

Ursula Winterfeld
Swiss Teratogen Information Service and Clinical Pharmacology Service, Centre Hospitalier Universitaire Vaudois (CHUV) and University of Lausanne, Lausanne, Switzerland

The increasing use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in women of reproductive age raises important clinical questions at the interface between metabolism, fertility, and pregnancy safety. Emerging evidence suggests potential benefits on ovulation and fertility in women with obesity and polycystic ovary syndrome. Consequently, their use in the preconception period is expanding.

However, GLP-1 RAs are not recommended during pregnancy due to the absence of randomized controlled trials in pregnant populations and findings of reproductive toxicity in animal studies. Current recommendations advise discontinuation prior to conception, particularly for long-acting agents. Despite this, real-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

world data indicate increasing exposure during early pregnancy, often in the context of unplanned pregnancies.

This situation requires distinguishing between two different clinical questions: the potential teratogenic risk associated with early pregnancy exposure, and the metabolic consequences of treatment discontinuation before conception. Addressing these questions demands different types of evidence and has distinct implications for clinical counseling.

This presentation will review the available data on preconception benefits of GLP-1 RAs, summarize current knowledge on pregnancy outcomes following inadvertent exposure, including recent findings from the European Network of Teratology Information Services (ENTIS), and discuss emerging evidence on metabolic changes after discontinuation. Finally, implications for counseling women treated with GLP-1 receptor agonists who are planning pregnancy or present with early exposure will be discussed.

S3.1 - Novel diagnostic strategies and personalized treatment for obesity

Abstract Unavailable

Abstract citation ID: lvag096.015

S3.2 - RNA processing: another regulatory layer of islet cell function

Lori Sussel
Barbara Davis Center for Diabetes, University of Colorado, Aurora, United States

Emerging data from both mouse models and human islets indicate that islet cells dynamically regulate RNA metabolism in response to environmental cues. Because β cells must rapidly adapt to fluctuations in nutrient availability, RNA processing offers a fast yet durable layer of regulatory control, but this level of regulation remains relatively understudied. In addition, cell type–specific aberrant splicing and the resulting protein isoforms contribute to β cell dysfunction in both T1D and T2D. Our work has identified RNA-binding proteins (RBPs) and altered splicing programs that influence islet cell identity and β cell function. We and others have also shown that N6-methyladenosine (m6A)—the most abundant and best-characterized RNA modification in mammals—differs in abundance between diabetic and non-diabetic donor islets, and emerging evidence suggests that this modification impacts both alternative splicing and cell differentiation. To define these mechanisms, we are using mouse models with disruptions in m6A regulatory pathways combined with single-cell long-read sequencing to determine how RNA modifications control islet cell–specific splicing and functional outcomes.

Abstract citation ID: lvag096.016

S3.3 - Latest advances in amylin therapeutics for obesity treatment

Thomas Lutz
University of Zurich, Institute of Veterinary Physiology, Zurich, Switzerland

The pancreatic hormone amylin has originally been discovered in and isolated from pancreatic islet amyloid deposits. In few species only, including primates and felines, the amylin molecule has the propensity to aggregate into oligomers and eventually mature amyloid fibrils. However, monomeric hormonal amylin produces a large variety of beneficial metabolic effects that make the non-fibrillar forms of amylin a fascinating candidate for the treatment of metabolic diseases. Amylin is co-synthesized and co-secreted with insulin, and it is an important control of eating, mainly by its physiological effect on meal-ending satiation. Chronically, amylin and its receptor analogues also lead to substantial weight loss. Here, I will review the current knowledge on the central nervous system pathways mediating amylin's metabolic effects and how this may translate in effective pharmacotherapy. Amylin receptor pharmacology is complex because of the existence of several distinct amylin receptor subtypes, and we only start to understand the specific actions mediated by these subtypes. The latter aspect is also relevant to understand potential differences in tolerability among different amylin receptor agonists which are in different phases of clinical developments.

Abstract citation ID: lvag096.017

S4.1 - Emerging genetic factors in young-onset and familial pituitary tumors

Adrian Daly
Department of Endocrinology, Centre Hospitalier Universitaire de Liège, University of Liège, Liège, Belgium

Clinically evident pituitary adenomas affect 1:1000 individuals and most cases remain genetically unexplained. Pituitary adenomas have a very limited repertoire of known germline genetic causes and most affect neuroendocrine pathways. Among these, the most prevalent are rare loss of function (LOF) variants in AIP that cause young onset and familial isolated pituitary adenomas (FIPA), primarily acro-gigantism and prolactinomas. Duplications disrupting a conserved topologically associating domain (TAD) at GPR101 cause sporadic and familial X-linked acrogigantism (X-LAG). Pituitary adenomas also form part of genetic syndromes including multiple endocrine neoplasia (MEN) 1, MEN4, MEN5, and Carney complex. Recent genetic research has highlighted the major contribution of germline deleterious variants to tumorigenesis across many tissue types. In particular, young age at diagnosis and a positive family history of tumors are two key indicators of the presence of underlying germline deleterious genetic variants in cancer-related molecular pathways. These approaches are beginning to be applied to anterior pituitary tumors in both selected/focused screening populations and in unselected patient groups. Recent work using NGS panels has linked deleterious variants in DNA mismatch repair (MMR) genes to the development of pituitary adenomas in rare instances. Using whole exome sequencing and clinical databases, groups have identified pathogenic variants in genes like PMS2, MSH2, and MLH1 in various populations. While some of these variants occurred in individuals with Lynch syndrome (and undergoing screening), others occur in patients with sporadic pituitary tumors without a known family history of Lynch syndrome. While established risk genes like AIP and MEN1 remain significant players in pituitary tumorigenesis, the broader landscape of DNA

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

repair genes may play a larger role than previously appreciated. In this presentation, we will trace existing knowledge on pituitary tumorigenesis and cancer risk genes and will highlight new research from our international research collaboration examining the potential contribution of novel pituitary risk genes in the etiology of aggressive young-onset pituitary tumors and FIPA. These emerging findings may have relevance for genetic counseling and could expand targeted management strategies in patients with pituitary tumors.

S4.2 - Age-related changes in pituitary function

Abstract Unavailable

Abstract citation ID: lvag096.018

S4.3 - Approach to older patients with a pituitary adenoma: challenges and future directions

Niki Karavitaki
Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, United Kingdom

Non-functioning pituitary adenomas account for the majority of pituitary tumours detected in the elderly population. They usually present with pressure effects to surrounding structures (mainly visual deterioration or manifestations of hypopituitarism) or they can be detected incidentally. Other types of pituitary adenomas are less common and can relate with increased morbidity and mortality.

The presence of various comorbidities in the older patients affecting their frailty and fitness for surgery pose challenges for the surgical resection of pituitary adenomas in this age group. Nonetheless, a number of contemporary studies have suggested that complication rates after transsphenoidal surgery do not differ from those encountered in younger patients. Furthermore, satisfactory endocrine remission rates have been reported for functioning tumours. In non-functioning pituitary adenomas, the decisions for surgical intervention and its specific aims should rely on multidisciplinary team discussion with the contribution of anaesthesiology and geriatric medicine and after balancing the pros and cons of active management versus observation alone. Further strategies for use of adjuvant radiotherapy post-operatively should also be individualised taking into account the risk of tumour regrowth and its clinical sequelae over time.

Studies that will allow the development of reliable risk stratification and will guide the evidence-based selection of optimal management pathways in older patients with pituitary adenomas are needed.

Abstract citation ID: lvag096.019

S5.1 - Heat stress effects on ovarian function and fertility

Aileen Keating
Iowa State University, Ames, United States

Female infertility is a consequence of heat stress and has been recognized in production animals for decades and more recently in women. Systemically, heat stress compromises intestinal barrier integrity and elevates circulating insulin, both physiological perturbations that can independently compromise female fertility. In production animals, heat stress is phenotypically characterized by anovulation, reduced conception rates, and low pregnancy maintenance. In women, heat stress is linked with preterm birth, birth defects, fetal growth restriction and death and altered ovarian function. Ovarian endocrine disruption and molecular sequelae due to heat stress have been partially identified. Using pig and mouse models, the impacts of heat on ovarian follicle number, ovarian steroid hormone concentrations and the ovarian proteome have been characterized. Reduced female fertility is detrimental not only to quality of life in humans, but also to animal welfare, agricultural economics/sustainability and human food security. Thus, identifying mechanisms that compromise female fertility is needed for developing mitigation strategies.

Abstract citation ID: lvag096.020

S5.2 - Human in utero exposures to air pollution

Paul Fowler
University of Aberdeen

WHO estimates that over 99% of all humans are exposed to excess air pollution. At the same time air pollution is ubiquitous globally, transported around the world in the atmosphere. Air pollution includes gases like ozone, CO, O_3, nitrogen dioxides chemicals like lead, sulphur, particulate matter (PM), including PM_{10} and $PM_{2.5}$ μm micro and nanoparticles. These particles consist of metals, black carbon and plastics. Overall air pollution is a complex mixture: acids, inorganic compounds, organic chemicals, soot, metals, soil/dust particles, and biological materials. Components of air pollution also including endocrine disrupting chemicals and man-made chemicals, such as “forever chemicals”, PFAS. Exposure to air pollution in utero is a cause of multiple developmental deficits and post-natal health deficits and affects millions of pregnancies globally. The presentation will introduce air pollution, examples of adverse consequences and summary of major issues of concern. In addition, issues, such as the movement of pollutants between air and water and other matrices will be discussed.

Abstract citation ID: lvag096.021

S5.3 - Thyroid hormone system–disrupting effects on neurosensory system development—lessons learned from the zebrafish model

Lisa Baumann
Vrije Universiteit Amsterdam

Early vertebrate development is partly regulated by thyroid hormones (THs) and can therefore be disrupted by environmental pollutants that interfere with the TH system (thyroid hormone system–disrupting chemicals, THSDCs). Because THs play a key role in neurosensory development, these systems represent sensitive endpoints for detecting endocrine disruption in humans and environmental non-target species, such as fish. Using the popular (eco)toxicology model zebrafish (Danio rerio), we examined the impact of model THSDCs on several neurosensory structures and assessed whether early-life effects are reversible. THSDC exposure induced pronounced alterations in eye development, including changes in size, pigmentation, and retinal cell

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

structure. Specificity of effects was confirmed by molecular analyses (TH levels and transcriptomics) and behaviour assays. Notably, these effects showed partial reversibility after a short recovery period. Based on this work, zebrafish eye development assessment is currently undergoing OECD validation as a standardized thyroid-related endpoint in fish. In addition to extensive results on THSD-induced effects on eye development, preliminary data indicating that early TH system disruption also affects the brain and olfactory epithelium development in zebrafish embryos will be presented. Using transgenic zebrafish lines and confocal microscopy, we observed developmental changes in total brain volume and in olfactory epithelium area, suggesting broader neurosensory sensitivity to TH perturbation. Together, these data demonstrate that multiple components of the zebrafish neurosensory system respond to THSDCs during early development, with potential for recovery effects. Because the endocrine system is highly conserved across vertebrates, these findings from zebrafish may also provide insights relevant to human thyroid-dependent neurosensory development and potential vulnerabilities to TH system disruption.

Abstract citation ID: lvag096.022

S6.1 - New models on pheochromocytoma: organoids

Patricia Dahia
Division of Hematology and Medical Oncology, University of Texas Health Science Center at San Antonio, San Antonio, Texas, United States

Pheochromocytomas and paragangliomas (PPGLs) are rare chromaffin cell-derived neuroendocrine tumors derived from sympathetic (catecholamine-producing) or parasympathetic (nonsecretory) lineage, frequently driven by dysregulation of hypoxia-inducible factor (HIF) signaling, particularly HIF-2α. Although often benign, PPGLs can metastasize unpredictably, with limited therapeutic options once disseminated. Progress has been hindered by the lack of robust preclinical models, especially those that capture their molecular complexity and microenvironmental influences. To address this gap, we established patient-derived tumor organoids (PDOs) from 35 PPGLs, comprising a broad spectrum of clinical and molecular phenotypes. The organoids retained key immunohistochemical, genomic, transcriptomic, and catecholamine-secretory features of their parental tumors. PPGL organoids cultured under hypoxic conditions generally exhibited enhanced viability, supporting hypoxia as a driver of cell survival. Hypoxia activated HIF-1α and expanded *ASCL1*-positive cell populations, suggesting a shift toward a more immature chromaffin state. In contrast, long-term normoxic cultures activated hypoxia inducible factor 2α (HIF-2α) and acquired a hybrid sympathoblast–mesenchymal identity in subpopulations with upregulation of extracellular matrix and cell cycle markers, independent of genotype. These PDO features resemble high-risk neuroblastoma subtypes and establish a molecular parallel suggestive of shared lineage plasticity and pathogenic programs, which are also detectable in primary PPGLs. Drug screening across a library of up to 51 drugs and combinations revealed both shared and unique vulnerabilities, with response rates to belzutifan resembling clinical observations. The CDK4/6 inhibitor abemaciclib, previously unexplored in PPGLs, elicited the strongest activity. Abemaciclib-responsive PDOs and their matched tumors, including a metastatic sample, exhibited epithelial mesenchyme transition enrichment, nominating potential biomarkers for patient stratification. Our results establish PDOs as a novel platform for modeling neuroendocrine tumor biology, reveal microenvironment-driven plasticity in PPGLs with potential translational relevance, and identify actionable vulnerabilities in a disease with few effective systemic therapies.

S6.2 - Use of artificial intelligence in management of pheochromocytoma

Abstract Unavailable

Abstract citation ID: lvag096.023

S6.3 - Cardiovascular complication of pheochromocytoma and paraganglioma

Ondrej Petrák
General University Hospital in Prague, III. internal clinic—clinic of endocrinology and metabolism, Praha, Czech Republic

Background: Adrenaline-producing tumors are mostly characterized by a sudden release of catecholamines with episodic symptoms. Noradrenergic ones are usually less symptomatic and characterized by a continuous overproduction of catecholamines that are released into the bloodstream. Their effects on the cardiovascular system can thus be different. The aim of this study was to determine the prevalence of cardiovascular complications by catecholamine phenotype.

Methods: We retrospectively analyzed data on the prevalence of cardiovascular events in 341 consecutive patients with pheochromocytoma and paraganglioma treated from 1995 to 2023. Biochemical catecholamine phenotype was determined based on plasma or urinary catecholamines and metanephrines.

Results: According to the phenotype, 153 patients had noradrenergic pheochromocytoma and paraganglioma and 188 had adrenergic pheochromocytoma and paraganglioma. In the whole sample, the incidence of serious cardiovascular complications was 28% (95 patients), with no difference between the phenotypes or sexes. The noradrenergic phenotype had significantly more atherosclerotic complications (composite end point of type 1 myocardial infarction and symptomatic peripheral artery disease; odds ratio, 3.58 [95% CI, 1.59-8.83]; $P = .003$), while the adrenergic phenotype more often had type 2 myocardial infarction and takotsubo-like cardiomyopathy (OR, 0.24 [95% CI, 0.09-0.57]; $P = .002$). These changes remained even after adjustment for conventional risk factors of atherosclerosis.

Conclusions: We found a 28% incidence of cardiovascular complications in a consecutive group of patients with pheochromocytoma and paraganglioma. Patients presenting with a noradrenergic phenotype have a higher incidence of atherosclerotic complications, while the adrenergic phenotype is associated with a higher incidence of acute myocardial damage due to takotsubo-like cardiomyopathy.

Abstract citation ID: lvag096.024

S7.1 - Focus on Osteogenesis imperfecta viewpoint

Neil Gittoes

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom

Osteogenesis imperfecta (OI) is a heterogeneous group of rare, heritable disorders of connective tissue characterised primarily by increased bone fragility and reduced bone mass. Most forms arise from pathogenic variants affecting type I collagen synthesis, structure, or processing, leading to impaired bone matrix quality and abnormal skeletal biomechanics. Clinical severity ranges from mild with few fractures to perinatal lethality. In most forms of OI, fracture risk is highest during the period of linear growth, and during adolescence, fracture risk reduces rapidly. Bisphosphonates remain the mainstay of medical therapy, and in children, the evidence base is stronger for fracture prevention and attendant improvements in bone density. Recent data in adults questions the role of bisphosphonates and teriparatide in conferring a meaningful benefit in fracture prevention. Newer anabolic and targeted molecular approaches—such as sclerostin inhibition and TGF–β pathway modulation—show emerging promise. Optimal care is multidisciplinary, incorporating endocrinology, orthopaedics, physiotherapy, and genetics to improve function, mobility, and quality of life.

From a generalist perspective, recognising a rare syndrome of fracture susceptibility can be challenging when a child or young adult presents with a fracture, which is a common occurrence, usually linked to an active lifestyle. Often, the number of fractures and mechanism of injury can highlight suspicion of such susceptibility. This talk will review features of OI that should be considered when faced with a young adult with fractures.

S7.2 - Focus on hypophosphatasia viewpoint

Abstract Unavailable

Abstract citation ID: lvag096.025

S7.3 - Focus on X-linked hypophosphatemia

Catherine Chaussain
Université Paris Cité, Paris, France

Bones and teeth are the most important mineralized tissues in the body. They share several mechanisms related to their development and mineralization, including the signaling pathways that regulate the differentiation of their cell types.[1,2] Therefore, dental complications are a common morbidity in patients with endocrine disorders. Depending on the disorder, either the tooth structure, its morphology, or the number of teeth may be affected. Rare bone disorders related to the mineral homeostasis or affecting genes encoding a component of the extracellular matrix can dramatically affect tooth mineralization. As a consequence, patients may endure early tooth loss, or high susceptibility to caries, periodontitis or pulp infections.[1,2,3] The aim of this presentation will be to present the dental aspects of rare endocrine diseases and the impact of their complications on the patient's quality of life. In addition, we will show how a thorough dental examination can support the diagnosis of a rare endocrine disorder, and how ultrastructural examination of the tooth can provide new insights into the pathophysiological mechanisms associated with the disorder. In addition, we will discuss how the ultrastructural examination of the tooth can reveal how a systemic treatment improves the mineralization process. Overall, this presentation will urge the need to include a dentist as part of the multidisciplinary team caring for the patient.

References

1. Kovacs CS, Chaussain C, Osdoby P, Brandi ML, Clarke B, Thakker RV. The role of biomineralization in disorders of skeletal development and tooth formation. *Nat Rev Endocrinol*. 2021;17(6):336-349.
2. Opsahl Vital S, Gaucher C, Bardet C, Rowe PS, George A, Linglart A, Chaussain C. Tooth dentin defects reflect genetic disorders affecting bone mineralization. *Bone*. 2012;50(4):989-97.
3. McKee MD, Hoac B, Addison WN, Barros NM, Millán JL, Chaussain C. Extracellular matrix mineralization in periodontal tissues: noncollagenous matrix proteins, enzymes, and relationship to hypophosphatasia and X-linked hypophosphatemia. *Periodontol 2000*. 2013;63(1):102-22.

S7.4 - Focus on non-surgical hypoparathyroidism

Abstract Unavailable

S7.5 - Focus Pseudohypoparathyroidism

Abstract Unavailable

Abstract citation ID: lvag096.026

S8.1 - Strategies for clinical screening of MEN1 mutation carriers

Gerlof D. Valk
University Medical Center Utrecht, Utrecht, The Netherlands

Multiple Endocrine Neoplasia type 1 (MEN1) is a rare autosomal dominant hereditary syndrome caused by inactivation mutations in the *MEN1* gene. MEN1 patients are predisposed to tumors of endocrine and non-endocrine organs. The clinical management of mutation carriers is challenging because of the variable penetrance and the unpredictable course of the disease. Due to limited available evidence, the 2012 Clinical Practice Guidelines for MEN1 were predominantly based on expert opinion, leaving room for interpretation and variation in practices. However, the more protocolized screening increased the evidence on the natural course of the syndrome. The updated (2025) MEN1 clinical practice recommendations offer more evidence based refinements in the management of patients based on three systematic reviews and a Delphi consensus procedure.

Clinically diagnosed patients have a different clinical course compared to mutation carriers with now addressed consequences for clinical management. As for primary hyperparathyroidism, subtotal parathyroidectomy is now the initial procedure of choice. Guidance is given on the timing of initial parathyroidectomy as well as on the controversial topic of unilateral clearance in young patients. Neuroendocrine tumors (NETs) generally have an indolent course but still lead to a 10-15 years shorter life expectance because aggressive cases do occur. The main challenge is to balance between a less intensive surveillance and timely treatment. Pituitary adenomas are most often prolactinomas

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and nonfunctioning microadenomas with an excellent prognosis and good response to therapy. Clinically relevant manifestations are already seen at the pediatric age and recommendations are now given on mutation screening in children of a MEN1 parent and subsequent initiation of screening for manifestations. In conclusion, more guidance is given for care tailored to the needs of the individual patient and improving outcomes on an individual basis. Studies are now needed to define predictors of tumor behavior and effects of more individualized interventions.

Abstract citation ID: lvag096.027

S8.2 - GER surgical strategies for patients with MEN1 (parathyroid, pancreas)

Detlef Bartsch
Dept. Visceral-, Thoracic- and Vascular Surgery, University Hospital Marburg, Marburg, Germany

Surgical management plays a central role in the treatment of MEN1-associated disease, but remains challenging due to the multifocal and recurrent nature of these tumors. This presentation focuses on contemporary surgical strategies for MEN1 associated primary hyperparathyroidism (pHPT) and pancreatic neuroendocrine tumors (pNETs). PHPT occurs in more than 90% of patients. Because multiglandular disease is the rule, the standard surgical approaches include subtotal parathyroidectomy or total parathyroidectomy with autotransplantation, however, nowadays focussed, limited resection is also considered. Key considerations include timing of surgery, prevention of persistent or recurrent disease, and management of reoperative neck surgery. pNET represent a major determinant of MEN1-related morbidity and mortality. Surgical decision-making is complex due to the frequent multiplicity of lesions and the variable biological behavior of functional and non-functional tumors. Current strategies balance the risks of duodenopancreatic surgery with the oncologic benefits of tumor removal. Indications for resection, operative techniques such as enucleation versus formal pancreatic resection, local ablative treatments and surveillance strategies will be discussed.

S8.3 - Integrative management of MEN1: timing, targets, and translational perspectives,

Abstract Unavailable

S9.1 - LH beyond the gonads/non canonical effects of gonadotropins

Abstract Unavailable

Abstract citation ID: lvag096.028

S9.2 - Expanding horizons of kisspeptin: from sexual behaviour to skeletal health

Alexander Comninos
Imperial College London, Imperial College Healthcare NHS Trust, London, United Kingdom

Kisspeptin is best known as the master regulator of the reproductive hormone axis, yet growing evidence suggests its influence extends well beyond reproductive hormone control. In this lecture, I will discuss how kisspeptin signalling represents an important integrative pathway linking reproductive biology with behaviour and skeletal health.

Drawing on translational work spanning experimental models and human studies, I will present evidence demonstrating that kisspeptin influences aspects of sexual and emotional behaviour, providing insight into how reproductive neuroendocrine signals may shape human behavioural responses. Our findings highlight a broader role for kisspeptin in modulating human behaviour, with potential therapeutic implications for disorders of mood, emotion and sexual desire.

I will then discuss recent work exploring the role of kisspeptin in bone biology. Reproductive status is closely linked to skeletal health, and research from our group and others suggests that kisspeptin may positively influence bone metabolism. Understanding these pathways could open avenues for novel therapeutic approaches in metabolic bone disease.

Together, these findings illustrate the expanding physiological and pharmacological horizons of kisspeptin, positioning it as a key modulator of reproductive, behavioural and skeletal biology.

Abstract citation ID: lvag096.029

S9.3 - Non-canonical effects of non-reproductive factors on reproduction

Eva González Suárez
Spanish National Cancer Research Centre (CNIO), Tumor Biology and Immunology program, Madrid, Spain

The hypothalamic-pituitary-gonadal axis (HPG) controls pubertal development, sexual maturation, and fertility. We identified a role of hypothalamic microglia in controlling the HPG axis through Rank signaling. Whole-body and microglia Rank depletion led to hypogonadotropic hypogonadism (HH) resulting from an alteration in gonadotropin-releasing hormone (GnRH) neuron function. In addition, we identified rare gene variants of RANK in patients with HH. Transcriptional profiling upon Rank loss revealed defective microglia activation and morphological alterations in the median eminence, decreasing the contacts and engulfment of GnRH terminal projections and impairing GnRH neuronal responses to kisspeptin. Overall, our data uncover the microglia as regulator of GnRH neuronal function through Rank signaling, with potential implications for reproductive maturation and fertility

Dra. Eva Gonzalez is PhD in Molecular Biology, is a Senior scientist and group leader of the Transformation and Metastasis laboratory, at the Spanish National Cancer Research Center (CNIO) in Madrid, Spain.

S10.1 - EDCs and neuroendocrine control of male and female reproduction

Abstract Unavailable

S10.2 - Linking endocrine disruption to health outcomes—from cohorts to mechanisms and risk assessment

Abstract Unavailable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.030

S10.3 - Early life exposure to EDC and cognitive function in humans and animals

Sakina Mhaouty-Kodja
Development Adaptation & Aging, Sorbonne University—Institut de Biologie Paris Seine, Paris, France

Human populations are exposed to chemical substances released in the environment through agricultural and industrial activities. Among these chemicals, endocrine disrupting compounds (EDC) have the ability to interfere with the endocrine system leading to adverse effects. Epidemiological studies suggested associations between EDC exposure and reduced markers of the cognitive function. Exposure of rodents to EDC exhibiting either thyroid or sex steroid disrupting activities was shown to interfere with cognitive processes. In particular, exposure to environmentally relevant doses of phthalates, used as plasticizers and identified as anti-androgens, impacted learning and memory, reduced dendritic spine density, increased neuroinflammation and blood brain permeability, and altered the kynurenine pathway of tryptophan metabolism in the hippocampus.

However, as human populations are exposed to mixtures of chemicals, it is important to get insights into their effects and mechanisms following developmental exposure. This was performed in mice through exposure of dams to an EDC mixture identified in human breast milk. The obtained data show that male and female offspring born from exposed dams exhibited altered temporal order memory, novel object recognition and anxiety state level. The underlying cellular and molecular mechanisms are under investigation.

An overview of all these human and experimental data will be given, with a special focus on how they can be integrated to assess the risk or hazard for human cognitive health to EDC exposure.

S11.1 - Update on systemic therapies for paraganglioma and pheochromocytoma

Abstract Unavailable

S11.2 - Alpha- vs beta-emitting radionuclide therapies in endocrine oncology: are we ready for routine clinical application?

Abstract Unavailable

S11.3 - Reframing the therapeutic landscape in GEP-NETs: lessons beyond the NETTER-2 trial

Abstract Unavailable

S12.1 - Fingerprints of increased susceptibiliy for adrenal crises—insights from the German registry for adrenal insufficiency

Abstract Unavailable

S12.2 - Pitfalls in the prevention and management of adrenal crises—patient's perspective

Abstract Unavailable

Abstract citation ID: lvag096.031

S12.3 - Management of CAH across the life span

Henrik Falhammar
Department of Endocrinology, Metabolism and Diabetes, Karolinska University Hospital, Stockholm, Sweden

Management of congenital adrenal hyperplasia (CAH) requires a lifelong, multidisciplinary approach that adapts to the evolving physiological and psychosocial needs of each patient. 21-hydroxylase deficiency accounts for 95%-99% of all CAH. Classic CAH due to 21-hydroxylase deficiency typically presents in infancy, necessitating early diagnosis through newborn screening and prompt initiation of glucocorticoid and mineralocorticoid therapy to prevent adrenal crises. During childhood, management centers on optimizing growth and development while avoiding both undertreatment—associated with hyperandrogenism—and overtreatment, which risks iatrogenic Cushingoid features and impaired growth potential. Regular monitoring of hormones, growth velocity, and bone age is essential, alongside careful titration of therapy.

The transition to adolescence introduces new challenges, including puberty induction or modulation, fertility considerations, metabolic risk, and gender identity or body image concerns. A structured transition program supports the shift toward autonomous disease management and ensures continuity of care. In adulthood, treatment goals broaden to include preservation of fertility, cardiometabolic health, bone density, and psychological well-being. Women may face issues related to menstrual function, polycystic ovarian morphology, or sexual health, whereas men may develop testicular adrenal rest tumors requiring surveillance.

Adrenal crisis is most common during childhood but can occur at any age and is the most common cause of death in CAH and is therefore of utmost importance to prevent.

Throughout life, emerging therapies—including modified-release hydrocortisone, CRF1 antagonists, and gene-based approaches—offer potential to reduce androgen excess and glucocorticoid exposure. Comprehensive care should integrate endocrinologists, surgeons, psychologists, reproductive specialists, and genetic counsellors. Effective lifelong management of CAH requires individualized therapy, anticipatory guidance through key developmental stages, and ongoing evaluation of both clinical outcomes and quality of life.

Abstract citation ID: lvag096.032

S13.1 - CCN3, a maternal brain hormone stimulating bone building

Thomas Ambrosi
UC Davis, University of California Davis, Sacramento, United States

During lactation, the high calcium demand for milk production leads to substantial bone loss, compounded by a sharp drop in estrogen. We discovered that cellular communication network factor 3 (CCN3), a brain-derived hormone secreted by a subset of neurons in the arcuate nucleus, compensates for this deficit by acting as a potent osteoanabolic factor. CCN3 increases skeletal stem cell activity, enhances bone

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

remodeling, and accelerates fracture repair in mice of both sexes in experimentally-induced and age-related osteoporosis. Physiologically, CCN3 expression rises during lactation, and its reduction causes maternal bone loss and impaired offspring survival under low-calcium conditions. Results of non-human primate serum sample analysis bolster translational implications of these findings. In sum, we identify CCN3 as a maternal brain hormone essential for skeletal adaptation and a promising therapeutic target to build bone.

S13.2 - Regulation of stem cells in bone regeneration

Abstract Unavailable

Abstract citation ID: lvag096.033

S13.3 - Fibroblast growth factor 23 (FGF23) and bone mineralization

Marie-Helene Lafage-Proust
Université Jean Monnet—INSERM UMR 1059 Sainbiose, Saint Priest En Jarez, France

Bone mineralization is a tightly regulated process involving two complementary phases: primary mineralization, corresponding to the rapid deposition of hydroxyapatite crystals within the osteoid matrix, and secondary mineralization, a slower process leading to progressive crystal maturation and increased mineral density. These processes critically depend on systemic and local regulation of calcium–phosphate homeostasis.

Phosphate plays a central role in skeletal mineralization, as a substrate for hydroxyapatite formation. Its systemic balance is maintained through coordinated actions of the kidney, intestine, and bone, under hormonal control including FGF23, Vitamin D and PTH.

Fibroblast growth factor 23 (FGF23), a bone-derived hormone mainly produced by osteocytes, is a key regulator of phosphate metabolism. FGF23 increases renal phosphate excretion and suppresses 1,25-dihydroxyvitamin D synthesis, thereby decreasing intestinal phosphate absorption. Through these actions, FGF23 indirectly modulates bone mineralization by controlling phosphate availability.

In turn, FGF23 is regulated by dietary phosphate load, Vitamin D and PTH. In addition, recent data unraveled the effects of inflammation and iron metabolism on FGF23 control.

Beyond its systemic indirect effects, accumulating evidence suggests that FGF23 may exert direct actions on osteoblasts activity and matrix mineralization independently of its renal effects.

This presentation will briefly report current knowledge on bone mineralization, phosphate metabolism, and FGF23 biology, highlighting both established pathways and emerging concepts regarding direct skeletal effects of FGF23 and new regulation pathways.

Abstract citation ID: lvag096.034

S14.1 - Tissue specific thyroid hormone signalling

Balázs Gereben
HUN-REN Institute of Experimental Medicine, Budapest, Hungary

The human thyroid gland primarily synthesizes thyroxine (T4), a metabolically stable prohormone requiring mostly extrathyroidal peripheral deiodination to T3 for cellular activity. The hypothalamic-pituitary-thyroid (HPT) axis maintains a relatively stable circulating thyroid hormone (TH) level. However, TH signaling within the brain exhibits rapid, cell-type specific modulation, demonstrating a capacity for local regulation largely independent of circulating TH concentrations. T3 production in the brain is largely dependent on the type 2 deiodinase (D2), a selenoenzyme predominantly expressed in glial cells—specifically astrocytes in extrahypothalamic regions and tanycytes within the hypothalamus. Globally, hypothyroidism affects hundreds of millions of individuals, and current standard-of-care treatment predominantly utilizes L-T4 monotherapy. Although this approach effectively normalizes thyroid-stimulating hormone (TSH) levels, a significant proportion (~10%-20%) of patients experience persistent residual symptoms, notably cognitive dysfunction often described as “brain fog”, suggesting tissue hypothyroidism and substantially impacting quality of life. Utilizing our Thyroid Hormone Action Indicator (THAI) mouse model, we have recently elucidated a molecular mechanism underlying the incomplete restoration of T3-dependent brain functions despite normalized TSH following L-T4 treatment. This mechanism involves glial subtype-specific differential regulation of D2 ubiquitination. Specifically, while tanycytic D2 in the mediobasal hypothalamus with direct impact on HPT function remains resistant to T4-mediated, ubiquitination-dependent inhibition and maintains sufficient T3 production for TSH normalization, D2 activity in extrahypothalamic astrocytes throughout the brain parenchyma is impaired by excess T4. This highlights the potential need for individualized assessment of tissue-level TH action in select patient populations. Our newly developed, minimally invasive methodology for evaluating human tissue TH action will be also discussed, that incorporates novel biomarkers and a Machine Learning-based predictive system.

Abstract citation ID: lvag096.035

S14.2 - Towards precision endocrinology: personalizing TSH reference ranges using genetic profiles

Aleksander Kus

Thyroid-stimulating hormone (TSH) is the cornerstone of thyroid function assessment, yet its interpretation relies on broad population-based reference ranges that may not reflect individual physiology. Increasing evidence indicates that TSH levels are strongly influenced by genetic factors, resulting in substantial inter-individual variability but relatively stable intra-individual setpoints. This suggests that integrating genetic information can refine TSH interpretation and advance a precision medicine approach in thyroidology.

A recent population-based study demonstrated that a polygenic score (PGS), constructed from common genetic variants associated with TSH regulation, explained a meaningful proportion of variability in TSH concentrations, exceeding the proportion explained by FT4 and other clinical determinants. Individuals stratified by genetic risk presented distinct TSH distributions, supporting the concept of genetically determined setpoints within the hypothalamic–pituitary–thyroid axis. Applying genetically informed reference ranges resulted in substantial (~25%-30%) reclassification of individuals previously labelled with subclinical thyroid dysfunction, which could alter treatment decisions in these patients.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Complementary research also highlights the strong genetic architecture of autoimmune thyroid disease (AITD). A PGS based on multiple genetic variants associated with thyroid autoimmunity was able to identify individuals at an increased risk of developing AITD in the general population. Moreover, among the individuals diagnosed with subclinical hypothyroidism, individuals with higher PGS score presented a higher risk of progression to overt thyroid dysfunction. This showed that PRS can potentially improve the diagnostic accuracy in thyroid hormone deficiency as well as help to predict the clinical course of subclinical disease.

Together, these findings underscore the potential of genetics to improve future clinical decision-making and set the research directions for personalized, genetically informed management of thyroid dysfunction.

S14.3 - T4 monotherapy vs T4/T3 combination therapy

Abstract Unavailable

Abstract citation ID: lvag096.036

S15.1 - Adipocytes in a dish: the benefits and blind spots of in vitro fat modeling

Johan Fernø
Haukeland University Hospital

Cell culture models are central to studying adipocyte biology, and primary human adipose tissue progenitor cells (ASPCs) are widely used because they better reflect in vivo biology and capture inter-individual variation compared to immortalized cell lines. However, these models have limitations, including restricted expansion capacity, artifacts introduced during tissue processing, and uncertainty about how well different 2D and 3D adipocyte models represent mature adipocytes and intact adipose tissue. Here, we present data on how in vitro culture conditions influence the identity and function of primary human ASPCs. Using single-cell flow cytometry and bulk RNA sequencing, we show that ASPCs undergo substantial shifts in cell-surface marker expression and transcriptional programs during culture. These molecular changes are accompanied by altered responsiveness to adipogenic stimuli, reflected in cellular lipid accumulation. We further compare adipocyte differentiation in primary 2D and 3D culture models and assess their similarity to mature adipocytes from the same donors. Finally, we analyze mature adipocytes isolated from subcutaneous and visceral depots across numerous donors to determine how depot-specific functional characteristics are preserved ex vivo. Our findings reveal how standard culture conditions reshape ASPC biology and highlight some important limitations of commonly used in vitro adipocyte models. We also provide insight into how 2D and 3D adipocyte models recapitulate distinct aspects of mature adipocyte biology and demonstrate that mature adipocytes retain depot-specific signatures even under ex vivo conditions.

S15.2 - Human adipose tissue development and therapeutic potential

Abstract Unavailable

S15.3 - Unveiling adipose populations linked to metabolic health in obesity

Abstract Unavailable

Abstract citation ID: lvag096.037

S16.1 - Genetic causes of pituitary tumours

Sunita De Sousa
Royal Adelaide Hospital, Adelaide, Australia

Familial pituitary tumours are thought to account for 5% of all pituitary adenomas, relating to germline variants in *AIP, MEN1, CDKN1B, PRKAR1A, SDHA, SDHB, SDHC*, *SDHD* and *MAX*. In addition, germline or mosaic *GPR101*-containing X chromosome microduplications produce the X-linked acrogigantism (X-LAG) phenotype, and postzygotic gain-of-function variants in *GNAS* produce McCune-Albright syndrome.

Amongst sporadic pituitary adenomas, somatic variants are detected in *GNAS* and *USP8* in approximately 50% of somatotrophinomas and corticotrophinomas, respectively. Widespread somatic copy number variation is also frequently found on tumour testing of functioning pituitary adenomas and aggressive non-functioning pituitary adenomas. Recently, somatic variants in *TP53*, *ATRX* and *SF3B1* in pituitary adenomas have been proposed as harbingers of aggressive tumour behaviour. Outside of the pituitary literature, somatic variants in the mismatch repair (MMR) genes and *BRAF* have been demonstrated to predict tumour responses to immune checkpoint inhibitor therapy and BRAF inhibitor therapy, respectively.

Our increasing scientific understanding of the genetic causes of pituitary tumours has been paralleled by improved clinical access to genetic technologies, meaning that clinicians are now able to consider genetic testing in their patients with pituitary tumours. Germline testing may guide pituitary tumour management, gene-specific tumour surveillance, cascade testing and reproductive planning, whilst somatic testing offers—at least theoretically—the possibility of targeted tumour therapy.

This talk will provide an updated overview of the germline and somatic genetic changes found in pituitary adenomas and translation of these developments into a clinical approach to genetic testing in patients with pituitary adenomas.

Abstract citation ID: lvag096.038

S16.2 - Stem cells in development of pituitary tumours

Karine Rizzoti
The William Harvey Research Institute, London, United Kingdom

Postnatal pituitary stem cells give rise to most adult gonadotrophs.

Gonadotrophs are pituitary endocrine cells essential for reproduction, producing luteinizing hormone (LH) and follicle-stimulating hormone (FSH) that act on the gonads to drive germ cell maturation and steroidogenesis, under the control of hypothalamic GnRH and gonadal feedback. They first appear in the embryonic pituitary and expand after birth; although they can show heterogeneous responses to GnRH, they appear so far as transcriptionally relatively homogeneous.

We have recently shown that adult murine gonadotrophs have an unsuspected dual origin: most adult gonadotrophs are in fact generated postnatally, originating from pituitary stem cells from early postnatal life up to puberty, while embryonic gonadotrophs are maintained in a distinct domain in the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

gland. Postnatal gonadotroph differentiation occurs independently of GnRH signalling and gonadal hormones. The existence of gonadotrophs with distinct developmental origins has implications for how reproductive function is established and regulated in health and disease.

- Gonadotrophs first appear in the embryonic pituitary and expand postnatally.
- Postnatal expansion result from differentiation of pituitary stem cells.
- Pituitary gonadotrophs have a dual origin, most being generated postnatally, with a small proportion of embryonic gonadotrophs persisting.
- Postnatal expansion occurs independently of GnRH.
- We are investigating the implications of these distinct developmental origins for reproductive function in health and disease.

Abstract citation ID: lvag096.039

S16.3 - Management of pituitary microadenomas: a practical approach

Tina Dusek
Zagreb University School of Medicine

Pituitary microadenomas, defined as pituitary adenomas smaller than 10 mm in diameter, are increasingly detected due to widespread use of high-resolution imaging. While many are incidental findings, a significant proportion are hormonally active and clinically relevant. A practical, patient-centred approach is essential to ensure appropriate evaluation, avoid overdiagnosis, and guide optimal management.

This lecture will provide a structured framework for the assessment and management of pituitary microadenomas. Key steps include careful clinical evaluation, targeted biochemical testing to identify hormone hypersecretion (particularly prolactin, growth hormone, and ACTH excess), and appropriate use of magnetic resonance imaging. Special emphasis will be placed on distinguishing true pathological lesions from incidentalomas and avoiding unnecessary interventions.

Management strategies vary depending on tumour functionality. Prolactinomas are primarily treated with dopamine agonists, whereas other functioning adenomas may require surgical intervention. In contrast, non-functioning microadenomas are often managed conservatively with periodic monitoring. The role of follow-up imaging and hormonal reassessment will be discussed, along with current guideline recommendations.

Through clinical cases and evidence-based recommendations, this session aims to equip clinicians with practical tools for decision-making in everyday practice, balancing early detection with avoidance of overtreatment.

Joint Sessions

JS1.1 - Bilateral nodular adrenocortical diseases, from micronodular in children to macronodular in adults

Abstract Unavailable

Abstract citation ID: lvag096.040

JS1.2 - Biological differences between pediatric and adult adrenal tumours

Enzo Lalli
Inserm, Valbonne, France

Adrenal tumours in children and adults arise from the same organ but exhibit important differences in biology, clinical behaviour and therapeutic responses. Paediatric adrenocortical tumours (ACTs) are rare, often hormonally active and frequently associated with germline mutations, particularly in *TP53*, reflecting strong genetic predisposition. In contrast, adult adrenocortical carcinomas (ACCs) are typically sporadic, genetically heterogeneous and characterized by chromosomal instability and recurrent somatic alterations in *TP53*, *CTNNB1* and *ZNRF3*. Developmental context further distinguishes these tumours: the paediatric adrenal cortex retains foetal features that influence cell differentiation, tumour phenotype and hormone secretion, whereas adult tumours arise from a differentiated adrenal environment.

These differences manifest clinically: children commonly present with androgen excess, rapid tumour growth and localized disease, whereas adult tumours more often exhibit cortisol excess and are diagnosed at the stage of advanced disease. Histopathological criteria established for adult tumours, such as the Weiss score, often overestimate malignancy in paediatric cases, necessitating paediatric-specific indices like the Wieneke scoring system. Epigenetic and transcriptomic analyses reinforce this divergence, showing foetal-like gene expression in paediatric tumours and more dedifferentiated, proliferation-associated signatures in adult tumours.

Understanding these age-specific biological and molecular distinctions is crucial for accurate diagnosis, prognostication and treatment planning. Paediatric adrenocortical tumours may respond differently to chemotherapy and mitotane compared with adults, highlighting the risk of inappropriate extrapolation of adult treatment protocols.

My presentation will integrate data on epidemiology, developmental biology, molecular genetics and clinical outcomes to provide a comprehensive overview of the differences between paediatric and adult adrenal tumours. Emphasis will be placed on the implications for tailored diagnostic criteria, therapeutic strategies and the need for international collaborative research to optimize patient outcomes across age groups.

Abstract citation ID: lvag096.041

JS1.3 - Clinical management of children with adrenal cortical cancer

Verena Wiegering
Universitätsmedizin Frankfurt, Frankfurt, Germany

Pediatric adrenocortical carcinoma (ACC) is a rare and aggressive malignancy arising from the adrenal cortex, with an estimated incidence of 0.2-0.3 cases per million children per year. Despite its rarity, ACC represents one of the most clinically significant endocrine tumors in childhood due to its potential for rapid progression and frequent hormone secretion. In pediatric patients, ACC often presents with signs of hormonal excess, most commonly virilization caused by androgen overproduction, but may also include features of Cushing syndrome or mixed endocrine

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

syndromes. Early recognition of endocrine symptoms can facilitate earlier diagnosis, which is a key determinant of outcome.

The cornerstone of curative treatment for pediatric ACC is complete surgical resection of the primary tumor. Achieving an R0 resection remains the most important prognostic factor for long-term survival. Surgical management should ideally be performed in specialized centers with experience in pediatric oncologic and endocrine surgery to minimize tumor rupture and ensure appropriate staging. Adjuvant therapy may be considered depending on tumor stage, resection status, and risk stratification. The adrenolytic agent mitotane has been used in selected cases, often in combination with cytotoxic chemotherapy regimens such as etoposide, doxorubicin, and cisplatin for advanced or metastatic disease.

Pediatric ACC is frequently associated with genetic predisposition syndromes, particularly germline TP53 mutations as seen in Li–Fraumeni syndrome. Therefore, genetic counseling and testing are recommended for affected patients and their families. Multidisciplinary management involving pediatric oncology, endocrinology, surgery, genetics, and supportive care is essential to optimize outcomes. To continuously improve understanding, treatment, and prognosis, international networks and expert tumor boards such as ENSAT-PACT are essential.

Prognosis depends largely on stage at diagnosis, completeness of tumor resection, and biological tumor behavior. While localized disease treated with complete resection can have favorable outcomes, advanced or metastatic ACC remains challenging to treat. Continued international collaboration and clinical research are critical to improving risk stratification, treatment strategies, and survival in this rare pediatric malignancy.

JS2.1 - Special considerations

Abstract Unavailable

JS2.2 - Diagnosis

Abstract Unavailable

Abstract citation ID: lvag096.042

JS2.3 - European Society of Endocrinology and Endocrine Society Joint Arginine Vasopressin (AVP) deficiency guideline: updates, insights and next steps

Olaf Dekkers
Department of Clinical Epidemiology, Lumc, Leiden, The Netherlands

This presentation will cover recommendations from the forthcoming joint ESE-ES Clinical Guideline for the Diagnosis and Management of Arginine Vasopressin Deficiency (AVP-D), a rare condition previously known as central diabetes insipidus. A structured framework for distinguishing AVP-D from primary polydipsia and AVP resistance through baseline tests, as well as advanced testing, eg, copeptin-based stimulation testing, will be provided. Therapeutic strategies centered on individualized desmopressin treatment will be discussed, emphasizing the prevention of hyponatraemia through “treatment breaks” and patient education. Special considerations will be addressed such as AVP-D after pituitary surgery or traumatic brain injury, and management during pregnancy. Ultimately, the guidelines aim to standardize specialist care to maintain electrolyte balance and enhance the quality of life for patients with this complex water-regulatory disorder.

JS2.4 - Postoperative considerations

Abstract Unavailable

JS2.5 - Treatment

Abstract Unavailable

JS3.1 - Treatment of chronic hyponatraemia

Abstract Unavailable

JS3.2 - Methodology & methodologic pitfalls of assessing correction rates

Abstract Unavailable

Abstract citation ID: lvag096.043

JS3.3 - Preventing and treating overcorrection and the osmotic demyelination syndrome

Ewout Hoorn
Erasmus Medical Center, Rotterdam, The Netherlands

This presentation will cover recent insights into the incidence and risk factors for overcorrection of hyponatraemia and the development of osmotic demyelination syndrome. Furthermore, the recommendations from the 2026 ESE-ERA European Hyponatraemia Guideline on these topics will be discussed, including their implications for clinical practice.

JS3.4 - Symptomatic hyponatraemia and hypertonic saline

Abstract Unavailable

Abstract citation ID: lvag096.044

JS3.5 - Introduction, classification of hyponatraemia, differentiating causes of hyponatraemia

Mark Sherlock
Department of Endocrinology, Beaumont Hospital, Dublin, Ireland

This presentation will cover recent insights into the incidence and risk factors for overcorrection of hyponatraemia and the development of osmotic demyelination syndrome. Furthermore, the recommendations from the 2026 ESE-ERA European Hyponatraemia Guideline on these topics will be discussed, including their implications for clinical practice.

Abstract citation ID: lvag096.045

JS4.1 - Diabetes subclassification using ANDIS: from five clusters to clinical impact

Emma Ahlqvist
Clinical Sciences Malmö, Lund University, Malmö, Sweden

Adult-onset diabetes is characterized by considerable heterogeneity in metabolic presentation, disease progression, and risk of complications. Traditional diagnostic categories, which largely distinguish only between autoimmune and non-autoimmune forms, provide limited resolution for understanding this variation. The ANDIS cohort was created to systematically enroll all newly diagnosed cases of diabetes in a defined region and to collect standardized clinical, biochemical, and longitudinal

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

data. Using these data, we applied unsupervised clustering methods to examine whether patterns in routinely measured clinical variables could reveal more granular subgroups within non-autoimmune diabetes.

This analysis identified five reproducible clusters (SAID, SIDD, SIRD, MOD, and MARD) each characterized by distinct profiles in glycemia, insulin secretion, insulin resistance, body composition, age at onset, and markers of autoimmunity. Follow-up studies within ANDIS and replications in several independent cohorts have demonstrated that these subgroups show meaningful differences in glycemic progression, therapy needs, and rates of complications such as kidney disease. These findings suggest that subclassification may help explain why individuals with seemingly similar initial diagnoses experience markedly different trajectories over time.

In this presentation, I will summarize the development of the five-cluster model, the evidence supporting its reproducibility, and key results from longitudinal analyses within the ANDIS cohort. I will focus on what the clusters reveal about underlying disease mechanisms and how these data-driven subgroups compare with existing clinical markers used in diabetes assessment. The aim is not to propose immediate changes to routine clinical care, but to present how systematic population-based data collection and unbiased analytical approaches can improve our understanding of diabetes heterogeneity and provide a framework for generating more targeted hypotheses in diabetes research.

Abstract citation ID: lvag096.046

JS4.2 - Omics approaches to Asian Diabetes: genetic and molecular insights

Soo Heon Kwak
Internal Medicine, Seoul National University Hospital, Seoul, South Korea

The clinical landscape of type 2 diabetes (T2D) is undergoing a paradigm shift from a glucose-centric approach to a more nuanced, stratification-based strategy. This evolution is particularly crucial for East Asian (EA) populations, whose metabolic phenotypes—characterized by early beta-cell failure and distinct fat distribution—often deviate from Western models. In this symposium, we present a comprehensive framework that bridges multidimensional omics data to clinical phenotypes, aiming to decode the biological heterogeneity of T2D through computational methods and large-scale Korean biobank data.

Central to our approach is a deep learning-based integration of genomics, proteomics, and metabolomics. By mapping these high-dimensional data into a clinically relevant latent space, we identified four robust T2D subtypes that significantly outperform traditional single-omics models in terms of classification accuracy (ARI 0.78). Our analysis reveals that the molecular drivers of these subtypes are fundamentally different; for instance, the Mild Age-Related Diabetes (MARD) subtype is predominantly characterized by proteomic signatures, whereas the Severe Insulin-Resistant Diabetes (SIRD) subtype is more closely linked to metabolic dysregulation. Crucially, these molecular clusters are directly tied to clinical outcomes, with SIRD showing a heightened prevalence of chronic kidney disease and the Severe Insulin-Deficient (SIDD) subtype correlating strongly with diabetic retinopathy.

To further ground these findings in population-specific biology, we established a “Multi-Omics Atlas” of 5438 Korean individuals. This resource allowed us to identify over 1000 proteometabolic signatures and, more importantly, 138 EA-specific genetic signals that are absent in European cohorts like the UK Biobank. A standout discovery is the causal link between the ALDH2 protein and the metabolite 2-hydroxyisovalerate, a branched-chain amino acid metabolite uniquely associated with insulin resistance in East Asians. Through Mendelian randomization and colocalization, we demonstrate how these population-specific genetic architectures dictate systemic metabolic responses, providing a molecular explanation for the EA-specific T2D phenotype.

Taken together, this integrated research highlights that the future of diabetes management lies in understanding the interplay between genetic predisposition and molecular manifestations. By leveraging deep learning for precise subtyping and identifying EA-specific molecular markers, we provide a robust foundation for population-specific precision medicine. These insights not only enhance our understanding of diabetes heterogeneity but also pave the way for identifying novel, targeted therapeutic interventions tailored to the East Asian population.

Abstract citation ID: lvag096.047

JS4.3 - Data-driven subclassification of type 2 diabetes in Korea: from clinical phenotyping to precision intervention

Sang Youl Rhee
Endocrinology and Metabolism, Digital Health, Kyung Hee University College of Medicine, Seoul, South Korea

Background: Type 2 diabetes mellitus (T2DM) is a pathophysiologically heterogeneous disease. Its clinical phenotype in East Asians differs substantially from Western populations, with impaired insulin secretion—rather than insulin resistance—playing a predominant role. Subclassification frameworks derived from European cohorts may therefore not adequately capture Korea-specific phenotypes, necessitating data-driven approaches tailored to this population.

Methods: Using exploratory factor analysis applied to a multicenter retrospective cohort of 6603 middle-aged Korean T2DM patients from three tertiary hospitals (2008-2020), we identified distinct metabolic patterns and examined their associations with diabetes-related complications using Cox proportional hazard models, adjusted for age, sex, medications, and comorbidities.

Results: Three clinically distinct metabolic patterns were identified: the Obesity and Hypertension pattern (OH-P), the Liver Function-related HyperGlycemia pattern (LFHG-P), and the Decreased Kidney Function pattern (DKF-P). Each pattern conferred a unique complication risk profile. The OH-P was associated with increased peripheral vascular disease risk (HR 1.26; 95% CI 1.02-1.57), while the LFHG-P — characterized by hyperglycemia, dyslipidemia, and elevated liver enzymes—was associated with higher risks of myocardial infarction (HR 1.79; 95% CI 1.13-2.82) and atrial fibrillation (HR 1.54; 95% CI 1.07-2.23). The LFHG phenotype appears Korea-specific, potentially reflecting genetically reduced insulin secretory capacity compounded by high-carbohydrate dietary patterns.

Conclusions: These findings demonstrate that ethnicity-aware, multivariate clinical phenotyping can meaningfully resolve metabolic heterogeneity in Korean T2DM and identify pattern-specific complication risks. Advancing from retrospective EMR-based

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

approaches toward prospective, multimodal data collection—integrating genetics, imaging, and lifestyle variables—represents the next critical step. To this end, we are initiating a Korea National Institute of Health-funded multi-center prospective study, with the presenter as principal investigator, to develop precision complication prediction models tailored to the Korean population.

JS5.1 - The reduced life expectancy and treatment options for RTHbeta

Abstract Unavailable

JS5.2 - The psychosocial consequences of living with a pituitary condition

Abstract Unavailable

Abstract citation ID: lvag096.048

JS5.3 - Transversal working group on genomic testing

Thomas Eggermann
Center for Human Genetic and Clinical Genomics, Medical Faculty, RWTH University Aachen, Aachen, Germany

To faciliate focused activities for topical issues in genomic testing, ENDO-ERN has established a transversal working group (WG) in 2024. The major purposes of the WG group are to improve guidelines, identify gaps and updates in the field of genetic testing of endocrine disorders; to smooth and make genetic testing guidelines applicable, which consider daily routine and the best standard for genetic testing ensuring cooperation with other societies and avoiding double work; to suggest a standardised genetic testing regime whenever possible to guarantee a standarised testing procedure all over Europe; to orchestrate and to channel the activities of Endo-ERN in the field of genetics, to avoid fragmentation and unhelpful developments in genetic testing. In addition to a general overview on the WG, the presentation will focus on the joint activities to achieve a joint agreement on genetic testing and reporting from the clinical point of view, and the cooperation of ENDO-ERN with the European Society of Human Genetics.

JS5.4 - Introduction on endo-ERN initiatives (with a focus on the EndoCompass paper)

Abstract Unavailable

Abstract citation ID: lvag096.049

JS5.5 - The peadiatric thyroid cancer registry

Hanneke van Santen
Department of Pediatric Endocrinology, Wilhelmina Children's Hospital, UMCU, Princess Maxima Center for Pediatric Oncology, Utrecht, The Netherlands

Although differentiated thyroid carcinoma (DTC) is the most frequent endocrine pediatric cancer, it is rare in childhood and adolescence. While tumor persistence and recurrence are not uncommon, mortality remains extremely low. Complications of treatment are however reported in up to 48% of the survivors. Due to the rarity of the disease, current treatment guidelines are predominantly based on the results of small observational retrospective studies and extrapolations from results in adult patients. In order to develop more personalized treatment and follow-up strategies (aiming to reduce complication rates), there is an unmet need for uniform international prospective data collection and clinical trials.

The European pediatric thyroid carcinoma registry aims to collect clinical data for all patients ≤18 years of age with a confirmed diagnosis of DTC who have been diagnosed, assessed, or treated at a participating site. This registry is a component of the wider European Registries for Rare Endocrine Conditions project which has close links to Endo-ERN, the European Reference Network for Rare Endocrine Conditions. A multidisciplinary expert working group was formed to develop a minimal dataset comprising information regarding demographic data, diagnosis, treatment, and outcome. We constructed an umbrella-type registry, with a detailed basic dataset. In the future, this may provide the opportunity for research teams to integrate clinical research questions.

Abstract citation ID: lvag096.050

JS6.1 - Gestational diabetes: a critical window for cardiovascular prevention

Laura Lopez
Sanatorio Santa Rosa, Santa Rosa, Argentina

Background: Gestational Diabetes Mellitus (GDM) is now recognized as a profound "metabolic stress test" that unmasks a woman's underlying cardiovascular (CV) and metabolic vulnerability. This talk explores GDM not as a transient condition, but as a chronic phenotype identifying women at high risk for future disease.

Methods: We synthesized evidence from systematic reviews involving over five million women and recent clinical trials, including the "Steady Sugar" study, to evaluate the magnitude of cardiovascular risk (CVR) and the impact of Continuous Glucose Monitoring (CGM) on clinical outcomes.

Findings: Women with a history of GDM have a twofold higher risk of future major CV events, which manifests within the first decade postpartum. Crucially, progression to type 2 diabetes (T2DM) explains only 23.3% of this risk, suggesting that GDM is an independent marker of early vascular dysfunction. In this context, technology has proven to be a vital ally; real-time CGM identifies nocturnal and postprandial excursions missed by traditional monitoring. The "Steady Sugar" trial demonstrated that CGM use significantly improves outcomes, reducing unscheduled cesarean sections (20.0% vs 44.4%) and neonatal intensive care admissions compared to standard care.

Conclusions: GDM represents a unique clinical opportunity to identify and intervene in a high-risk vascular phenotype before overt disease occurs. A comprehensive management strategy must transition from reactive glucose monitoring to a continuum of care that integrates advanced technologies during pregnancy and rigorous postpartum surveillance. By combining 6-week reclassification, lifelong annual monitoring, and primordial prevention through breastfeeding, clinicians can effectively shift the trajectory of cardiovascular health for this population.

JS6.2 - Cardiovaascular health in menopause: key aspects and management

Abstract Unavailable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.051

JS6.3 - The cardiometabolic–hepatic axis in menopause

Poli Mara Spritzer
Universidade Federal do Rio Grande do Sul, Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil

The perimenopause is associated with an increase in cardiometabolic risk driven in part by estrogen deficiency. In this setting, the cardiometabolic–hepatic axis describes the interconnected metabolic disturbances linking cardiovascular risk factors, metabolic syndrome, and metabolic dysfunction–associated steatotic liver disease (MASLD).

Declining estrogen levels contribute to adverse changes in lipid metabolism, body composition, and vascular function. Around the time of the final menstrual period, total cholesterol, LDL-C, and apolipoprotein B increase, while visceral fat accumulation promotes central obesity, insulin resistance, and metabolic syndrome. Concurrently, the prevalence and severity of MASLD rise, with postmenopausal women exhibiting a higher risk of advanced fibrosis and loss of the relative protection observed during premenopausal years.

Management should prioritize lifestyle intervention, with 7%-10% weight loss associated with improvements in hepatic steatosis, inflammation, and fibrosis. Healthy dietary patterns, regular physical activity, and comprehensive control of cardiometabolic risk factors are essential. Incretin-based therapies offer promising multisystem benefits by targeting both hepatic and cardiometabolic pathways. For patients with noncirrhotic MASH and stage F2-F3 fibrosis, a liver-directed pharmacologic option has also recently become available in some countries. In selected perimenopausal and early postmenopausal women with vasomotor symptoms and MASLD, transdermal estrogen-based hormone therapy may offer additional metabolic and hepatoprotective effects, although this approach requires further validation in prospective trials.

In conclusion, perimenopause represents a critical window for cardiovascular and hepatic risk assessment. Effective management should integrate lifestyle modification, cardiometabolic optimization, and individualized pharmacologic strategies based on fibrosis stage and comorbidity profile.

ESE EYES Symposium

Abstract citation ID: lvag096.052

EYS1.1 - Using genomics to characterize features of aggressiveness in PitNETs”

Nesrine Benanteur
Institut Cochin, Equipe Bertherat, Paris, France

Aggressive evolution of pituitary neuroendocrine tumors (PitNETs) is rare, and metastatic spread is even more uncommon. As a result, defining aggressiveness and malignancy in PitNETs remains difficult, making these outcomes challenging to predict and understand. The aim of our work was to establish a molecular definition of aggressiveness in PitNETs using integrated genomic approaches.

PitNET samples from 206 patients were analyzed. Associations between nine clinicopathological features of aggressiveness and tumor omics profiles were investigated. The omics data included transcriptome, DNA methylation, chromosomal alterations, and gene mutations. In addition, clonal tumor evolution was monitored longitudinally in seven patients.

Among the nine clinicopathological features of aggressiveness evaluated, only rapid progression, progression after radiotherapy, Ki67/MIB1 proliferation index ≥10%, temozolomide treatment, metastases, and specific death were associated with distinct omics signatures. In contrast, tumour maximal diameter ≥40 mm, cavernous invasion, and sphenoid invasion did not show associations with specific molecular profiles.

Although the omics signatures linked to these features of aggressiveness partially overlapped, they remained distinct between corticotroph and mammo-somato-thyrotroph tumor lineages. Within each lineage, a shared molecular signature of aggressiveness was identified, characterized by a proliferative transcriptome signature combined with DNA hypermethylation. Alterations in several genes were associated with aggressive features, including mutations in known cancer-related genes such as *TP53* and *CDKN2A*, as well as alterations in *LRP1B*, identified here as a novel PitNET-associated gene. In contrast, alterations in *USP8* and *GNAS* were not associated with aggressive features.

Integrating gene alterations with methylome and transcriptome signatures allowed the identification of a subset of molecularly aggressive PitNETs. Notably, these molecular signatures remained globally stable throughout disease progression, despite increasing aggressiveness and potential clonal divergence.

Overall, this integrated multi-omics analysis provides a histomolecular definition of aggressiveness in PitNETs. Prospective cohort studies will be required to validate these molecular signatures and determine their prognostic value.

EYS1.2 - RNA processing defects in craniopharyngiomas and pituitary tumors”

Abstract Unavailable

EYS1.3 - Insight into ESE Young Endocrinologists and Scientists (EYES) activities

Abstract Unavailable

Abstract citation ID: lvag096.053

EYS1.4 - Out of sync: circadian dysregulation in cortisol excess

Elisabeth Nowak
Department of Internal Medicine IV, Ludwig-Maximilians-Universität, Munich, Germany

- Endogenous cortisol excess disrupts circadian rhythmicity, and emerging evidence shows circadian misalignment is an independent driver of cardiometabolic morbidity.
- The talk challenges reliance on single time-point diagnostics, highlighting the limitations of current tests in capturing dynamic cortisol patterns.
- It underscores the clinical burden of sleep-wake disruption and fatigue, which remain underrecognised and undertreated in routine endocrine care.
- It provides novel insights into objective assessment using actigraphy to characterise sleep-wake patterns and circadian

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

metrics, alongside emerging data on altered clock gene expression in cortisol excess.
- Finally, it offers an outlook on circadian-informed management, including chronotherapy to restore physiological rhythms and improve outcomes.

EYS1.5 - Celebrating excellence: EYES observership programme, sixth cycle

Abstract Unavailable

EUWIN Symposium

Abstract citation ID: lvag096.054

EW1.1 - Thyroid diseases: exploring sex differences in prevalence, treatment pattern and outcomes

Helena Filipsson Nyström
Department of Endocrinology, Institution of Medicin, Göteborg, Sweden

This 20-minute presentation will explore gender-specific patterns in the prevalence, diagnosis, and outcomes of thyroid diseases.

Hypo- and hyperthyroidism shows a clear female predominance, both in hypothyroidism, Graves' disease and toxic multinodular goitre, although the underlying mechanisms differ. Graves' disease occurs throughout adult life, with incidence peaks following pregnancy and during menopause, whereas toxic nodular goitre and hypothyroidism increase with age.

Thyroid dysfunction is common during pregnancy, underscoring the importance of appropriate, pregnancy-specific reference ranges for thyroid hormones to ensure accurate diagnosis and optimal treatment. The presentation will also address the effects of mild iodine deficiency during pregnancy. In addition, the impact of thyroid disorders on mental health, brain function, and cognitive performance in adults will be discussed.

Abstract citation ID: lvag096.055

EW1.2 - Obesity and type 2 diabetes: sex differences in risk factors, treatment responses, and long-term complications

Alexandra Kautzky-Willer
Department of Medicine III, Medical University of Vienna, Vienna, Austria

Obesity and type 2 diabetes are chronic diseases which are dramatically increasing worldwide leading to lower health- and lifespan of the patients and high costs and an enormous burden on the public health care system. Both biological and psychosocial factors, environment and lifestyle are involved in the pathogenesis of these metabolic disorders and thus important sex- and gender-based differences are evidenced. These differences have also important implications for lifestyle intervention (nutrition and exercise) and drug therapy. At the global level, prevalence of obesity is higher in women than men, including higher rates of preclinical obesity, especially at young age. Type 2 diabetes mellitus is usually diagnosed at a younger age and lower body fat mass in men compared to women. Women with newly diagnosed type 2 diabetes commonly have a more unfavourable risk factor profile including higher prevalence of hypertension. Psychosocial stress might play a prominent role in diabetes risk in women who also show higher levels of diabetes distress and higher prevalence of depression which further exacerbates their cardiometabolic risk. There are differences between men and women regarding comorbidities, the manifestation of complications and the initiation of and adherence to therapy. Women with diabetes show greater relative risk of CVD and mortality than men. Thus, more research on sex and gender differences, including the pathophysiologcal mechanisms, is necessary to increase the evidence in the future.

New Scientific Approaches

Abstract citation ID: lvag096.056

NSA1 - Harnessing the microbiome to improve health and prevent disease

Wendy Russell
Rowett Institute

The enteroendocrine system of the gastrointestinal tract is the largest endocrine organ in the human body. It plays an important role in the regulation of many physiological processes and altered secretion patterns are associated with several disorders. This talk will focus on the role of diet and in particular the functional output of the microbiome to impact on this system, with potential outcomes for human health.

Abstract citation ID: lvag096.057

NSA2 - Modeling GnRH neurons development

Taneli Ravio
Department of Physiology, University of Helsinki, Helsinki, Finland

Modeling human GnRH neuron development using hPSCs—from protocol development to disease modeling

Understanding human GnRH neuron biology has long been limited by the inaccessibility of primary human tissue and the unique developmental origin of these neurons. Human pluripotent stem cells (hPSCs) provide a powerful platform to overcome these limitations, enabling the reconstruction of developmental trajectories, identification of key signaling mechanisms, and modeling of human reproductive disorders in a patient-specific context.

In this presentation, I will discuss how the field has evolved from initial protocol development toward mechanistic insight and disease modeling, and finally toward reconstructing increasingly complex elements of the human reproductive axis.

Pioneering the field: from concept to reproducible protocol

Our early work in the field was driven by a fundamental question: is it possible to generate GnRH neurons from hPSCs at all? Initial differentiation attempts in my laboratory were based on a strategy to mimic olfactory placode differentiation, but this resulted in limited efficiency and unclear cellular identity. A major breakthrough was achieved with the development of a protocol combining dual SMAD inhibition, FGF8b treatment, and NOTCH inhibition. This approach enabled robust and reproducible generation of GnRH neurons and formed the basis of the key publication in Stem Cell Reports (Lund et al, 2016; PMID: 27426041). Thus, the field transitioned from proof-of-concept to a reproducible and disseminated

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

methodology that enabled broader exploration of human GnRH neuron biology.

From developmental biology to mechanism

Once a reliable and reproducible protocol was established, our focus shifted toward understanding the mechanisms that drive GnRH neuron specification. We demonstrated that GnRH neuron differentiation is sensitive to FGF8b dose, suggesting that their specification is not a binary process but is quantitatively regulated (Yellapragada et al. 2022; PMID: 35833364). In parallel, inhibition of FGFR1 signaling was shown to impair GnRH neuron formation, highlighting the importance of the FGF8–FGFR1 axis. These findings suggest that FGF signaling acts at the level of neural progenitor cells, influencing cell fate decisions and regional identity. Decoding the transcriptional landscape at the single cell level, we were subsequently able to demonstrate developmental trajectories of hPSC-derived GnRH neurons (Wang et al 2022; PMID: 36153707). Also, WNT inhibition during dual SMAD inhibition phase was shown to contribute to GnRH ontogeny. This raises the possibility that multiple developmental routes may exist and/or that GnRH neuron specification is more plastic than previously assumed, but still the FGFR1-FGF8 signaling appears to be the key. Emerging data, including our ongoing work on *DLX5* may further expand our understanding in this context, although these findings are still under investigation.

Disease modeling: translating developmental insight

One of the most important advances enabled by these models is the ability to study human disease mechanisms directly in GnRH neurons. In the context of precocious puberty, we have investigated the role of *MKRN3* and *DLK1* in GnRH neuron ontogeny from hPSCs (Yellapragada et al. 2019 PMID: 30800097; Eskici et al. 2025; PMID: 4092404). Similarly, we have modelled gonadotropin deficiency induced by mutations in genes such as *POGZ* (Eskici et al. 2023; PMID: 37619992, and *MADD* (Pulli et al. 2024; PMID: 38775154) by employing our hPSC-derived model. Overall, these studies demonstrate that hPSC-derived GnRH neurons provide a powerful system to functionally validate genetic findings and link them to specific developmental mechanisms.

Past, present, and future

The trajectory of the field can be viewed along three axes. In the past, the key question was whether GnRH neurons could be generated from human stem cells. In the present, the focus is on understanding the signaling pathways and developmental mechanisms that govern their specification, as well as applying these insights to disease modeling. Looking to the future, the field is moving toward increasing biological complexity. This includes the development of three-dimensional models, incorporation of migration and network formation, and expansion to additional cell types. A particularly exciting direction is the generation of kisspeptin neurons from hPSCs, which act upstream of GnRH neurons and are critical regulators of reproductive function. Combining GnRH and kisspeptin neurons in integrated systems may ultimately allow reconstruction of key elements of the human reproductive axis in vitro.

Take-home message

The field has evolved from protocol development to mechanistic understanding and disease modeling, and is now moving toward system-level reconstruction of human reproductive neuroendocrinology. Human pluripotent stem cell models are no longer only a tool to generate GnRH neurons—they are becoming a platform to understand, and ultimately rebuild, the human reproductive axis.

NSA3 - AI and detection of vertebral fractures

Abstract Unavailable

Debate Sessions

Abstract citation ID: lvag096.058

D1.1 - Surgery in mild autonomous cortisol secretion—against

Ioannis Ilias
Department of Endocrinology, Hippokration General Hospital, Athens, Greece

Background: Mild autonomous cortisol secretion (MACS) is commonly observed in adrenal incidentaloma patients and it leads to an increased prevalence of arterial hypertension, diabetes mellitus, and other cardiometabolic comorbidities. The indication of adrenalectomy in these patients is not well defined.

Objective: To critically review the data supporting both the surgical and conservative management of MACS, specifically vis-à-vis clinically relevant outcomes, patient safety, and guidelines.

Methods: Analysis of the literature along with the 2023 ESE-ENSAT guidelines.

Results: Adrenalectomy could be beneficial for surrogate endpoints including hypertension and glycemic control. However, the original literature, which is mainly retrospective and heterogeneous, does not provide conclusive information. More importantly, improvement in hard endpoints, has never been proven. Surgically treated patients show a high incidence of postoperative adrenal insufficiency, which may be prolonged. MACS typically has an indolent natural history, with a low annual probability of progressing to overt Cushing's syndrome. The majority of publications regarding surgery for MACS appear to be neutral or positive about the matter, however, negative views have increased after 2019.

Conclusions: In the absence of convincing evidence for improved survival or cardiovascular outcomes, and given the significant risk of harm, adrenalectomy should not be the default treatment for MACS. Conservative management with aggressive treatment of comorbidities and selective use of medical therapy should be considered to be the ethical and evidence-based default, reserving surgery for highly selected patients with clearly progressive or refractory disease.

D1.2 - Surgery in mild autonomous cortisol secretion—against

Abstract Unavailable

D1.3 - Surgery in mild autonomous cortisol secretion—pro

Abstract Unavailable

D1.4 - Surgery in mild autonomous cortisol secretion—pro

Abstract Unavailable

D2.1 - Rebuttal

Abstract Unavailable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

D2.2 - Crossing the medial wall of the cavernous sinus: surgical innovation or heresy in invasive pituitary adenomas—heresy

Abstract Unavailable

D2.3 - Rebuttal

Abstract Unavailable

D2.4 - Crossing the medial wall of the cavernous sinus: surgical innovation or heresy in invasive pituitary adenomas—surgical innovation

Abstract Unavailable

Meet the Expert Sessions

MTE1 - Bone quality in endocrine diseases

Abstract Unavailable

MTE3 - Diagnosis and targeted treatment of primary aldosteronism

Abstract Unavailable

MTE4 - Novel growth hormone receptor antagonists; atomic mechanism(s) of receptor binding and new uses

Abstract Unavailable

Abstract citation ID: lvag096.059

MTE5 - Medullary thyroid cancer: from genetics to clinic

Antonio Matrone[1,2]

[1]*Department of Clinical and Experimental Medicine, Unit of Endocrinology, University Hospital of Pisa, Pisa, Italy;* [2]*Unit of Endocrinology, Department of Clinical and Experimental Medicine, University Hospital Of Pisa, Pisa, Italy*

The current presentation consistently highlights that molecular profiling is central to modern management of medullary thyroid carcinoma (MTC). RET mutations drive nearly all hereditary cases and the majority of sporadic and advanced MTC, making germline testing mandatory in all patients and somatic testing essential in advanced disease for prognostic stratification and therapeutic decisions. Hereditary cases, particularly if MTC is driven by molecular alteration of the RET gene linked to the phenotype of type 2 Multiple Endocrine Neoplasia (MEN 2), need careful and specific management. It should be considered that the gene carriers, those still not affected by MTC but who carry the RET mutation, need to be followed up in a specific manner. From a clinical perspective, biochemical markers, calcitonin, and CEA, are key tools across the disease continuum. Calcitonin is crucial for early diagnosis and screening in selected thyroid nodules, while postoperative levels and doubling times are strong prognostic indicators and guide follow-up intensity. Imaging is used in a stepwise approach, escalating from ultrasound and CT scan, mainly total body with i.v. contrast medium, to functional imaging (ie, 18F-DOPA PET) in cases of biochemical or structural persistence.

Management differs by risk:

- **Low-risk or cases that are cured after surgery** can often be managed with active surveillance and tailored follow-up based on biomarker trends.
- **Advanced MTC cases** require a more careful follow-up to identify those in which active therapy is needed. The progressive MTC cases, mainly according to progressions defined by a specific imaging, require systemic therapy, initiated based on tumor burden, progression rate, and symptoms rather than biochemical elevation alone.

Therapeutically, multikinase inhibitors (vandetanib, cabozantinib) improve progression-free survival but are limited by toxicity and resistance. In contrast, highly selective RET inhibitors (selpercatinib) represent a major advance, offering higher response rates, better tolerability, and activity even after prior treatments—though restricted to RET-mutant disease and still challenged by resistance mechanisms. Overall, integrating molecular data, biomarkers, and imaging enables a personalized, risk-adapted approach that improves outcomes across both early and advanced MTC.

MTE6 - Risk communication in stage 1 and 2 type 1 diabetes,

Abstract Unavailable

MTE7 - Reducing exposure: practical tips for everyone

Abstract Unavailable

MTE8 - Long term results in pituitary adenoma surgery

Abstract Unavailable

MTE9 - Graves orbitopathy: what therapy and when?

Abstract Unavailable

MTE10 - Clinical management of VHL syndrome

Abstract Unavailable

MTE11 - Treatment of adrenocortical carcinoma—standard therapy and experimental approaches (including CART)"

Abstract Unavailable

MTE12 - Meet the EndoCompass expert

Abstract Unavailable

Meet the Expert Basic Scientist Sessions

MTEBS1 - Latest insights of cryo-EM structures in the Thyroid field

Abstract Unavailable

MTEBS3 - Liquid biopsy biomarkers in Neuroendocrine Tumours: advancing diagnosis, prognosis, and therapeutic management

Abstract Unavailable

MTEBS2 - Neurobiology of stress response

Abstract Unavailable

MTEBS5 - How to measure EDCs?

Abstract Unavailable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.060

MTEBS4 - Seeing is believing: imaging live cell behaviour in the pituitary gland

Patrice Mollard
University of Montpellier, Institute of Functional Genomics, CNRS UMR5203, INSERM U1191, Montpellier, France

Advanced *in vivo* imaging technologies have revolutionized our understanding of pituitary gland function by revealing the critical importance of three-dimensional cellular organization in hormone secretion in mouse models. Using innovative approaches such as two-photon microscopy, intra-vital microscopes fitted with long-distance objectives and GRIN lens-equipped miniscopes in awake mice, researchers have demonstrated that pituitary endocrine cells are organized in intermingled 3D multicellular networks rather than functioning as isolated units. These networks generate coordinated calcium signals that translate hypothalamic signals into precisely-timed hormone pulses released into the bloodstream. The integration of high-resolution *in vivo* imaging with spatial transcriptomics and single-cell multi-omics now helps identify key ion channels, signaling molecules, and plasticity mechanisms governing these cellular networks. These findings challenge classical views of pituitary function and reveal that spatial cellular organization is fundamental to endocrine homeostasis. Furthermore, this integrated approach offers unprecedented opportunities to understand pituitary disorders at the cellular and molecular level, potentially leading to improved diagnostic tools and therapeutic strategies. While direct high-resolution imaging of the human pituitary remains technically challenging due to its anatomical location, insights from genetically-modified mouse models provide translatable knowledge that bridges fundamental research and clinical applications in endocrinology.

Pre-Congress Events

PCC1.1 - Symposium 1: growth hormone deficiency—GH replacement in suvivors of Cancer—new concensus

Abstract Unavailable

Abstract citation ID: lvag096.061

PCC1.2 - Symposium 1: growth hormone deficiency—GHD in Cushing's disease: diagnosis and management

Kevin CJ Yuen
Barrow Pituitary Center, Barrow Neurological Institute and St. Joseph's Hospital and Medical Center, University of Arizona College of Medicine, Phoenix, AZ, United States

Growth hormone deficiency (GHD) occurs in Cushing disease (CD) patients mainly because of treatment-related effects (eg, pituitary surgery and radiation therapy), but tumor mass effect may also contribute to the development of GHD in the minority of CD patients due to corticotroph macroadenomas. However, several comorbidities associated with active CD may persist after remission of hypercortisolism. Growth hormone deficiency shares many clinical features seen in CD patients, and its presence after disease remission worsens the systemic complications caused by previous hypercortisolism. In patients with active hypercortisolism, GH secretion is suppressed, but may recover after disease remission is achieved. Hence, GH testing should only be performed at least 1-2 years after remission for the correct diagnosis. Treatment for GHD (either daily or long-acting GH formulations) in CD adult patients has been associated with improvements in body composition, muscle strength, exercise capacity, quality of life, cardiovascular health, bone mineral density and reversal of metabolic dysfunction-associated steatotic liver disease, whereas for GHD in CD pediatric patients, improvement in adult height is one of the major goals of GH replacement. While generally safe, GH replacement requires careful monitoring to ensure effectiveness and tolerance (particularly hyperglycemia) in treated patients.

PCC1.3 - Symposium 1: growth hormone deficiency—rethinking GH deficiency: genetic diversity and treatment outcomes in children

Abstract Unavailable

PCC1.4 - Symposium 2: the efficacy and safety of long-acting GH a report from a GRS consensus workshop—adult perspectives

Abstract Unavailable

PCC1.5 - Symposium 2: The efficacy and safety of long-acting GH a report from a GRS consensus workshop—paediatric perspectives

Abstract Unavailable

PCC1.6 - Symposium 2: the efficacy and safety of long-acting GH a report from a GRS consensus workshop—similarities and differences with daily GH replacement

Abstract Unavailable

PCC1.7 - Symposium 3: GH from bench to bedside and registries—aging and the GH/IGF-I axis in mice models

Abstract Unavailable

PCC1.8 - Symposium 3: GH from bench to bedside and registries—The Pituitary Society Lecture

Abstract Unavailable

PCC1.9 - Symposium 3: GH from bench to bedside and registries—The SAFE-survivors study—using registries for studying the safety of long-acting growth hormone in cancer survivors

Abstract Unavailable

PCC2.1 - AE-PCOS Society News

Abstract Unavailable

Abstract citation ID: lvag096.062

PCC2.2 - Cell type-specific endometrial dysfunctions across the menstrual cycle in polycystic ovary syndrome

Tanja Turunen[1], Congru Li[1], Riikka Arffman[2], Gustaw Eriksson[1], Tina Gorsek Sparovec[1], Ulla Saarela[2], Angelica Lindén Hirschberg[3], Terhi Piltonen[2] and Elisabet Stener-Victorin[1]
[1]*Karolinska Institutet, Solna, Sweden;* [2]*Medical Research Center, Department of Obstetrics and Gynecology, University of Oulu and*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Oulu University Hospital, Research Unit of Clinical Medicine, Oulu, Finland; [3]Department of Women's and Children's Health, Department of Gynecology and Reproductive Medicine, Karolinska Institutet and Karolinska University Hospital, Solna, Sweden

Polycystic ovary syndrome (PCOS) affects 11%-13% of reproductive-aged women and is characterized by hyperandrogenism, polycystic ovarian morphology, and menstrual irregularities. It is a major cause of anovulatory infertility and affected women have an increased risk of implantation failure and miscarriage, likely due to endometrial dysfunction. Recently, we published the first PCOS Endometrial Cell Atlas (PECA 1.0), which revealed cell-type-specific disease signatures in proliferative-phase endometrium. Here, we comprehensively characterize how different cell types and their transcriptomic signatures evolve across the menstrual cycle in PCOS by establishing PECA 2.0. pEndometrial biopsies were obtained, after informed consent, from women with and without PCOS who had similar age and BMI ($P > .05$ two-tailed Welch's t-test). Combined with the PECA 1.0 study (12 PCOS, 5 controls), our current single-nuclei (sn) RNA-seq dataset of 62 samples covers proliferative (7 PCOS, 7 controls), early secretory (6 PCOS, 3 controls), mid-secretory (7 PCOS, 5 controls), and late secretory phases (4 PCOS, 3 controls), as well as the anovulatory state (3 PCOS). Libraries were prepared from snap-frozen biopsies using Chromium GEM-X technology v 4.0 (10X Genomics). After data quality control, the final PECA 2.0 dataset included 998 832 high-quality nuclei: 625 593 from PCOS and 373 239 from control endometrium. We identified four main clusters: epithelial ($n = 478$ 789), stromal ($n = 453$ 832), immune ($n = 55$ 708), and endothelial cells ($n = 10$ 503). Reintegration revealed 11 epithelial, 7 stromal, 5 endothelial, and 16 immune cell subpopulations. The proliferative phase PCOS endometrium has a decreased proportion of proliferative stromal cells (56.26%) compared to controls (92.96%; Mann-Whitney U, adj. $P = .124$; Levene's test, adj. $P = .018$). Moreover, disrupted decidualization was demonstrated by a decreased proportion of decidualized stromal cells in PCOS late secretory phase samples (45.77%) compared to controls (59.98%; Mann-Whitney U, adj. $P = .124$; Levene's test, adj. $P = .011$). Levene's test results indicate significantly greater variability in these cell proportions in PCOS samples. The PCOS Endometrial Cell Atlas across the menstrual cycle, PECA 2.0, maps cellular heterogeneity and reveals transcriptomic signatures of endometrial dysfunction in PCOS at high resolution. This resource provides a foundation for developing precise diagnostic tools, targeted therapies, and preventive strategies to improve endometrial health.

Abstract citation ID: lvag096.063

PCC2.3 - In vitro endometrium of insulin resistant women with polycystic ovary syndrome

Anja Dekanski[1], Gustaw Eriksson[1], Tanja Turunen[1], Timotej Strmen[2], Tina Gorsek Sparovec[1], Angelica Lindén Hirschberg[3], Elin Chorell[2], Nayere Taebnia[1] and Elisabet Stener-Victorin[1]

[1]Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden; [2]Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden; [3]Department of Women's and Children's Health, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

Introduction: Endometrial dysfunction in polycystic ovary syndrome (PCOS) can lead to reduced fertility, miscarriage, and higher endometrial cancer risk. Additionally, our recent PCOS endometrial single-cell atlas shows cell type specific transcriptomic disease signatures. *In vitro* endometrial systems mirroring the PCOS tissue of origin is crucial for future mechanistic insight and novel target testing. We hypothesized that PCOS-associated endometrial disease features can be preserved in primary human endometrial epithelial organoids (EEOs) and single-layer stromal cells, under optimized conditions.

Methods: We established and characterized EEOs ($n = 4$ PCOS; $n = 4$ controls) and stromal cells ($n = 6$ PCOS; $n = 6$ controls) from proliferative phase endometrial biopsies of women with and without PCOS. Women with PCOS were hyperandrogenic and insulin resistant. Both cell systems were differentiated with 10 nM estradiol and 1 uM progesterone. EEOs and stromal cells were collected for bulk RNA sequencing and stained for typical differentiation markers. In stromal cells, we also performed lipidomics using liquid chromatography coupled to quadrupole time-of-flight mass spectrometry, and cellular bioenergetics using Seahorse XFe96. Additionally, we used a PCOS-like anovulatory hormonal environment and a healthy hormonal environment with estrogen, progesterone and androgen levels fluctuating. We tried EEO stimulation in these hormonal environments in both a static and microfluidic setting.

Results: In the initial EEO set-up very few transcriptomic differences were captured between PCOS and Control origin cells. In stromal cells, progesterone receptor staining was reduced, and maximal respiration trended lower in PCOS. Differentially expressed genes (DEGs) in stromal cells included upregulation of fibro activation protein (*FAP*) gene and downregulation of *CARD16*. Lipidomics analysis showed PCOS stromal cells uniquely accumulated insulin-resistance-associated ceramides during differentiation. At day 14, PCOS stromal cells had significantly elevated C20-ceramide and reduced cardiolipins. Fluctuating hormonal environment and the microfluidics setting were able to recapitulate more of the transcriptomic differences between PCOS and Control in EEOs.

Conclusions: Preliminary data shows that in the static hormonal environment *in vitro*, that does not closely recapitulate neither the normal menstrual cycle nor the PCOS irregular menstrual cycle, the EEOs lose most of their PCOS phenotype *in vitro*, while stromal cells retain more of it. Mimicking the PCOS-like and healthy-like hormonal environment and using microfluidics exacerbated transcriptomic differences in EEOs. Stromal cells from women with PCOS had DEGs related to proliferation and inflammation, and lipid dysregulation associated with metabolic dysfunction. In the next steps we are establishing co-culture systems to combine EEOs and stroma, but also adipose and endometrial cells.

PCC2.4 - Increased prospective cardiovascular disease risk in 127 517 Nordic women withPAGE 3polycystic ovary syndrome. A national cohort study

Abstract Unavailable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

PCC2.5 - Inhibition of the androgen-activating enzyme AKR1C3 selectively decreases systemic and intra-adipose 11-oxygenated androgens in women

Abstract Unavailable

PCC2.6 - Limited utility of cluster analysis in polycystic ovary syndrome for defining clinically meaningful subtypes and case–control discrimination in unselected populations

Abstract Unavailable

PCC2.7 - Manipulation of peripheral androgen signaling in the treatment of PCOS-associated metabolic dysfunction

Abstract Unavailable

PCC2.8 - Reduced circulating and skeletal muscle MOTS-c expression in women with polycystic ovary syndrome: evidence for disrupted mitochondrial-derived peptide regulation

Abstract Unavailable

PCC2.9 - Session 1—blocking AMH in a spontaneous rat model of PCOS

Abstract Unavailable

Abstract citation ID: lvag096.064

PCC2.10 - Session 1 -targeting the androgen receptor to treat cardiometabolic complications in PCOS

Damian Romero
Pharmacology and Toxicology, University of Mississippi Medical Center, Jackson, United States

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder in reproductive-age women and is strongly associated with hyperandrogenemia and cardiometabolic dysfunction. Hyperandrogenic phenotypes are particularly prone to obesity, insulin resistance, dyslipidemia, and adipose tissue dysfunction. Although androgen receptor (AR) signaling is central to the pathophysiology of these abnormalities, traditional antiandrogens are limited by safety concerns, including hepatotoxicity. Thus, innovative strategies to modulate AR activity with improved specificity and safety are urgently needed.

We investigated the therapeutic potential of selective AR degradation using the PROTAC ARV-110 in a well-established hyperandrogenemic mouse model of PCOS. Peripubertal dihydrotestosterone (DHT) exposure induced increased body weight, adiposity, glucose intolerance, hypercholesterolemia, and hyperleptinemia. ARV-110 dose-dependently reduced AR protein levels across metabolic tissues and attenuated DHT-mediated increases in body weight and fat mass, without affecting lean mass. Treatment improved glucose homeostasis, reduced circulating leptin, and favorably modified the adiponectin to leptin ratio, a marker of adipose tissue dysfunction.

Unbiased proteomic analyses were performed in both liver and kidney to define tissue-specific molecular responses. In the liver, ARV-110 was the primary driver of proteomic remodeling, broadly altering metabolic, translational, and proteostatic pathways, with high-dose treatment producing pathway disruptions consistent with hepatotoxicity. In the kidney, DHT was the dominant driver of molecular change, markedly altering gene expression programs related to translation, ribosomal activity, and protein quality control. ARV-110 produced a dose-dependent modulation of these DHT-induced signatures in hyperandrogenemic mice, partially reversing multiple translational and proteostatic pathways, particularly at the higher dose, although renal profiles were not fully restored to control patterns.

These findings establish targeted AR degradation as a mechanistically novel and potentially transformative therapeutic strategy for hyperandrogenemia-driven cardiometabolic disease in PCOS, offering a precision approach that moves beyond receptor blockade toward selective modulation of androgen signaling.

PCC2.11 - Session 2—GLP-1 and GLP-1/GIP receptor agonists in PCOS

Abstract Unavailable

PCC2.12 - Session 3—Saroglitazar/PPAR gamma agonist in PCOS treatment

Abstract Unavailable

PCC2.13 - Session 4—targeting cannabinoids and incretins in the treatment of PCOS

Abstract Unavailable

PCC2.14 - Unraveling the role of hyperandrogenism in the development of metabolic dysfunction-associated steatotic liver disease (MASLD) in polycystic ovary syndrome

Abstract Unavailable

PCC2.15 - Update meeting wrap up and promotion of annual meeting

Abstract Unavailable

PCC3.1 - Symposium 4: covert actions of GH—GH and fibrosis in human models

Abstract Unavailable

PCC3.2 - Symposium 4: covert actions of GH—GH and fibrosis in mice models

Abstract Unavailable

Abstract citation ID: lvag096.065

PCC3.3 - Symposium 4: covert actions of GH—GH and liver fat content

Karen Miller
Massachusetts Hospital and Harvard Medical School

Metabolic dysfunction-associated steatotic liver disease (MASLD) is highly prevalent, associated with significant morbidity and there are currently few FDA-approved treatments available for the condition. Insights from preclinical models as well as from patients with acromegaly and organic growth hormone deficiency in patients with hypopituitarism have led to the investigation of the impact of growth deficiency and administration in the pathophysiology of MASLD. Our randomized, double-blind trial of physiologic GH administration

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

demonstrated improvement in hepatic endpoints in patients with obesity and MASLD without pituitary disorders. Further studies are ongoing with the ultimate goal of understanding the mechanisms of the impact of GH administration on liver fat, inflammation and fibrosis. Future studies are needed to guide screening and monitoring of MASLD-related outcomes in patients with GH deficiency.

PCC3.4 - Symposium 4: covert actions of GH—impact of nutrition on somatotroph axis: a potential role in acromegaly treatment

Abstract Unavailable

PCC4.1 - Comparison of ultrasound-based thyroid cancer risk stratification systems

Abstract Unavailable

PCC4.2 - Fine needle biopsy technique

Abstract Unavailable

Abstract citation ID: lvag096.066

PCC4.3 - Practical session—thyroid ultrasound—practical demonstration, ultrasound-guided fine needle aspiration technique—practical demonstration, radiofrequency ablation for Thyroid nodules—practical demonstration

Filip Gabalec, David Fibigr, Tereza Grimmichova, Jan Jiskra, Jan Kratky and Darina Reva
4th Department of Internal Medicine—Hematology, University Hospital Hradec Králové, University Hospital Hradec Kralove and Charles University, Faculty of Medicine in Hradec Kralove, Hradec Králové, Czech Republic

This workshop will present the basic principles and technical aspects of radiofrequency ablation (RFA) used in the treatment of thyroid nodules. The procedure and the moving-shot technique will be demonstrated under ultrasound guidance. Participants will have the opportunity to practice the technique in a safe educational environment using simulation models prepared from gelatin as well as biological tissue models such as chicken breast and liver. These models allow realistic training of needle placement, electrode manipulation, and basic ablation techniques without risk to patients. The workshop aims to provide physicians with practical experience and a better understanding of the RFA procedure.

Abstract citation ID: lvag096.067

PCC4.4 - Radiofrequency ablation for thyroid nodules

Darina Reva
Otorhinolaryngology and Head and Neck Surgery, Regional Hospital Pardubice and Faculty of Health Studies, University of Pardubice, Pardubice, Czech Republic

Introduction: Radiofrequency ablation (RFA) is a minimally invasive treatment method that has become an established alternative to surgery for selected benign thyroid nodules. The procedure is performed under ultrasound guidance and allows targeted thermal destruction of nodular tissue while preserving the surrounding thyroid parenchyma and thyroid function. RFA has been increasingly adopted in clinical practice due to its favorable safety profile and good clinical outcomes.

Methods: This presentation will provide an overview of the technical principles of ultrasound-guided RFA for thyroid nodules. The procedure, including patient preparation, equipment, and the moving-shot technique, will be described. Particular attention will be given to ultrasound guidance during the procedure, protection of surrounding structures, and strategies to minimize complications. Expected clinical outcomes such as nodule volume reduction and improvement of compressive or cosmetic symptoms will also be discussed.

Conclusions: Radiofrequency ablation represents a safe and effective minimally invasive treatment option for thyroid nodules. Understanding the technical aspects of the procedure and appropriate ultrasound guidance is essential for achieving optimal outcomes and minimizing complications in clinical practice.

PCC4.5 - Thermal ablation for Thyroid nodules—indications, risks, and benefits

Abstract Unavailable

Abstract citation ID: lvag096.068

PCC4.6 - Ultrasound features associated with Thyroid Cancer

Tereza Grimmichova
Department of Internal Medicine, University Hospital Královské Vinohrady and Third Faculty of Medicine, Prague, Czech Republic

Thyroid nodules are frequently found in the thyroid gland; between 19% and 67% of individuals are found to have nodules on high-resolution ultrasound, with 5%-10% being malignant. The most common thyroid cancer is papillary cancer (PTC); in particular, papillary microcarcinoma is frequently found incidentally. Despite the striking increase in incidence over the last decades, the mortality rate for thyroid cancer has remained low. However, there are rising trends in incidence-based mortality for thyroid cancer, particularly in cases of advanced-stage papillary thyroid cancer.

It is crucial to correctly stratify the malignancy risk of nodules to balance overdiagnosis against the risk of overlooking clinically significant tumors. Sonography is the most sensitive method for thyroid nodule examination. Risk stratification systems known as TIRADS (Thyroid Imaging Reporting and Data System) were developed using specific ultrasound features to estimate the likelihood of malignancy and provide guidance on whether fine-needle aspiration (FNA) biopsy is warranted. TIRADS must use a combination of sonographic features to properly establish the risk of thyroid nodules.

Implementing TIRADS should lead to standardized reporting, improved communication, unified recommendations, and a reduction in unnecessary FNAs. While there are currently many overlapping risk stratification systems, the International TIRADS (I-TIRADS) lexicon has been developed as a first step toward a unified, universally accepted system. It defines specific thyroid nodule features—illustrated with sonograms—such as composition, echogenicity, margins, direction of growth (shape), echogenic foci (including microcalcifications), and lymph node status. Typical sonographic features of a thyroid nodule with a

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

higher risk of malignancy include a solid composition, a markedly hypoechoic appearance, irregular margins, a taller-than-wide shape, microcalcifications, and signs of extrathyroidal extension. Interobserver agreement for individual sonographic features is usually fair to good, with substantial agreement regarding the indication for fine-needle aspiration biopsy. In summary, TIRADS provides a user-friendly and clinically necessary framework for assessing thyroid nodules.

PCC4.7 - Ultrasound of neck lymph nodes

Abstract Unavailable

PCC5.8 - Hypogonadism and obesity: practical questions and solutions

Abstract Unavailable

PCC5.9 - Introduction to andrology

Abstract Unavailable

PCC5.10 - Male infertility: the genetic etiology and its management

Abstract Unavailable

Abstract citation ID: lvag096.069

PCC5.11 - The EAA guidelines on Klinefelter syndrome

Jolanta Slowikowska-Hilczer
Medical University of Łódź

Among patients with Klinefelter syndrome (KS) clinical features are highly variable; however, the most common characteristics include severely impaired spermatogenesis and Leydig cell dysfunction, resulting in azoospermia and hypergonadotropic hypogonadism. In addition, a broad spectrum of neurocognitive and psychosocial manifestations has been described, along with an increased prevalence of cardiovascular, metabolic, and bone-related disorders, which may contribute to the elevated morbidity and mortality observed in KS. Moreover, compared with the general male population, patients with KS appear to have a higher prevalence of coagulation and autoimmune disorders. Both genetic and epigenetic mechanisms related to the supernumerary X chromosome, as well as testosterone deficiency, contribute to this pathological profile.

The majority of patients with KS are diagnosed in adulthood, although symptoms may already become apparent during infancy, childhood, or adolescence. An expert panel of academicians appointed by the EAA developed the first consensus guidelines for the management of KS. These guidelines provide recommendations and practical suggestions for the care of patients with KS across different developmental stages, from childhood and adolescence to adulthood. The recommendations are based on recent research findings, as well as expert evaluation and validation.

PCC5.12 - What an endocrinologist should know about the diagnosis and management of erectile dysfunction?

Abstract Unavailable

PCC6.1 - Session 1. Treatment of chronic hypoparathyroidism in adults—emerging therapies

Abstract Unavailable

PCC6.2 - Session 1. Treatment of chronic hypoparathyroidism in adults—hormone replacement therapy—for who and when?

Abstract Unavailable

PCC6.3 - Session 1. Treatment of chronic hypoparathyroidism in adults—rationale for first line (conventional) therapy—when is it enough?

Abstract Unavailable

PCC6.4 - Session 2. Fracture risk in parathyroid disorders—bone in parathyroid disorders

Abstract Unavailable

Abstract citation ID: lvag096.070

PCC6.5 - Session 2. Fracture risk in parathyroid disorders—fracture risk in hypo—and hyperparathyroidism

Neil Gittoes
University of Birmingham, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom

Rare bone and mineral disorders often masquerade as common clinical problems, leading to delays in accurate diagnosis and optimal management. This symposium, part of the ESE Rare-CaPaB Educational Programme, brings together expert clinicians to illustrate how typical presentations—such as fragility fractures in young adults and seizures with hypocalcemia—can conceal underlying rare etiologies. Through two case-based discussions, the session highlights multidisciplinary perspectives across osteogenesis imperfecta, hypophosphatasia, X-linked hypophosphatemia, non-surgical hypoparathyroidism, and pseudohypoparathyroidism. By integrating focused viewpoints from endocrinology, metabolic bone disease, and related specialties, the program aims to improve recognition, diagnostic pathways, and tailored treatment strategies for these rare conditions.

Abstract citation ID: lvag096.071

PCC6.6 - Session 2. Fracture risk in Parathyroid disorders prevention and treatment of fractures in hypo—and hyperparathyroidism

Stefan Pilz
Medical University of Graz

The basic concept of fracture prevention is based on assessment of fracture risk with tools such as FRAX and evaluating whether it exceeds intervention thresholds for anti-osteoporosis drugs. Historically, fracture risk thresholds were set to match the risk level of persons with previous fragility fractures, and this aligned well with cost-effectiveness calculations. Due to price reductions for bisphosphonates over time, these medications may nowadays be cost-effective in patients well below current intervention thresholds, thereby contributing to debates on thresholds for anti-osteoporosis drugs.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Fracture prevention in patients with primary hyperparathyroidism (PHPT) can be done by parathyroidectomy, anti-osteoporosis drugs or a combination of them. Anti-fracture efficacy of parathyroidectomy in PHPT patients has not been documented in the few randomized controlled trials (RCT), but these investigations were limited by eg, low participant numbers and several sorts of potential bias such as group differences in anti-osteoporosis drugs. Large observational studies have documented significantly lower fracture incidence in PHPT patients undergoing parathyroidectomy as compared to those managed conservatively. Importantly, this fracture risk reduction was similar in patients with and without osteoporosis and in those with and without a guideline indication for parathyroidectomy. The current PHPT guidelines from the Fifth International Workshop recommend parathyroidectomy in PHPT patients with a T-score of ≤ -2.5 at the hip, spine or 1/3 radius and/or a prevalent vertebral fracture or incident low-trauma fracture during follow-up. For diagnostic purposes, bone mineral density (BMD) measurements and vertebral fracture screening are recommended in PHPT. Evaluations of FRAX in PHPT patients were released after publication of the 2022 PHPT guidelines and showed that FRAX provides reasonable fracture prediction though moderately underestimates fracture probabilities in PHPT. Whether and how to use FRAX in PHPT patients for decisions on parathyroidectomy remains unclear and the task for future guideline revisions. PHPT patients with low BMD who do not undergo parathyroidectomy can be treated with anti-osteoporosis drugs such as eg, bisphosphonates or denosumab. Evidence suggests that i.v. bisphosphonate treatment with zoledronate one to three months after parathyroidectomy results in a higher BMD as compared to parathyroidectomy alone, but several questions remain on the efficacy and optimal timing of a combination therapy with parathyroidectomy and anti-osteoporosis drug treatment. Clinicians should be aware that cinacalcet can effectively lower calcium in PHPT patients but does not increase BMD, though it may well be combined with anti-osteoporosis drugs if needed.

Patients with chronic hypoparathyroidism (HypoPT) do not have a significantly increased risk of major osteoporotic fractures in large registry studies. The Revised European Society of Endocrinology Clinical Practice Guideline for the treatment of HypoPT suggests assessing fracture risk as recommended for the general population. Pharmacological anti-osteoporosis treatment in HypoPT should also be performed by adhering to general population guidelines, but considering the potential risk of hypocalcemia with antiresorptive treatments in these patients.

PCC6.7 - Session 3. Primary hyperparathyroidism—defining optimal management—current and future medical options

Abstract Unavailable

Abstract citation ID: lvag096.072

PCC6.8 - Session 3. Primary hyperparathyroidism—defining optimal management—debate—parathyroidectomy should be performed in cases of mild PHPT—for the motion

Jens Bollerslev

Department of Endocrinology, Morbid Obesity and Preventive Medicine, Oslo University Hospital, Oslo, Norway

Primary hyperparathyroidism (PHPT) is a prevalent disease especially in peri- and postmenopausal women,[1,2] where most patients are asymptomatic and diagnosed based on biochemical work-up for various, non-calcium related reasons. Nevertheless, these patients do present subtle metabolic abnormalities that might be related to the increased PTH rather than the slightly elevated calcium level.[3-5]

A series of international workshops during the last three and a half decades have discussed the management of asymptomatic PHPT, with only modest changes in indications for parathyroidectomy (PTX), the only curative treatment.[6,7] In asymptomatic PHPT patients with organ manifestations there is an indication for PTX, but these manifestations are purely defined,[5] and thereby a matter of discussion.[8]

Based on clinical markers on morbidity, recent data indicate that it seems safe to observe truly asymptomatic PHPT patients without organ manifestations for at least a decade. These data include kidney function, all fractures and overall mortality.[9-11] However, whereas bone turnover normalizes in PHPT by PTX with a subsequent normalization of BMD, long-term observation without intervention is followed by a state of high bone turn-over and a continuous loss of bone mass, including in the axial skeleton.[10] These data are of concern for bone health during long-term observation without intervention in asymptomatic PHPT.

Most patients do have PHPT due to a single, benign parathyroid adenoma accessible for cure by PTX.[3] PTX of a single adenoma has a very high cure rate (>98%) in specialized centers, with a low recurrence rate (about 1% in a ten-year perspective).[12]

As the population grow older with a healthier and more active elderly population, a more pro-surgery approach for asymptomatic PHPT should be considered and discussed,[1-15] including cost-effective/benefit analyses.[8]

References

1. Lundgren E, Rastad J, Thrufjell E, Akerström G, Ljunghall S. Population-based screening for primary hyperparathyroidism with serum calcium and parathyroid hormone values in menopausal women. *Surgery*. 1997;121(3):287-294. https://doi.org/10.1016/S0039-6060(97)90357-3
2. Siilin H, Rastad J, Ljunggren O, Lundgren E. Disturbances of calcium homeostasis consistent with mild primary hyperparathyroidism in premenopausal women and associated morbidity. *J Clin Endocrinol Metab*. 2008;93(1):47-53. https://doi.org/10.1210/jc.2007-0600
3. Cardoso LM, Rolighed L, Amrein K, et al. Advances in the clinical management of Parathyroid disorders: report from the 2024 workshop by the ESE Educational Program on Parathyroid disorders. *Eur J Endocrinol*. 2025;193:R65-R88. https://doi.org/10.1093/ejendo/lvaf204
4. Bollerslev J. The important players in primary hyperparathyroidism. *Clin Endocrinol (Oxf)*. 2013;79(6):774-775. https://doi.org/10.1111/cen.12291
5. Bollerslev J, Marcocci C, Sosa M, Nordenström J, Bouillon R, Mosekilde L. Current evidence for recommendation of surgery, medical treatment and vitamin D repletion in mild

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

primary hyperparathyroidism. *Eur J Endocrinol*. 2011;165(6):851-864. https://doi.org/10.1530/EJE-11-0589
6. NIH Conference. Diagnosis and management of asymptomatic primary hyperparathyroidism: consensus development conference statement. *Ann Intern Med*. 1991;114(7):593-597. https://doi.org/10.7326/0003-4819-114-7-593
7. Bilezikian JP, Khan AA, Silverberg SJ, et al. Evaluation and management of primary hyperparathyroidism: summary statement and guidelines from the fifth international workshop. *J Bone Miner Res*. 2022;37(11):2293-2314. https://doi.org/10.1002/jbmr.4677
8. Bollerslev J, Cetani F, Gittoes N, Rolighed L. Individualized management of primary hyperparathyroidism. *J Intern Med*. 2026;299:650-669. https://doi.org/10.1111/joim.70089
9. Heck A, Pretorius M, Lundstam K, et al. No effect of surgery on kidney and cardiovascular risk factors in mild primary hyperparathyroidism: secondary analyses from a 10-year randomized controlled trial. *Eur J Endocrinol*. 2024;191(3):354-360. https://doi.org/10.1093/ejendo/lvae109
10. Lundstam K, Pretorius M, Bollerslev J, et al. Positive effect of parathyroidectomy compared to observation on BMD in a randomized controlled trial of mild Primary Hyperparathyroidism. *J Bone Miner Res*. 2023;38(3):372-380. https://doi.org/10.1002/jbmr.4763
11. Pretorius M, Lundstam K, Heck A, et al. Mortality and morbidity in mild primary Hyperparathyroidism: results from a 10-year prospective randomized controlled trial of parathyroidectomy versus observation. *Ann Intern Med*. 2022;175(6):812-819. https://doi.org/10.7326/M21-4416
12. Zaman M, Raveendran L, Senay A, Sayles H, Acharya R, Dhir M. Long-term recurrence rates after surgery in primary hyperparathyroidism. *J Clin Endocrinol Metab*. 2023;108(11):3022-3030. https://doi.org/10.1210/clinem/dgad316
13. Hassan-Smith ZK, Criseno S, Gittoes NJL. Mild primary hyperparathyroidism-to treat or not to treat? *Br Med Bull*. 2019;129(1):53-67. https://doi.org/10.1093/bmb/ldy042
14. Milat F, Ramchand SK, Herath M, et al. Primary hyperparathyroidism in adults-(part I) assessment and medical management: Position statement of the Endocrine Society of Australia, the Australian & New Zealand endocrine surgeons, and the Australian & New Zealand Bone and Mineral Society. *Clin Endocrinol (Oxf)*. 2024;100(1):3-18. https://doi.org/10.1111/cen.14659
15. Zhu CY, Nguyen DT, Yeh MW. Who benefits from treatment of primary hyperparathyroidism? *Surg Clin North Am*. 2019;99(4):667-679. https://doi.org/10.1016/j.suc.2019.04.007

PCC6.9 - Session 3. Primary hyperparathyroidism—defining optimal management—debate—parathyroidectomy should be performed in cases of mild PHPT -against the motion

Abstract Unavailable

PCC7.1 - Novelties in DM treatment—immunotherapy as new type of treatment for type 1 diabetes

Abstract Unavailable

PCC7.2 - Novelties in DM treatment—monitoring blood glucose: new options and what can we learn from the experience in diabetes?

Abstract Unavailable

Nurse Sessions

N1.1 - Environmental chemical exposures and female fertility

Abstract Unavailable

Abstract citation ID: lvag096.073

N1.2 - Immunotherapy induced endocrinopathies

Helen Turner
Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford University Hospitals NHS Trust, Oxford, United Kingdom

Immune checkpoint inhibitors are a new group of monoclonal antibodies against checkpoints in normal T Lymphocyte activation enabling immune system activation in order to target cancer cells. They have transformed the management of an increasing spectrum of malignancies. However immune related adverse effects are common, and endocrine dysfunction is frequently observed.

Guidelines exist to help guide clinical care, and the monitoring and management of the endocrinopathy seen with checkpoint inhibitors involves a partnership with Oncology. In the 15 years since first used, there has been an increase in patients needing specialist investigation, management, follow-up and advice/support in Endocrine Departments.

Patients may have pre-existing endocrine problems, or receive glucocorticoid treatment for other immune related inflammatory adverse effects and need steroid safety advice, or may have an incidentally detected abnormality detected in an endocrine organ.

The endocrine specialist nurse is integral to all these aspects and collaboration with oncology is essential for optimal patient outcomes.

N2.1 - Optimizing melatonin: from sleep physiology to clinical chronotherapy

Abstract Unavailable

N2.2 - Eat: nutrition and hormone secretion

Abstract Unavailable

N2.3 - Sport: hormones, friend and foe

Abstract Unavailable

N3.1 - InvolveMe: a digital communication tool for post-surgery pituitary patient follow-up

Abstract Unavailable

N3.2 - The use of CGM's in non-diabetic care

Abstract Unavailable

N3.3 - Technological alternatives in adrenal insufficiency management: what's here, what's coming

Abstract Unavailable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

N3.4 - Project: a home care educational program for patients with acromegaly supports people with complex needs

Abstract Unavailable

How Do I... Sessions

Abstract citation ID: lvag096.074

H1.1 - How do I manage thyroid emergencies (thyrotoxic crisis and myxedema coma)

Corin Badiu

Thyroid emergencies—thyrotoxic crisis (thyroid storm) and myxedema coma—are life-threatening conditions requiring immediate admission to an Intensive Care Unit (ICU). Both conditions are often triggered by precipitating events such as infection, surgery, or trauma which should be promptly treated in a multi-disciplinary approach.

1. Management of Thyrotoxic Crisis (Thyroid Storm)

Management follows a multimodality approach to block the production, release, and peripheral effects of thyroid hormones. Clinical diagnosis is often supported by the Burch-Wartofsky Point Scale (BWPS), where a score above 45 is highly suggestive of storm. When treating thyroid storm, we should consider the five "Bs":

1. Beta-blocker
2. Block synthesis (ie, antithyroid drugs);
3. Block release (ie, iodine);
4. Block T4 into T3 conversion (ie, high-dose propylthiouracil [PTU], propranolol, corticosteroid);
5. Block enterohepatic circulation (ie, cholestyramine)

Several drugs are critical in intervention:

Beta-Blockers: Administer immediately to control heart rate and reduce adrenergic symptoms. Propranolol: Used to manage symptoms. It is preferred because it also helps block the peripheral conversion of T4 to T3. Esmolol: IV infusion may be used for rapid titration in the ICU. Take care to avoid vascular collapse.

Block Synthesis (*Thionamides*): Administer agents such as Propylthiouracil (PTU) or Methimazole to stop new hormone production. PTU is often preferred initially because it also inhibits the peripheral conversion of T4 to T3. Administer thionamides every 4-6 hours, due to rapid metabolism of these drugs during thyroid storm, orally, rectally or via a nasogastric (NG) tube in the unresponsive patient with a loading PTU dose of 600 mg followed by doses of 200-250 mg every 6 h.

Block Release (*Inorganic Iodine*): Administer Lugol's solution or SSKI to block hormone release. Critical: Wait at least one hour after the first thionamide dose to prevent providing "fuel" for further hormone synthesis.

Block T4 into T3 conversion—*Glucocorticoids*: Use Hydrocortisone to inhibit T4 to T3 conversion and treat potential relative adrenal insufficiency.

Block enterohepatic circulation (cholestyramine) 4 g orally two to four times each day.

Supportive Care: All actions are performed in ICU setting, ensuring adequate rehydration, repletion of electrolytes, treatment of comorbid disease such as infection until stabilization. Use cooling blankets and acetaminophen for fever. Avoid salicylates (Aspirin), as they can displace thyroid hormones from binding proteins and worsen the crisis. Plasmapheresis is a second-line "rescue" therapy used for patients with thyroid storm who are refractory to standard medical management or have contraindications to first-line. Refractory cases are defined as failure to improve within 24-48 hours of starting standard multidrug therapy.

2. Management of Myxedema Coma

Myxedema coma represents the most severe and life-threatening manifestation of hypothyroidism, characterized by multiorgan dysfunction. It is a medical emergency that requires immediate admission to an ICU. Clinical diagnosis is suspected on Popevenciuc score evaluating multiorgan dysfunction across six clinical and metabolic domains: thermoregulatory, central nervous system, cardiovascular, gastrointestinal, metabolic disturbances and precipitating event. A score above 60 is suggestive of myxedema coma.

Treatment must begin as soon as the diagnosis is suspected, often before laboratory confirmation, due to high mortality rates (30%-60%).

1. Glucocorticoids: Administer Hydrocortisone IV (100 mg iv) every 8 hours to address potential adrenal insufficiency before thyroid hormone replacement to avoid triggering an adrenal crisis. Thyroid hormones increase the metabolism of cortisol. If the patient has underlying adrenal insufficiency (common in autoimmune or pituitary causes), starting thyroid treatment alone can trigger a fatal adrenal crisis.

2. Thyroid Hormone Replacement: T4 (Levothyroxine): Administer via IV loading dose, often 200-400 µg, followed by a daily maintenance dose. Since the gut is often edematous and absorption is poor, medications must be given IV. T3 (Liothyronine) may be added for more rapid action, administered via IV initially, then at intervals, taking care about cardiovascular action. Monitor for arrhythmias or myocardial ischemia, especially in elderly patients or those with known heart disease.

3. Supportive care and monitoring in ICU setting: frequent checking of mental status, body temperature, cardiovascular status, and electrolytes are mandatory. The following topics should be considered:

Airway: Anticipate the need for mechanical ventilation for respiratory failure or airway compromise.

Rewarming: Use passive measures like warming blankets; avoid aggressive active rewarming to prevent vasodilation and cardiovascular collapse.

Fluids: Treat hyponatremia with water restriction; use hypertonic saline only if levels are extremely low or seizures occur.

In conclusion, thyroid emergencies, despite rare, requires a multidisciplinary approach, involving prompt admission into ICU and treatment of precipitating factors. Limited access to specific drugs (PTU, Colestiramine, IV thyroxine or T3) in some countries might pose problems in the prompt management of these disorders.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.075

H1.2 - How do I manage differential diagnosis of hypoglycemia

Emanuel Christ
Novo Nordisk Pharma Switzerland, Basel, Switzerland

Plasma glucose concentrations depend on glucose appearance rate, ie, a combination of exogenous carbohydrate intake in the postabsorptive and gluconeogenesis and glycogenolysis in the fasting state and glucose disappearance rate ie, uptake of glucose in the target tissues. The main organs for gluconeogenesis and glycogen storage are the liver and the kidney. The main regulatory hormones to keep the glucose concentration within normal range are insulin and its counterregulatory hormones such as glucagon, epinephrine, cortisol and growth hormone.

If hypoglycemia is documented the management of differential diagnosis follows the pathophysiology. In an ill or medicated patient, hypoglycemia is only one of the symptoms in a clinical context and the etiology of hypoglycemia is straightforward, ie, known diabetes on insulin or insulin secretagogues, critical illness including severe kidney or liver failure or counterregulatory hormone deficiencies. The very rare etiology of hypoglycemia in the context of a non-islet cell tumor (often neoplasia of mesenchymal origin with a high tumor burden and secretion of IGF-2) is also part of the differential diagnosis.

More challenging is the seemingly well individual with an autonomous insulin secretion, also called endogenous hyperinsulinemic hypoglycemia (EHH). Clinically these patients present with the classical Whipple's triad and a panoply of mainly neurological symptoms while the symptoms of the sympathetic nervous system are often less pronounced due to hypoglycemia unawareness. Weight gain, however, is often recorded. Hypoglycemia may occur postprandially (after postgastric bypass hypoglycemia or the insulin autoimmune hypoglycemia) or fasting (benign and malignant insulinoma, non-insulinoma-pancreatogenous-hypoglycemia, factitious).

The focus of this talk will include investigations of EHH (biochemical proof of EHH and localization of insulinoma using conventional and molecular imaging). New developments in this area are presented.

Abstract citation ID: lvag096.076

H1.3 - How do I manage mild autonomous cortisol secretion (MACS)

Alessandro Prete
Department of Metabolism and Systems Science, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom

Mild autonomous cortisol secretion (MACS) is no longer a niche endocrinology problem. As adrenal incidentalomas are detected with increasing frequency, clinicians are being asked ever more often to decide who should be tested, how far investigation should go, and which patients may benefit from intervention. Yet MACS rarely presents in black and white: it lies on a clinical spectrum, overlaps with common cardiometabolic disease, and raises difficult questions around surgery, conservative care, postoperative adrenal insufficiency, and long-term follow-up.

This talk will provide a practical approach to the management of MACS. It will cover who should and should not be investigated, how to interpret diagnostic tests, and how to assess cardiometabolic risk in a structured way. It will also address the decisions clinicians find hardest: when to recommend adrenalectomy, how to approach bilateral disease, how to manage postoperative glucocorticoid replacement and recovery of the hypothalamic-pituitary-adrenal axis, and when patients can be safely followed in primary care.

Oral Communications

Abstract citation ID: lvag096.077

OC1.1 - ECE_3815 - Pregnancy outcomes by thyroid autoantibody status in euthyroid and subclinical hypothyroid women- insights from a nationwide cohort study

Uri Yoel[1,2], Merav Fraenkel[1,2] and Tamar Eshkoli[1,2]
[1]*Endocrinology, Soroka University Medical Center, Beer Sheva, Israel;* [2]*Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel*

Background: Although an increased risk of miscarriage has been well documented in women with subclinical hypothyroidism and thyroid autoantibodies, the independent effect of thyroid autoimmunity on other obstetric outcomes, particularly among euthyroid and subclinical hypothyroid women, remains unclear.

Objective: To evaluate pregnancy outcomes and complications, excluding miscarriage, according to thyroid autoantibody status among euthyroid and subclinical hypothyroid women.

Methods: All live-birth pregnancies (2013-2022) among Clalit Health Services-insured women were screened. Pregnancies in women aged ≥18 years with available thyrotropin (TSH) and thyroid autoantibody (anti–thyroid peroxidase and/or anti–thyroglobulin) measurements were included; women with a history of hypothyroidism or levothyroxine treatment were excluded. Pregnancies were stratified by thyroid function and autoantibody status into euthyroid (mean pregnancy TSH <4 mIU/L) or subclinical hypothyroid (TSH ≥4 mIU/L), with or without thyroid autoantibodies (one or both). To address confounding, antibody-positive and antibody-negative groups were balanced using inverse probability weighting (IPW) based on propensity scores estimated from maternal age, ethnicity, socioeconomic status, use of in vitro fertilization, history of recurrent pregnancy loss, and smoking. Analyses included univariate comparisons of obstetric outcomes and weighted quasi-Poisson regression to estimate adjusted incidence rate ratios for composite pregnancy complications.
Results: Of 338 352 screened live-birth pregnancies, 25 484 were included in the final analysis. In univariate analyses, most maternal and neonatal outcomes were clinically comparable across groups. Although statistically significant differences were observed for selected outcomes such as gestational diabetes, labor induction, assisted delivery, premature rupture of membranes, and certain placental or amniotic fluid abnormalities, these differences were inconsistent across comparisons and did not reflect clinically meaningful increases in severe outcomes. In weighted Poisson regression analyses, thyroid antibody positivity among euthyroid women was associated with a slightly lower rate of composite pregnancy complications compared with antibody-negative euthyroid women (IRR 0.92, 95% CI 0.89-0.96). No association between thyroid antibody status and composite complications was observed among women with subclinical

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hypothyroidism (IRR 1.01, 95% CI 0.91-1.12). Importantly, no significant difference was identified between euthyroid antibody-negative women and subclinical hypothyroid antibody-positive women (IRR 0.96, 95% CI 0.91-1.01).

Conclusions: Thyroid antibody positivity was not associated with clinically meaningful increases in pregnancy complications among euthyroid or subclinical hypothyroid women. These findings suggest that, in the absence of overt hypothyroidism, thyroid autoimmunity alone may not warrant intensified obstetric monitoring.

Abstract citation ID: lvag096.078

OC1.2 - ECE_1905 - Efficacy of radioactive iodine of 15 mCi in treatment in pediatric patients with Graves' disease: a prospective multicenter study

Chenghang Liu and Bin Liu
Department of Nuclear Medicine, West China Hospital, Sichuan University, Chengdu, China

Objective: Currently, there is a lack of consensus on activity of radioactive iodine (RAI) to be administered for pediatric patients with Graves' disease. This prospective multicenter study aimed to investigate that the efficacy of 15 mCi RAI in treatment of pediatric patients with Graves' disease, and to determine risk factors influencing treatment failure.

Methods: From October 2021 to March 2025, pediatric patients (aged ≤21 years) with Graves' disease who had been prepared for RAI therapy were prospectively recruited at 4 tertiary hospitals in Southwest China. All enrolled patients were given 15 mCi RAI. Remission and failure rates were evaluated at 6 months post-RAI. Statistical analysis was performed using logistic regression.

Results: A total of 102 patients were enrolled in the study (mean [range] age, 18 [12-21] years; 83 females [81%]). The cure rate of 15 mCi RAI treatment was 79.4%, including 75 patients (73.5%) with hypothyroidism, 6 (5.9%) with euthyroidism. Multivariable logistic regression analysis demonstrated that disease duration, thyroid mass, and TRAb titers were significantly associated with the therapeutic efficacy. The disease duration of >8 months (OR = 11.30, 95% CI = 2.72-46.93), thyroid mass of >43.5 g (OR = 4.30, 95% CI = 1.17-15.72), and TRAb titers of >8.5-fold the upper normal limits (OR = 7.38, 95% CI = 1.73-31.50) were independent risk factors for therapeutic failure.

Conclusions: For the treatment of pediatric patients with Graves' disease, the use of a fixed-activity of 15 mCi RAI has a high success rate without additional measurements or calculations. The adoption of a standard dose of 15 mCi RAI may help implementing a streamlined and uniform RAI therapy process for pediatric patients with Graves' disease.

Abstract citation ID: lvag096.079

OC1.3 - ECE_3490 - Teprotumumab efficacy in long- and short-duration thyroid eye disease: post hoc analysis of four trials

Prem Subramanian[1], George Kahaly[2], Sara Wester[3], Zhenxun Wang[4], Tomoko Hayashida[4], Juan Ayala-Haedo[4] and Terry Smith[5]

[1]*Sue Anschutz-Rodgers University of Colorado Eye Center, Aurora, United States;* [2]*Department of Medicine I, Johannes Gutenberg University (JGU) Medical Center, Mainz, Germany;* [3]*Bascom Palmer Eye Institute, University of Miami, Miami, United States;* [4]*Amgen Inc., Thousand Oaks, United States;* [5]*Department of Ophthalmology and Visual Sciences, W. K. Kellogg Eye Center, and Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, United States*

Teprotumumab, an insulin-like growth factor-1 receptor inhibitor, has demonstrated efficacy treating signs & symptoms of thyroid eye disease (TED) in patients with high or low clinical activity score (CAS) and short & long duration TED. We evaluate pooled efficacy data of teprotumumab in patients with TED <1-year & ≥1-year disease duration, independent of disease activity as measured by CAS.

Data from patients with moderate-severe TED were pooled from teprotumumab clinical trials. Patients were to receive 8 infusions of teprotumumab. Observed proptosis response (≥2 mm-improvement), CAS response (≥2-point improvement in patients w/baseline CAS ≥3), overall response (proptosis + CAS response in patients with baseline CAS ≥3), diplopia response (Gorman scale ≥1-point improvement in patients with baseline score >0), & TED-specific Graves' Ophthalmopathy Quality of Life (GO-QoL, 0-100 scale) score improvement are reported among teprotumumab-treated patients with TED diagnosis <1 or ≥1 year.

Teprotumumab-treated patients from clinical trials were pooled: Phase 2 (NCT01868997) & OPTIC (NCT03298867), OPTIC open-label extension (OPTIC-X[NCT03461211]), OPTIC-J (jRCT2031210453), OPTIC-J open-label extension, Phase 4 (NCT04583735), and Phase 4 open-label extension. For the <1-year TED duration group ($n = 144$), 43 Phase 2, 41 OPTIC, 16 OPTIC-X, 27 OPTIC-J, and 17 OPTIC-J open-label patients were included. For the ≥1-year group ($n = 81$), 42 Phase 4, 12 Phase 4 open-label, 21 OPTIC-X and 6 OPTIC-J open-label patients were included. TED duration was mean (SD) of 6.5 (2.9) months for the <1-year TED duration group($n = 144$) and 46.7 (29.5) months and for the ≥1-year group ($n = 81$); 88% (127/144) and 84% (68/81) completed treatment, respectively. At week 24, observed proptosis response was 82% (113/137) for shorter TED duration and 72% (54/75) for longer duration; change from baseline was mean (SD) −3.0 (1.7) mm ($n = 137$) and -2.6 (1.6) mm ($n = 75$), respectively. The observed overall response rate at week 24 was 80% (98/123) and 71% (12/17), observed diplopia response rate was 66% (69/104) and 57% (17/30), and complete resolution of diplopia was observed in 50% (52/104) and 47% (14/30), respectively. Additionally, clinically meaningful improvements in overall GO-QoL scores were observed in both groups as well as for the appearance and visual function subscales.

Although patients with earlier treatment had higher response rates overall, those treated with teprotumumab had clinically meaningful responses regardless of time since TED diagnosis or level of disease activity across all endpoints.

Abstract citation ID: lvag096.080

OC1.4 - ECE_1840 - IL-17$^+$ γδ T cells mediate thyroid hormone excess–induced metabolic dysfunction

Hyon-Seung Yi[1,2]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Daejeon, South Korea; [2]Internal Medicine, Endocrinology and Metabolism, Chungnam National University, Daejeon, South Korea

Background and Research Aim: Thyrotoxicosis induces systemic catabolic effects such as muscle wasting and bone loss, traditionally attributed to direct actions of thyroid hormones (TH) on target tissues. However, the immune mechanisms linking TH excess to metabolic pathology remain unclear. This study aims to determine whether γδ T cells mediate TH-induced musculoskeletal dysfunction and to elucidate the underlying immunometabolic mechanisms.

Methods: To address this question, we employed a translational approach combining patient samples and experimental models. Immune and metabolic parameters were profiled in newly diagnosed Graves' disease patients before and after 12 weeks of methimazole treatment. In parallel, a murine model of TH excess was established via intraperitoneal T4 injection. γδ T cells were analyzed using flow cytometry, single-cell RNA sequencing (scRNA-seq), and paired γδ TCR sequencing. Functional validation was performed using TCRδ knockout (KO) mice, IL-17A neutralization, adoptive γδ T cell transfer, and in vivo stable isotope tracer infusion to quantify lipid turnover and oxidative metabolism.

Results: TH excess promoted the expansion of Vδ1 γδ T cells with heightened IL-17A expression in both humans and mice. In patients, normalization of thyroid function led to a reduction in IL-17A–producing γδ T cells, coinciding with improved muscle strength and bone density. scRNA-seq and TCR-seq revealed selective clonal enrichment of IL-17A–producing Vδ1 subsets under TH excess, supported by enhanced chromatin accessibility at IL-17A loci. In mice, TH-induced muscle weakness, fiber-type switching, and bone loss were all mitigated in TCRδ KO mice or with IL-17A antibody treatment. Metabolically, TH excess increased adipose lipolysis and suppressed muscle fatty acid oxidation, leading to accumulation of lipid intermediates—changes that were absent in TCRδ KO mice. TH also enhanced glycolysis and acetyl-CoA production in γδ T cells, promoting histone acetylation and IL-17A expression through epigenetic remodeling. Adoptive transfer of TH-activated γδ T cells partially recapitulated the muscle and bone phenotypes, while CD1d-deficient mice retained full γδ T cell responses, suggesting a CD1d-independent mechanism of activation.

Conclusions: Our findings establish Vδ1 γδ T cells as essential immunometabolic mediators of thyrotoxicosis. TH excess drives IL-17A expression through metabolic–epigenetic reprogramming, redefining thyrotoxicosis as an immune-driven endocrine disorder with implications for biomarker development and therapeutic targeting.

Abstract citation ID: lvag096.081

OC1.5 - ECE_3515 - Thyroid nodules in pediatric patients: which is the performance of the ultrasound risk stratification systems in identifying malignancy?

Carla Gambale[1], Giulia Lisi[1], Elisa Minaldi[1], Alessandro Prete[1], Eleonora Molinaro[1], Teresa Rago[1], Maria Scutari[1], Liborio Torregrossa[2], Rossella Elisei[1] and Antonio Matrone[1]

[1]Unit of Endocrinology, Department of Clinical and Experimental Medicine, University Hospital of Pisa, Pisa, Italy; [2]Molecular Pathology and Critical Area, Department of Surgical, Medical, University Hospital of Pisa, Pisa, Italy

Objectives: Thyroid nodules are quite rare in pediatric (≤18 years) patients; however, several studies reported a higher malignancy rate in this population. The aim of this study was to evaluate the ultrasound (US) characteristics of thyroid nodules in pediatric patients and to assess the performance of the main US risk stratification systems (RSS) in identifying malignant nodules. In addition, we investigated the correlation between US RSS categories and cytological findings.

Methods: We retrospectively analyzed US features and cytology results of a consecutive series of thyroid nodules diagnosed for the first time in pediatric patients at our department between 2016 and 2022. Nodules were classified according to EU-TIRADS, 2015 ATA, and AACE/ACE-AME systems, while cytology was reported according to the Italian Consensus classification.

Results: The study included 271 nodules from 221 patients. Most patients were females (74.2%), with a median age at cytological evaluation of 16 years (IQR 14-17). The median nodule size was 1.9 cm (IQR 1.4-2.9). Cytological diagnoses were TIR5 in 9.3%, TIR4 in 4.0%, TIR3b in 8.8%, TIR3a in 19.5%, TIR2 in 32.7%, TIR1C in 13.6%, and TIR1 in 12.1% of nodules. Ultrasound features were available for 216 nodules (79.7%). The thyroid was multinodular in 34.3% of cases. Most nodules were solid (74.1%), isoechoic (49.1%), wider than tall (80.6%), had well-defined margins (82.9%), and without calcifications (77.8%). Approximately one-third of nodules were classified as highly suspicious for malignancy according to all three RSS (EU-TIRADS 5: 35.2%; 2015 ATA high suspicion: 30.6%; AACE/ACE-AME high risk: 35.2%). However, in high-risk and low/intermediate-risk nodules, according to ultrasound features, only about 25% and 10% of cases were suspicious or malignant at citology (TIR4-TIR5), respectively.

Conclusions: Our findings indicate that the US risk stratification systems used at present are clinically poorly reliable in predicting malignancy in pediatric nodules and it would be desirable to have US dedicated risk stratification systems for children and adolescents.

Abstract citation ID: lvag096.082

OC1.6 - ECE_1657 - Percentage of mutated neoplastic cells predicts the risk of persistent/recurrent disease in a cohort of patients with BRAF-mutated papillary thyroid carcinoma

Simone Colombero[1,2], Ida Sicilia[1,2], Giacomo Credi[1,2], Giampiero Castellana[1,2], Anna Piazza[1,2], Dario De Biase[3,4], Arber Golemi[5], Elena Tabacchi[5], Elisa Lodi Rizzini[6], Thais Maloberti[3], Stefano Chillotti[7], Stefania Damiani[7], Giovanni Tallini[3,8], Valentina Vicennati[1,2], Uberto Pagotto[1,2] and Andrea Repaci[2]

[1]Department of Clinical and Medical Sciences (DIMEC), Alma Mater Studiorum-University of Bologna, Bologna, Italy; [2]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [3]Solid Tumor Molecular Pathology Laboratory, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [4]Department of Pharmacy and Biotechnology (FaBit), Alma Mater Studiorum-University of Bologna, Bologna, Italy; [5]Nuclear Medicine Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [6]Radiation Oncology, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [7]Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [8]Department of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Clinical and Surgical Sciences, Alma Mater Studiorum-University of Bologna, Bologna, Italy

Background: The BRAFV600E mutation is a pivotal oncogenic driver in Papillary Thyroid Carcinoma (PTC). While Variant Allele Frequency (VAF) is commonly used to quantify mutational burden, it is significantly influenced by the proportion of non-neoplastic cells within the sample, potentially underestimating the biological aggressiveness of the tumor.

Objectives: We evaluated whether the estimated percentage of mutated neoplastic cells (MNC)—calculated by correcting the VAF for sample tumor cellularity—provides superior predictive capacity compared to isolated VAF in defining the risk of recurrent or persistent disease (RPD).

Methods: We performed custom multigene NGS panel analysis on cytological or histological thyroid samples of 253 consecutive patients who underwent thyroid surgery for BRAFV600E PTC. We excluded patients with multiple coexisting mutations. For each sample, VAF was determined via sequencing, and the percentage of MNC was derived using a mathematical algorithm. Predictive performance for both variables was evaluated using ROC curves, Kaplan-Meier analysis, and a multivariate Cox model.

Results: The cohort ($n = 253$) showed a mean VAF of 21.4% and a median MNC percentage of 89.4% (IQR: 60.00-100.00%). Over a mean follow-up of 44.6 months, RPD occurred in 50 patients (19.8%). Association studies showed no significant differences in VAF between the RPD and disease-free groups ($P = .229$). Conversely, the percentage of MNC was significantly higher in RPD patients (median 100.0% vs 85.7%, $P = .013$). Univariate analysis revealed significant differences in the median MNC percentage according to tumor size <2 cm vs ≥2 cm (85.3% vs 97.5%, $P = .017$), minimal extrathyroidal extension (82.5% vs 92.9%, $P = .023$), and lymph node involvement <5 vs ≥5 (86.2% vs 98.0%, $P = .031$). ROC analysis confirmed VAF's ineffectiveness as a predictor of RPD (AUC 0.529; $P = .543$). In contrast, the MNC percentage demonstrated significant discriminative power (AUC 0.610; $P = .010$), allowing the identification of an optimal prognostic cut-off of 95.7%. Kaplan-Meier curves showed significantly worse progression-free survival for patients with MNC percentage ≥95.7% (Log Rank $P = .007$; median survival 86 months). Finally, multivariate Cox regression confirmed that a MNC percentage ≥95.7% is a strong independent predictor of recurrence (HR 3.88; 95% CI: 1.71-8.81; $P = .001$) together with male sex and higher stimulated thyroglobulin levels at radioiodine treatment.

Conclusions: Our findings suggest that the percentage of MNC is a more reliable prognostic biomarker than simple VAF. Achieving mutational quasi-homogeneity (≥95.7%) identifies a high-risk subgroup, emphasizing the importance of correcting molecular data for cellularity to achieve precise risk stratification.

Abstract citation ID: lvag096.083

OC2.1 - ECE_1752 - HMGA1 as a molecular link between insulin resistance and tau-driven neurodegeneration: evidence from human omics, genetics, and preclinical models

Maria Mirabelli[1], Francesco Saverio Brunetti[1], Eusebio Chiefari[1], Daniela Foti[2] and Antonio Brunetti[1]

[1]*Department of Health Sciences, Magna Græcia University, Catanzaro, Italy;* [2]*Department of Experimental and Clinical Medicine, Magna Græcia University, Catanzaro, Italy*

Introduction: Insulin resistance (IR) contributes to neurodegeneration, but the mechanisms linking impaired insulin signaling to tau pathology are unclear. High mobility group A1 (HMGA1), a key regulator of insulin receptor (INSR) transcription, may connect metabolic dysfunction and tauopathy. We examined whether reduced HMGA1 function increases susceptibility to IR and tau-driven neurodegeneration, and investigated the underlying mechanisms.

Methods: We used a translational, multi-system approach, including analyses of human post-mortem brain transcriptomics from Alzheimer's disease (AD)-relevant regions; *in silico* identification of HMGA1 binding motifs in the *MAPT* regulatory regions; cellular studies in retinoic acid (RA)-differentiated SH-SY5Y neurons; *MAPT* promoter luciferase assays following HMGA1 manipulation or pharmacological disruption; a case-control genetic study of the loss-of-function *HMGA1* variant rs146052672 with cognitive and cerebrospinal fluid (CSF) biomarker assessments; and in vivo validation in *Hmga1*-null mice.

Results: Bulk RNA-seq of hippocampal tissue from individuals with dementia revealed a robust inverse correlation between HMGA1 and MAPT expression, confirmed across tau-expressing neurons and glia by single-nucleus transcriptomics. MAPT levels remained largely stable across AD stages, suggesting early transcriptional setting rather than late induction. Computational analyses identified conserved HMGA1 binding motifs within repressive regions of the human and mouse *MAPT* promoter. In RA-differentiated SH-SY5Y cells, neuronal maturation was accompanied by reduced intracellular HMGA1, increased tau expression, decreased INSR levels, and heightened oxidative stress, alongside progressive increases in extracellular total tau and p-tau181. Promoter assays demonstrated that HMGA1 represses *MAPT* promoter activity in a dose-dependent manner, an effect lost with HMGA1 silencing or disruption of HMGA1-DNA binding. Clinically, the rs146052672 variant was more frequent in AD cases than controls (17.6% vs 5.0%; $P<.05$) and independently associated with tauopathy. Variant carriers exhibited a higher prevalence of diabetes, greater IR consistent with reduced INSR availability, worse cognitive performance (MMSE 14.7 ± 4.6 vs 19.7 ± 4.1; $P < .05$), and elevated CSF tau and p-tau181. These findings were mirrored in *Hmga1*-null mice, including hyperglycemia, increased brain tau and p-tau, reduced Insr expression, and AD-like neuropathological and behavioral features.

Conclusions: HMGA1 is a key transcriptional regulator linking IR to tau-driven neurodegeneration. By bridging IR and tau pathology, HMGA1 emerges as a promising biomarker and a potential therapeutic target in neurodegenerative disease.

Abstract citation ID: lvag096.084

OC2.2 - ECE_3929 - JUV-161 restores glucose homeostasis and skeletal muscle function in Type 2 diabetic mouse model

Vengadeshprabhu Karuppagounder, Ritwik Datta, Hee Ju Kim, Ashil Koranne, Annie Yang, Sharon Louie, Kimberly Crutcher, Ted Yu, Danielle Yi, Zhihua Li, Thach Mai,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Banmeet Anand, Colin Hislop, Priya Handa, Hanadie Yousef and Jeremy O'connell
Juvena Therapeutics, Redwood city, United States

Background: Loss of skeletal muscle mass and strength is a frequent yet underappreciated complication of type 2 diabetes (T2D), contributing to impaired glucose disposal and progressive metabolic dysfunction. Most antidiabetic therapies primarily address glycemia without directly improving muscle health. JUV-161 is a novel biologic identified through a machine learning driven, multi-omics platform designed to discover regenerative factors from stem cell–derived secretomes. This study examined whether JUV-161 can simultaneously improve metabolic control and muscle function in a severe murine model of T2D, alone and in combination with semaglutide.

Methods: Nine-week-old male db/db mice were assigned to four treatment arms ($n = 12$-15/group): vehicle, JUV-161 (48 mg/kg), semaglutide (6 nmol/kg), or JUV-161 combined with semaglutide. All treatments were administered daily by subcutaneous injection for 21 days. Longitudinal assessments included body weight, body composition by EchoMRI, and fasting glucose. Insulin sensitivity and glucose handling were evaluated during the final treatment week, along with forelimb and all-limb grip strength and in vivo hindlimb muscle force. At study termination, hindlimb muscle weights and circulating metabolic biomarkers were analyzed.

Results: Treatment with JUV-161 led to a progressive reduction in fasting glucose that was further enhanced when combined with semaglutide. Measures of insulin sensitivity demonstrated superior glucose clearance in JUV-161 treated animals, with the largest improvement observed in the combination group. Consistent with these findings, long-term glycemic control, assessed by HbA1c, was improved relative to vehicle controls (8.3%), with reductions observed for JUV-161 (7.2%), semaglutide (7.4%), and the combination (6.3%). Beyond glycemic control, JUV-161 favorably modulated circulating markers associated with liver function and systemic metabolism, with broader effects observed following combination therapy. Markers of muscle injury and renal stress were reduced in JUV-161 treated mice, while improvements in lipid-associated markers were specific to combination treatment. Functionally, JUV-161 significantly increased grip strength and enhanced gastrocnemius contractile performance across stimulation frequencies. These functional gains were accompanied by preservation of lean mass and significant increases in tibialis anterior and gastrocnemius muscle weights.

Conclusions: JUV-161 confers dual metabolic and musculoskeletal benefits in a severe model of T2D, improving glycemic control while enhancing muscle mass and function. These findings highlight JUV-161 as a promising first-in-class biologic that addresses both metabolic dysfunction and diabetes-associated muscle decline, supporting its translational potential either alone or in combination with established antidiabetic therapies.

Abstract citation ID: lvag096.085

OC2.3 - ECE_1423 - Research on the role of PRMT6 in promoting proliferation of pancreatic β-Cells

Changliu Xu, Shuhui Liang, Fenghua Lai, Nan Chen, Haipeng Xiao, Yanbing Li and Xiaopei Cao
The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Objective: Protein arginine methyltransferase 6 (PRMT6) is mainly localized in the nucleus, where it regulates gene transcription and controls the cell cycle, growth, and proliferation. Previous studies have shown that PRMT6 expression is significantly higher in the pancreatic islets of leptin-deficient obese diabetic mice (ob/ob) compared to control mice. This study aims to investigate the impact of PRMT6 on the proliferation of pancreatic β-cells.

Methods: In vitro, PRMT6 overexpression and knockdown models were established in mouse β-cell lines (MIN6 and β-TC6). Palmitic acid treatment was used to simulate a lipotoxic environment. Cell cycle distribution was analyzed by flow cytometry, and cell growth and proliferation were assessed using CCK8 assays and EdU incorporation assays. In vivo, 20 male C57BL/6J mice were fed a high-fat diet for 24 weeks and injected with recombinant adeno-associated virus vectors carrying either PRMT6 (AAV-PRMT6) or a negative control. Weekly measurements of body weight and fasting blood glucose were taken, and glucose and insulin tolerance tests were performed after 6 weeks.

Results: PRMT6 overexpression promoted the transition of the MIN6/β-TC6 cell cycle from G0/G1 to G2/S and increased cell growth and proliferation, while PRMT6 knockdown had the opposite effects. Palmitic acid treatment reduced cell growth, and knockdown of PRMT6 worsened this reduction. Overexpression of PRMT6 partially alleviated the palmitic acid-induced decrease in proliferation. In vivo, AAV-PRMT6-treated mice showed no significant differences in body weight, fasting blood glucose, or insulin tolerance compared to control mice. However, the glucose insulin tolerance tests revealed a significantly lower area under the curve for glucose levels in the AAV-PRMT6 group.

Conclusions: PRMT6 promotes the proliferation of pancreatic β-cells and improves glucose tolerance in diabetic mice. This suggests that PRMT6 may play a potential role in the regulation of β-cell proliferation and glucose homeostasis, providing insights into potential therapeutic strategies for diabetes.

Abstract citation ID: lvag096.086

OC2.4 - ECE_1405 - SGLT-2 inhibitor-induced erythrocytosis increases risk of lower limb amputation in persons with type 2 diabetes—a nationwide cohort study

Aidar Gosmanov[1,2] and Darren Gemoets[1]
[1]*Stratton VA Medical Center, Albany, United States;* [2]*Department of Medicine, Division of Endocrinology, Albany Medical College, Albany, United States*

The evidence is controversial whether type 2 diabetes (T2D) therapy with SGLT-2i can increase risk of lower limb amputations (LLA). Recent large-scale studies have clearly demonstrated that SGLT-2i cause erythrocytosis which in turn can potentially increase blood viscosity. The aim of this investigation was to assess incidence of LLA in T2D patients treated with SGLT-2i in presence and absence of erythrocytosis. In this retrospective cohort study we studied US Veterans with T2D who had complete medical records data, baseline hematocrit (Hct) <52.0%

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

measured within 1 year before the start of study, adequate adherence with SGLT-2i, no testosterone prescription, and no history of erythrocytosis or prior LLA and received care between 3/2013-12/2023. Among 691104 patients (mostly males (94.5%) and Caucasians (Whites 70.2%/Blacks 19.4%) with mean age 65.7 yrs) we identified control (no record of SGLT-2i use) and new SGLT-2i users and followed hematocrit for 1 year to identify those who developed new erythrocytosis defined as hematocrit ≥52%. Primary endpoints were odds ratio (OR) of new diagnosis of LLA calculated by logistic regression model adjusted for case-mix. The SGLT-2i use for 1 year resulted in significant hemoglobin A1c reduction and hematocrit increase compared with the control group and was associated with about 6-fold ($P < .001$) increase in erythrocytosis risk after adjusting for baseline characteristics: 0.58% of control patients developed erythrocytosis compared with 3.66% in the SGLT-2i group. In the models adjusted for multiple baseline characteristics, new-onset erythrocytosis in control group was not while in the SGLT-2i group was associated with 2.16-fold ($P < .001$) higher odds of LLA. For the first time, we demonstrated that, in a large T2D cohort, a new diagnosis of erythrocytosis defined by hematocrit ≥52% was accompanied by increased incidence of LLA in SGLT-2i-treated patients but not in those who received other anti-hyperglycemic agents. While further studies needed to confirm these findings, we recommend closely monitoring hematocrit trends in people with T2D receiving SGLT-2i.

Abstract citation ID: lvag096.087

OC2.5 - ECE_1969 - Interleukin-6 signaling modulates glucagon-stimulated gluconeogenesis from amino acids in humans

Hanna Litscher[1], Lena-Marie Leikam[1], Peter Plomgaard[2], Gerrit van Hall[3] and Beckey Trinh[1]
[1]Basel, Switzerland; [2]Rigshospitalet, The Centre for Physical Activity Research, Copenhagen, Denmark; [3]Rigshospitalet, Clinical Metabolomics Core Facility, Copenhagen, Denmark

Background: Over the past 25 years, interleukin-6 (IL-6) has been recognized not only as a key regulator of immune function but also as a context-dependent mediator of energy allocation. We previously demonstrated that chronic blockade of IL-6 signaling increases circulating plasma amino acid concentrations in healthy humans. Glucagon is a major regulator of amino acid metabolism, and patients lacking glucagon secretion after total pancreatectomy similarly exhibit hyperaminoacidemia. We therefore hypothesized that IL-6 signaling facilitates glucagon-induced amino acid catabolism and gluconeogenesis.
Methods: In this randomized, double-blind, placebo-controlled trial, 26 healthy participants were randomized 1:1 to receive either the IL-6 receptor antagonist tocilizumab (8 mg/kg body weight) or normal saline (placebo). After three weeks, overnight-fasted participants underwent a pancreatic clamp using octreotide, insulin, and glucagon to sequentially mimic low- and high-glucagon states, while insulin was maintained at basal fasting levels. A subset of 15 participants received concomitant infusion of stable isotope tracers (L-[3-^{13}C]alanine and [6,6-$^{2}H_2$]glucose). Sequential blood samples were collected throughout the clamp. The primary endpoint was the difference between groups in the maximal glucagon-induced reduction in total plasma amino acids. Key secondary endpoints included rates of gluconeogenesis and the contribution of alanine to gluconeogenesis assessed by tracer kinetics.

Results: No significant treatment effect was observed for the maximal reduction in total plasma amino acids during high glucagon (placebo: 344.1 ± 142.1 μmol/L [14.5 ± 6.2%] vs tocilizumab: 433.8 ± 168.5 μmol/L [18.1 ± 8.0%]) or for total rates of gluconeogenesis across clamp phases (all $P \geq .724$). In contrast, for gluconeogenesis from alanine, a significant treatment × phase interaction was observed ($P = .021$), with rates being 1% lower at baseline and 20% lower during high-glucagon conditions in the tocilizumab group. Similarly, the proportional contribution of alanine to total gluconeogenesis showed a significant treatment × phase interaction ($P = .011$), with reductions of 6% at baseline and 24% during high glucagon compared with placebo. These findings indicate a phase-dependent modulation of alanine-derived gluconeogenesis following IL-6 receptor blockade.

Conclusions: IL-6 signaling appears to facilitate glucagon-stimulated gluconeogenesis from amino acids in humans, particularly under high-glucagon conditions. This identifies IL-6 as a modulator of glucagon–amino acid interplay in human metabolism.

Abstract citation ID: lvag096.088

OC2.6 - ECE_2853 - Uncovering hidden metabolic patterns in healthy post-menopausal women

Alicia Santamaría-Quiles, Jesús Roca-García, Angela Rubio Tenor and Ines Pineda-Torra
Seville, Spain

Cardiovascular diseases remain the leading cause of mortality for women worldwide. Menopause marks a critical endocrine transition; the cessation of ovarian function and a reversal of the estrogen-to-androgen ratio elicit a pro-inflammatory and atherogenic metabolic shift, driving a sharp increase in cardiovascular risk.

The aim of this study was to characterize the metabolic landscape associated with menopause. We investigated the disparities between pre- and post-menopausal women employing targeted Nuclear Magnetic Resonance (NMR)-based metabolomics. This approach was further coupled with machine learning algorithms to determine how inflammation modulates these lipid profiles in post-menopausal women, with the ultimate goal of defining subclinical patterns relevant for early preventive strategies.

We recruited a cohort of pre- ($n = 68$; age 18-45) and post-menopausal women ($n = 59$; age 55-68; time since menopause: 0-28 years). All participants were healthy with no history of cardiovascular disease. Women on hormone replacement therapy, with autoimmune disorders, or with a recent vaccination (<3 weeks) were excluded. Serum metabolomic analysis was performed targeting lipoproteins, glycoproteins, low-molecular-weight metabolites, and lipid profiles. Finally, machine learning models were trained to identify a metabolic signature predictive of an inflammatory-associated lipid profile in post-menopausal women.

Post-menopausal women exhibited metabolic dysregulation driven by elevated lipids, pro-atherogenic apolipoprotein B, and inflammatory glycoproteins. In contrast, amino acid and glucose profiles remained largely unaltered, confirming that menopause-related risk is primarily mediated by lipid-inflammatory pathways. Metabolic variance was strongly

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

influenced by GlycA, an NMR biomarker reflecting acute-phase protein glycosylation. Given that chronic low-grade inflammation is a key driver of atherosclerosis progression, and GlycA serves as a robust predictor of subclinical cardiovascular risk, we used this biomarker to stratify post-menopausal women into high and low inflammation subgroups. While clinical profiles between inflammatory groups were mostly comparable, the high-inflammation subgroup displayed significantly higher systolic blood pressure, linking subclinical inflammation to vascular strain. A logistic regression model yielded the best performance (AUC: 0.945) identifying alanine, triglycerides, linoleic acid, omega-3 fatty acids, DHA, and large VLDL particles as primary drivers. Subsequently, an AutoScore analysis defined a selective 3-metabolite diagnostic signature validated in an independent test set (AUC: 0.869).

Our findings reveal the inflammatory nature of the post-menopausal metabolic landscape. We demonstrate that even in healthy women, inflammation drives specific metabolic patterns associated with heightened cardiovascular risk. Upon external validation, the identified metabolic signature would represent a powerful tool for early risk stratification, facilitating precision medicine interventions at a preclinical stage.

Abstract citation ID: lvag096.089

OC3.1 - ECE_1630 - Copy number variations define distinct genetic profiles and predict recurrence risk in Cushing's disease

Alexander Paul[1], Mario Detomas[1], Sabine Herterich[2], Silke Appenzeller[3], Laura Ölsner[3], Panagiota Arampatzi[4], Tom Gräfenhan[4], Fabian Imdahl[4], Coras Roland[5], Jörg Flitsch[6], Jürgen Honegger[7], Romand Rotermund[6], Anna Riester[8], Michael Buchfelder[9], Timo Deutschbein[1,10], Matthias Dottermusch[11], Alice Ryba[6], Camelia Monoranu[12], Martin Fassnacht[1], David S. Tourigny[13] and Silviu Sbiera[1]
[1]Department of Internal Medicine I, Division of Endocrinology and Diabetes, University Hospital Würzburg, Würzburg, Germany; [2]Department of Internal Medicine I, Central Laboratory, University Hospital Würzburg, Würzburg, Germany; [3]Comprehensive Cancer Center Mainfranken, University of Würzburg, Würzburg, Germany; [4]Core Unit Systems Medicine, University of Würzburg, Würzburg, Germany; [5]Insitute of Neuropathology, University Hospital Erlangen, Erlangen, Germany; [6]Department of Neurosurgery, University Hospital Hamburg-Eppendorf, Hamburg, Germany; [7]Department of Neurosurgery, University Hospital Tübingen, Tübingen, Germany; [8]Department of Medicine IV, LMU Munich, Munich, Germany; [9]Department of Neurosurgery, University Hospital Erlangen, Erlangen, Germany; [10]Medicover Oldenburg MVZ, Oldenburg, Germany; [11]Department of Neuropathology, University Hospital Hamburg-Eppendorf, Hamburg, Germany; [12]Insitute of Pathology, University of Würzburg, Würzburg, Germany; [13]School of Mathematics, University of Birmingham, Edgbaston, United Kingdom

Cushing's disease (CD) is caused by adrenocorticotropic hormone (ACTH)-secreting pituitary tumors. Despite various treatment options, patients still suffer from high recurrence rates, stressing the need to find better prognostic biomarkers and develop improved treatments. First, however, a comprehensive understanding of CD tumor biology is needed. Recurrent genetic alterations have been identified as potential drivers of tumorigenesis in CD. However, their impact at the molecular and clinical levels remains largely unknown. Therefore, we aimed to investigate the impact of genetic alterations at the genomic, chromosomal and transcriptomic levels in patient samples and on clinical outcomes.

Copy number variation (CNV) profiles of 129 CD tumors were assessed using whole exome sequencing (WES) or shallow whole genome sequencing (sWGS) and verified using FISH analysis. Mutations were determined using WES/WGS and Sanger sequencing. Transcriptomic changes were investigated using single-nucleus RNA sequencing (snRNA-seq.).

We identified high chromosomal losses and gains in 47/129 tumors, while the rest were CNV-low tumors. We found that CNV patterns were not random, as losses and gains were largely mutually exclusive across tumors, leading to further subgrouping into CNV-loss and CNV-gain tumors.

When examining variants, *USP8* mutations were enriched in CNV-low tumors, whereas *TP53* mutations were exclusively found in CNV-loss tumors which also showed higher tumor mutational burden and microsatellite instability.

CNV-loss tumors were enriched for pathogenic mutations in chromosome organization pathways with high cellular frequencies, suggesting a potential explanation for CNVs. We studied tumors from preceding and following surgery of the primary tumors and recurrences from five patients and revealed identical CNV profiles even after up to 994 days, underlining the high genomic stability despite massive genetic alterations.

Clinically, CNV-loss or CNV-gain tumors exhibited an approximately 30-fold increased risk of recurrence, highlighting CNVs as a potential prognostic biomarker.

At the transcriptomic level, snRNA-seq. analyses of nine CD tumors showed similarities between CNV-low (both *USP8* mutated and wild-type) and a CNV-gain tumor; however, there were strong differences compared to CNV-loss tumors. We could further show that chromosomal loss directly affected loss of corresponding transcripts, which may be exploited for clinical intervention.

Taken together, our study brings important new insights into tumor biology of CD by discovering CNV-defined tumor subgroups with strong differences in genetic characteristics, transcriptomic landscapes and clinical outcomes. CNV analysis of CD tumors and the high genomic stability may enable future prediction of recurrences and provide potential for novel and better patient-specific treatment options.

Abstract citation ID: lvag096.090

OC3.2 - ECE_2189 - Disrupted peripheral circadian clock gene expression in patients with Cushing's syndrome

Tim Terlutter[1], Elisabeth Nowak[1,2], Hanna F. Nowotny[1], Annie Sriramachandran[1], Pia Kruse[1], Marceli Chojnacki[1], Pia Wagner[1], Sarah Ilmberger[1], Elina Kotzeva[1], Stephanie Zopp[1], Martin Reincke[1] and Nicole Reisch[1]
[1]Munich, Germany; [2]Department of Medicine IV, LMU University Hospital, LMU Munich, Munich, Germany

Background: Endogenous Cushing's syndrome (CS) is characterised by a loss of physiological circadian cortisol rhythmicity, which contributes to typical comorbidities such as sleep disturbances, depression, and cardiometabolic complications. We aimed to investigate the effects of prolonged cortisol excess on peripheral circadian clock gene expression during active disease and in remission.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Methods: This prospective single-centre study included 54 patients with active CS (21 adrenal, 29 pituitary, 4 ectopic) and 54 sex-, age- and BMI-matched healthy controls. Seventeen patients (10 adrenal, 7 pituitary) were additionally assessed longitudinally during remission with persistent adrenal insufficiency and physiological hydrocortisone replacement therapy. Morning blood samples (8-12 AM) were collected and peripheral mononuclear blood cells were isolated within six hours using density gradient centrifugation. The mRNA expression of 11 core circadian clock genes (*CLOCK*, *ARNTL*, *CRY1*, *CRY2*, *PER1*, *PER2*, *PER3*, *NR1D1*, *TIMELESS*, *WEE1*, *CREB1*) was quantified by real-time qPCR.

Results: Patients with active CS showed significantly reduced mRNA expression of *CLOCK* ($P = .033$), *NR1D1* ($P = .0057$), *TIMELESS* ($P = .0039$), *PER2* ($P = .0004$), *PER3, CREB1* (both $P = .0002$), *ARNTL*, *CRY1*, and *CRY2* (all $P < .0001$). *PER1* and *WEE1* expression did not differ significantly between groups. No significant differences were observed between ACTH-dependent and -independent CS. After a median remission duration of 5.0 months (IQR 3.5-7.0), expression levels of *CLOCK*, *PER2*, *PER3*, *ARNTL*, *CRY1*, *CRY2*, and *CREB1* had normalised. In contrast, *NR1D1* was upregulated compared with both healthy controls ($P = .0003$) and patients with active CS ($P = .0011$). TIMELESS expression remained slightly, though not statistically significantly, lower relative to controls ($P = .069$). *WEE1* expression was reduced compared with patients with active CS ($P < .0001$).

Conclusions: Cortisol excess in CS is associated with broad alterations in peripheral circadian clock gene expression. Most changes are reversible after remission. However, persistent dysregulation of *NR1D1* indicates lasting circadian alterations and merits further investigation of downstream pathways and clinical associations.

Abstract citation ID: lvag096.091

OC3.3 - ECE_1982 - No circadian rhythmicity of neurophysin I, a surrogate marker for oxytocin

Cihan Atila[1,2], Rakithan Murugesu[1,2], Shalini Mekkattu[1,2], Deborah Rudin[2,3,4], Dino Lüthi[2,3,4], Matthias Liechti[2,3,4] and Mirjam Christ-Crain[1,2]

[1]Department of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland; [2]Department of Clinical Research, University of Basel, University Hospital Basel, Basel, Switzerland; [3]Division of Clinical Pharmacology and Toxicology, University Hospital Basel, Basel, Switzerland; [4]Department of Biomedicine, University of Basel, University Hospital Basel, Basel, Switzerland

Purpose: Oxytocin (OXT) plays key roles in social behaviour, stress regulation, and reproductive physiology. OXT deficiency has been described in pituitary disorders and is associated with increased anxiety and impaired prosocial behaviour. Despite growing clinical interest, the circadian regulation of OXT remains poorly defined, largely due to methodological limitations in measuring endogenous OXT. Neurophysin I (NP-I), a stable carrier protein co-released with OXT, represents a reliable surrogate marker. Characterizing the circadian profile of NP-I may therefore provide important insights into oxytocinergic function with implications for diagnostics and future replacement strategies.

Methods: This study is a secondary analysis of a prospective, observational trial conducted in healthy adults under highly standardized conditions. Thirteen participants underwent hourly blood sampling over 24 hours following overnight fasting, controlled fluid intake, standardized meals, and regulated light exposure and physical activity. All assessments were performed on the clinical research ward to minimize external influences on hormone secretion.

Results: Thirteen healthy participants (median age 23 years [IQR, 19-24]; 46% female; BMI 22.8 ± 1.6 kg/m^2) underwent 24-hour hormone profiling. NP-I concentrations ranged from 50 to 8607 pg/mL. The overall median NP-I concentration was 822 pg/mL [339-1392], with a mean of 1609 pg/mL (2084). Individual median 24-hour NP-I concentrations ranged from 143 pg/mL [114-186] to 7103 pg/mL [6380-7714]. Across participants, NP-I levels peaked at approximately 05:30 and reached a nadir at approximately 16:30. The estimated oscillation amplitude was small (35 pg/mL) and not statistically significant (95% CI-110 to 181; $P > .05$), indicating the absence of a robust population-level circadian rhythm. Female participants exhibited higher NP-I concentrations than males (median 1372 pg/mL [468-5344] vs 687 pg/mL [297-932]), with markedly elevated levels—approximately four- to five-fold higher—in two women using hormonal contraception.

Conclusions: Under resting, unstimulated conditions, circulating NP-I levels in healthy adults do not display significant circadian rhythmicity, suggesting stable basal oxytocinergic output. Exploratory findings indicate potential sex-related differences that warrant further investigation.

Abstract citation ID: lvag096.092

OC3.4 - ECE_1709 - Prolactinoma from the patients' perspective: clinical manifestations, treatment experiences and associated adverse effects, including a novel impulse control disorder questionnaire

Sara-Jessica Camerin[1], Katharina Schilbach[2], Timo Deutschbein[3], Emanuele Varaldo[4], Stephan Petersenn[3], Mario Detomas[5], Paul Loughrey[6], Julie Celine Refardt[7], Bettina Winzeler[8], Georgios Papadakis[9], Maria Mavromati[10], Kristina Isand[11], Queralt Asla Roca[12], Rebeca Marín Bueno[12], Ulf Elbelt[13], Martin Fassnacht[5], Schuetz Philipp[14], Niki Karavitaki[15], John Newell-Price[16], Maria Fleseriu[17], Juliana Drummond[18], Beatriz Santana Soares[18], Emanuele Ferrante[19], Miles Levy[20], Jürgen Honegger[21], Mirjam Christ-Crain[22], Emanuel Christ[1], Luigi Mariani[1], Michel Roethlisberger[1] and Cihan Atila[1]

[1]University Hospital Basel, Basel, Switzerland; [2]University Hospital München LMU, Basel, Germany; [3]University of Duisburg-Essen, Essen, Germany; [4]University of Turin, Turin, Italy; [5]University of Würzburg, Würzburg, Germany; [6]University of Dublin, Dublin, Ireland; [7]University of Rotterdam, Rotterdam, The Netherlands; [8]University of Zürich, Zürich, Switzerland; [9]University of Lausanne, Lausanne, Switzerland; [10]University of Geneva, Geneva, Switzerland; [11]North Estonia Medical Centre, Tallinn, Estonia; [12]University of Barcelona, Barcelona, Spain; [13]University Hospital Berlin Charite, Berlin, Germany; [14]University Medical Hospital Aarau, Aarau, Switzerland; [15]University of Birmingham, Birmingham, United Kingdom; [16]University of Sheffield, Sheffield, United Kingdom; [17]University of Oregon, Oregon, United

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

States; [18]Hospital of Clinics of the Federal University of Minas Gerais, Belo Horizonte, Brazil; [19]University of Milano, Milano, Italy; [20]University of Leicester, Leicester, United Kingdom; [21]University of Frankfurt, Frankfurt am Main, Germany; [22]University of Basel, Basel, Switzerland

Background: Prolactinomas are commonly treated with dopamine agonists (DA), which normalise prolactin levels in most patients. However, patient-reported long-term tolerability remains poorly characterised. Adverse effects—particularly impulse control disorders (ICDs)—may be underrecognized due to the lack of disease-specific screening tools and the limited feasibility of existing instruments developed for other conditions. This study assesses patient-reported treatment experiences and side effects across treatment modalities and introduces and evaluates a novel, brief ICD screening tool tailored to patients with prolactinoma.

Methods: International, cross-sectional survey study between 01/06/2025-02/01/2026, coordinated by the University Hospital Basel, Switzerland. Adults (≥18 years) with prolactinoma were recruited by their local physicians. The survey assessed symptoms at diagnosis, treatment history, DA-associated adverse effects, and behavioural changes. Impulsivity and ICDs were assessed using the Barratt Impulsiveness Scale (BIS), the Questionnaire for Impulsive–Compulsive Disorders in Parkinson's Disease (QUIP), and the newly developed BASEL-ICD-S questionnaire. Patients were analysed according to current DA exposure. Receiver operating characteristic (ROC) analyses were used to derive cut-offs for detecting high impulsivity and pathological ICD sub-domains in randomly assigned development and validation cohorts.

Findings: 528 patients were included (median age 40 years [31-49], 73% female, median disease duration 5 years [2-11]). Common manifestations at diagnosis included menstrual irregularities in women (82%), reduced libido in men (80%), as well as tiredness (70%) and mood changes (64%) overall. Primary treatment was medical in 87% and surgical in 9%, while 4% were newly diagnosed and had no treatment started. Among DA-treated patients ($n = 406$), the most frequent side effects were fatigue (51%), dizziness (43%), headache (38%), and gastrointestinal complaints (36%). BIS, QUIP, and BASEL-ICD-S total scores were higher in DA-treated than not DA-treated patients ($n = 406$) (all $P < .001$). High impulsivity (BIS score >74) was more frequent in DA-treated patients (22% vs 7%). A BASEL-ICD-S total score of ≥25 identified high impulsivity with good discrimination in both development (AUC 0.88) and validation cohorts (AUC 0.89), and with high negative predictive value (96%). Pathological ICDs in DA-treated patients included gambling (7.4% vs 1.6%), compulsive buying (28.1% vs 13.9%), and hypersexual behaviour (17.7% vs 5.7%). BASEL-ICD-S subscores demonstrated good to excellent discrimination across ICD domains (AUC ranges 0.75-0.99), with stable performance in the validation cohort (AUC 0.76-0.91).

Conclusions: Prolactinomas were associated with a substantial symptom burden. DA therapy was frequently accompanied by adverse effects, increased impulsivity, and other ICDs. The BASEL-ICD-S demonstrated robust performance as a brief screening tool for behavioural side effects in patients with prolactinoma.

Abstract citation ID: lvag096.093

OC3.5 - ECE_1667 - TP53 R248Q promotes immune escape of pituitary neuroendocrine tumors through cooperative interactions between SPP1+ TAMs and EndMT-CAFs

Wan Su[1], Zhang Ye[2], Yong Yao[2] and Lin Lu[1]
[1]Endocrinology, Peking Union Medical College Hospital, Beijing, China; [2]Beijing, China

Aggressive pituitary tumors remain difficult to manage due to invasive growth, frequent recurrence, and resistance to therapy and effective molecularly targeted treatments are still lacking. Accumulating evidence from previous clinical and genomic cohorts has demonstrated a high prevalence of TP53 alterations in aggressive pituitary tumors, implicating TP53 dysregulation as a potential driver of malignant progression. However, despite its established association with tumor aggressiveness, the mechanistic role of TP53 mutations in pituitary tumor biology—particularly in shaping tumor–stroma–immune interactions—remains poorly understood.

To address this gap, we integrated single-cell transcriptomics from 34 pituitary tumors with in vitro functional assays, including co-culture systems, collagen matrix contraction assays, flow cytometry, cytokine profiling, and a tri-culture Transwell model incorporating Trp53-mutant mouse pituitary tumor cell lines and patient-derived TP53-mutant tumor organoids.

Single-cell transcriptomic analysis of pituitary tumors revealed marked activation of the TP53 signaling pathway in aggressive case, together with occurrence of the hotspot mutation TP53(Arg248Gln). Detailed characterization of cancer-associated fibroblasts (CAFs) heterogeneity demonstrated a selective expansion of EndMT-CAFs in TP53-mutant tumors. Pseudotime modeling reconstructed fibroblast differentiation trajectories and identified a fibrosis-associated ECM program linked to EndMT (Endothelial-to-Mesenchymal Transition). Functionally, co-culture experiments demonstrated that TP53-mutant tumor cells induced EndMT-CAFs differentiation and promoted a pro-invasive CAF phenotype. In parallel, immune profiling revealed an enrichment of SPP1$^+$ tumor-associated macrophages (TAMs), reduced T-cell infiltration, and enhanced cytokine- and ECM-mediated communication networks in TP53-mutant tumors. Flow cytometric and cytokine analyses further showed that TP53 (Arg248Gln) tumor cells preferentially drove macrophage polarization toward an SPP1$^+$ TAM state through tumor-derived cytokine signals.

To interrogate coordinated stromal–immune interactions, a tri-culture Transwell system was established to model an immune-exclusion niche in vitro. Within this system, EndMT-CAFs and SPP1$^+$ TAMs cooperatively amplified ECM remodeling, forming a structured stromal barrier that enhanced tumor cell proliferation and invasion while restricting CD8$^+$ T-cell infiltration and effector function.

Collectively, these findings demonstrate that TP53(Arg248Gln) promotes pituitary tumor invasion by orchestrating EndMT-CAFs and SPP1$^+$ TAMs recruitment, thereby driving ECM remodeling and establishment of an immune-exclusion niche that supports tumor progression and immune escape. This work provides a mechanistic framework and potential therapeutic entry points for targeting aggressive pituitary tumors.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.094

OC3.6 - ECE_3431 - PitNET-associated SOX2+ pituitary stem cells: a transcriptomic landscape of 1534 patients

Bence Kövér[1], Ian Kruk[2], James Kaufman-Cook[1], Yasmine Kemkem[1], Miriam Vazquez Segoviano[1], Olivia Sherwin[1], Hui-Chun Lu[1] and Cynthia Andoniadou[1]

[1]*Centre for Craniofacial and Regenerative Biology, King's College London Guy's Campus, London, United Kingdom;* [2]*McGill University, Montreal, Canada*

The anterior pituitary gland contains SOX2+ pituitary stem cells (PSCs) that persist into adulthood. The role of PSCs remains obscure with regards to the initiation and maintenance of pituitary neuroendocrine tumours (PitNETs). To quantify the abundance and gene expression profile of tumour-associated PSCs, we carefully curated and uniformly reprocessed all publicly available human pituitary (healthy or PitNET) transcriptomic datasets (1441 bulk and 93 single-cell).

Analysis of bulk and single-cell samples in a shared embedding identified 5 broad PitNET subtypes, and a clear separation by transcription factor lineage (POU1F1+, NR5A1+, TBX19+). The majority of PitNETs with the clinical annotation "Null-cell" were clustered with NR5A1+ samples (85% (28/33)).

Cell type annotation of 93 single-cell samples (~420 000 cells) revealed the presence of PSCs in healthy pituitaries, and residual PSCs associated with PitNETs. Tumour-associated PSCs expressed known PSC markers, such as *SOX2*, *SOX9*, as well as newly identified markers in mice, such as *RUNX1*, *NFIB* or *SLIT2* (total of 3896 genes upregulated vs tumour cells). In addition, differential expression analysis revealed 1349 upregulated and 2298 downregulated genes in tumour-associated PSCs compared to healthy PSCs.

Across single-cell datasets, tumour-associated PSCs were present in 47% (37/78) of samples (POU1F1+ 47% (15/32); NR5A1+ 44% (8/18); TBX19+ 60% (9/15); Null-cell 33% (1/3)), at a median frequency of 1.8% of cells, as compared to 6.4% of cells in healthy tissue. To enable reproducible detection of cell types (including PSCs) in PitNET single-cell data, we release a machine learning-based annotation tool implemented in the *epitome_tools* Python package.

To further characterise stem cell abundance, we applied cell-specific marker signatures to deconvolute the cell type composition of 1441 high-quality bulk transcriptomic samples (1102 PitNETs, 339 Healthy). This analysis also identified a PSC compartment in 93% of healthy samples (316/339) and in at least 29% of PitNETs (POU1F1+ 36% (130/358); NR5A1+ 17% (39/225); TBX19+ 15% (26/167); Null-cell 15% (5/33)). In PitNETs, this analysis identified a median PSC abundance of 1.2%, compared to 3.3% in healthy tissue.

In summary, we find that SOX2+ PSCs are widely detectable across PitNET samples, regardless of tumour lineage or assay technology. In addition, tumour-associated PSCs exhibit an altered transcriptome compared to healthy PSCs, which might affect tumourigenesis. Importantly, none of the single-cell or bulk samples were fully composed of PSCs, suggesting that PitNETs always exhibit some level of differentiation. Follow-up work will examine the predictive power of PSC abundance on tumour invasion and recurrence.

Abstract citation ID: lvag096.095

OC4.1 - ECE_2808 - Chronic subcutaneous kisspeptin-10 sustains gonadotrophin secretion for 12 days without tachyphylaxis in healthy men

Jovanna Tsoutsouki[1,2], Arthur Yeung[1], Maria Phylactou[1,2], Kanyada Koysombat[1], Sandhi Nyunt[1], Megan Young[1], Aaran Patel[1], Elisabeth Daniels[1], Aureliane Pierret[1], Edouard G. Mills[1,2,3], Alexander Comninos[1,2,3], Ali Abbara[1,2] and Waljit Dhillo[1,2]

[1]*Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom;* [2]*Department of Endocrinology, Imperial College Healthcare NHS Trust, London, United Kingdom;* [3]*Endocrine Bone Unit, Imperial College Healthcare NHS Trust, London, United Kingdom*

Introduction: Kisspeptin is a key hypothalamic regulator of gonadotropin-releasing hormone and gonadotrophin (LH/FSH) secretion and has major therapeutic potential for hypogonadotrophic hypogonadism. While acute kisspeptin administration robustly stimulates gonadotrophin release in humans, concerns regarding receptor tachyphylaxis have limited its chronic clinical use. We evaluated, for the first time in humans, whether chronic subcutaneous administration of kisspeptin-10 can sustain gonadotrophin secretion without desensitisation.

Methods: In a randomised, single-blind, crossover, placebo-controlled study, healthy eugonadal men (18-40 years) received chronic subcutaneous kisspeptin-10 infusion via two paradigms: (1) continuous infusion (180 nmol/hr for 5 days, $n = 4$), with LH/FSH sampling every 15 minutes on days 1 and 5; and (2) intermittent infusion (150 nmol/hr for 8 hours daily with 16 hours rest for 12 days, $n = 7$), with 15-minute sampling on days 1, 8, and 12. Sampling sessions lasted up to 8.5 hours. In a subset ($n = 4$), an intravenous kisspeptin-10 bolus (1 nmol/kg) was administered immediately after cessation of the day-12 infusion to assess receptor responsiveness. Separate saline visits ($n = 12$) served as controls.

Results: Continuous 5-day kisspeptin-10 infusion induced robust gonadotrophin responses on both days. Mean gonadotrophin increases from baseline were significantly greater than saline (LH: -0.16 ± 0.19; FSH: -0.19 ± 0.08 IU/L) on day 1 (LH 4.11 ± 0.68 IU/L, $P < .0001$; FSH 0.84 ± 0.27 $P = .0003$) and day 5 (LH 1.65 ± 0.32, $P = .0039$; FSH 0.34 ± 0.21, $P = .049$), indicating partial but not complete attenuation by day 5.

Intermittent 12-day kisspeptin-10 administration sustained gonadotrophin secretion with mean LH increases from baseline significantly exceeding saline (-0.16 ± 0.19 IU/L) on day 1 (1.68 ± 0.25 IU/L; $P < .0001$), day 8 (1.04 ± 0.22 IU/L; $P = .006$), and day 12 (1.14 ± 0.33 IU/L; $P = .003$), with no significant decline across days. FSH showed similar patterns (mean increase in FSH from baseline in IU/L: saline -0.19 ± 0.07, vs day 1, $P < 0.0001$; vs day 8, $P = .030$; vs day 12, $P = .003$). Critically, an intravenous kisspeptin-10 bolus after 12 days elicited preserved gonadotrophin increases compared with saline (LH: 3.25 vs 2.76 IU/L; FSH: 0.61 vs 0.07 IU/L), confirming absence of receptor desensitisation.

Conclusions: This study provides the first evidence that chronic subcutaneous kisspeptin-10 administration can sustain gonadotrophin secretion in humans for up to 12 days without inducing tachyphylaxis. An intermittent infusion strategy preserves

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

kisspeptin receptor sensitivity while effectively activating the hypothalamic-pituitary-gonadal axis. These findings establish a clinically feasible protocol with strong translational potential for treating conditions characterised by hypothalamic kisspeptin deficiency, including functional hypothalamic amenorrhea and obesity-related hypogonadism.

Abstract citation ID: lvag096.096

OC4.2 - ECE_3288 - Dynamic endocrine responses to kisspeptin to decode hypothalamic-pituitary dysfunction in women with obesity

Sandhi Nyunt[1,2], Kanyada Koysombat[1,2], Megan Young[1], Agathoklis Efthymiadis[1,2], Patrick McGown[1,2], Aaran Patel[1,2], Bijal Patel[1,2], Arthur Yeung[1,2], Jovanna Tsoutsouki[1,2], Aureliane Pierret[1,2], Elisabeth Daniels[1,2], Maria Phylactou[1,2], Edouard G. Mills[1,2], Chioma Izzi-Engbeaya[1,2], Tricia Tan[1,2], Alexander Comninos[1,2], Ali Abbara[1,2] and Waljit Dhillo[1,2]

[1]Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom; [2]Department of Endocrinology, Imperial College Healthcare NHS Trust, London, United Kingdom

Background: Obesity frequently co-exists with and exacerbates polycystic ovary syndrome (PCOS). PCOS is characterised by increased hypothalamic GnRH neuronal activity, whereas animal models of obesity suggest that it reduces hypothalamic function. Kisspeptin stimulates hypothalamic GnRH neurons enabling direct assessment of hypothalamic dysfunction, whereas GnRH testing assesses pituitary responsiveness. Limited data exist evaluating hypothalamic and pituitary function in women with obesity, both with and without PCOS.

Methods: Women underwent an 8-hour assessment of LH pulsatility during the early follicular phase (days 1-5 of menstrual cycle), alongside dynamic endocrine testing with intravenous GnRH (100 µg) and kisspeptin-54 (9.6 nmol/kg) on separate occasions. Participants included lean eugonadal women (BMI 18.5-24.9 kg/m^2; LeEug; $n = 31$), obese eugonadal women (BMI ≥30 kg/m^2; ObEug; $n = 7$), lean women with PCOS (LePCOS; $n = 26$), and women with obesity and PCOS (ObPCOS; $n = 23$). Hormones were measured every 10-15 minutes. Baseline hormone concentrations were compared using Kruskal Wallis test with post hoc Dunn's test and hormone rises over time were analysed using two-way ANOVA.

Results: Median (IQR) of serum LH (IU/L) was lower with obesity in both eugonadal women and those with PCOS: ObEug (2.2, IQR 1.9-2.9), LeEug (3.5, 2.6-4.6), LePCOS (5.3, 3.3-7.4), ObPCOS (4.0, 2.6-5.5) ($P = .01$ for LePCOS vs obPCOS). Baseline FSH did not differ significantly between groups: ObEug (median 5.7, IQR 4.7-7.2), LeEug (5.6, 4.6-6.9), LePCOS (4.7, 4.2-6.1), ObPCOS (5.0, 4.7-5.7).

The LH rise from baseline following kisspeptin-54 was reduced in ObEug compared with LeEug women ($P = .043$). Likewise, the FSH rise from baseline following kisspeptin-54 in eugonadal women was reduced with obesity compared with lean women ($P = .0003$). However, obesity was associated with an increased FSH response to Kisspeptin-54 in women with PCOS ($P = .013$).

The LH ($P = .0008$) and FSH ($P < .0001$) responses to GnRH were reduced with obesity in eugonadal women. In women with PCOS, the FSH response was also reduced ($P = .02$), although the LH response was not significantly altered ($P = .3$).

Conclusions: Obesity is associated with reduced gonadotrophin concentrations, due to multiple mechanisms including increased renal clearance. Dynamic testing revealed that obesity attenuates pituitary responsiveness to GnRH. In contrast, we show for the first time that hypothalamic responses to kisspeptin were divergent, being increased in PCOS but reduced in eugonadal women. These data highlight fundamental differences between the neuroendocrine disturbances in women with PCOS and those due to obesity alone.

Abstract citation ID: lvag096.097

OC4.3 - ECE_1644 - Increased prospective cardiovascular disease risk in 127,517 Nordic women with polycystic ovary syndrome. a national cohort study

Dorte Glintborg[1], Meri-Maija Ollila[2], Noona Koskenkari[2], Jens-Jakob Møller[3], Daniella Calla[4], Frida Gyllenberg[4], Katrine Rubin[3], Paula Pesonen[2], Marianne Skovsager Andersen[1], Inger Sundström-Poromaa[4] and Terhi Piltonen[2]

[1]Department of Endocrinology, Odense, Denmark; [2]Oulu University Hospital, Oulu, Finland; [3]OPEN, Odense, Denmark; [4]Uppsala University, Uppsala, Sweden

Background: Cardiovascular disease (CVD) risk factors are prevalent in women with PCOS, but prospective data regarding CVD in population-based cohorts are limited.

Aim: To investigate prospective risk of CVD in Nordic women with PCOS.

Design: National register-based study in women with PCOS and age-matched controls originating from Denmark (PCOS Denmark, N = 27 298, controls, N = 135 019), Finland (PCOS Finland, N = 20 765, controls, N = 59 122), and Sweden (PCOS Sweden, N = 79 454, controls, N = 393 669). The main study outcome was CVD. CVD was defined according to ICD-10 diagnostic codes for major adverse cardiac events, pulmonary embolism and/or deep venous thrombosis. Cox regression analyses estimated HR with 95% CI and adjusted analyses included BMI and education.

Results: The median age at cohort entry was 28 years (Denmark) and 29 years (Finland and Sweden) and the median follow-up time was 8.0 to 10.0 years. The unadjusted hazard ratio (HR, 95% CI) for CVD in women with PCOS was 1.30 (1.20; 1.41) in Denmark, 1.45 (1.31; 1.60) in Finland, and 1.52 (1.44; 1.60) in Sweden. Models remained significant after adjusting for obesity and level of education. In a combined meta-analysis including all countries (PCOS, N = 127 517, controls, N = 587 810, the adjusted HR for CVD in women with PCOS was 1.32 (1.25; 1.39). In women with BMI <25 kg/m^2 and no type 2 diabetes, the adjusted HR for CVD risk was 1.40 (1.26; 1.55).

Conclusions: The risk of CVD was increased in women with PCOS across the three Nordic countries, also among women with BMI <25 kg/m^2.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.098

OC4.4 - ECE_2998 - Unraveling the role of hyperandrogenism in the development of metabolic dysfunction-associated steatotic liver disease (MASLD) in polycystic ovary syndrome

Andrea Rodriguez-Martin[1,2], Victor Serrano-Lopez[1,2], Esperanza Uceda-Rodriguez[1,2], Carmen Torres-Granados[1,2], Valentina Dorta-Bouza[3], Francisco Ruiz-Pino[1,2,4], Azahara Espejo-Cordero[1,2], Ana Belen Rodriguez[1,2,4], Rubén Nogueiras[3], Manuel Tena-Sempere[1,2,4] and Miguel Angel Sanchez-Garrido Nogueras[1,2,4]

[1]University of Cordoba, Cordoba, Spain; [2]Maimónides Biomedical Research Institute of Córdoba, Cordoba, Spain; [3]Deparment of Physiology (CIMUS), University of Santiago de Compostela, Santiago de Compostela, Spain; [4]CIBER Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Cordoba, Spain

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disorder among premenopausal women, characterized by hyperandrogenism and reproductive dysfunction. PCOS is often linked also to metabolic abnormalities, and women with PCOS have four-fold increased risk of developing metabolic dysfunction-associated steatotic liver disease (MASLD).

MASLD is a prevalent liver condition, affecting 35%-70% of women with PCOS. MASLD encompasses a spectrum of hepatic manifestations that begin with liver fat accumulation, which may progress to non-alcoholic steatohepatitis (NASH), a more severe stage of the disease that can lead to cirrhosis, liver failure and hepatocellular carcinoma.

Cumulative evidence suggests that the higher incidence of MASLD in PCOS women may be linked to the metabolic derangements associated with this endocrinopathy, including obesity and insulin resistance. Chronic hyperandrogenism might contribute also to the development of MASLD in women with PCOS. However, the mechanisms underlying MASLD in PCOS and the pathophysiological role of androgen excess in this condition remain unknown.

Here, we investigated the role of hyperandrogenism in MASLD pathogenesis using a well-validated murine model of PCOS, based on postweaning androgenization (PWA) of female mice, and a liver-specific androgen receptor knockout (LARKO) model. In PWA mice, we characterized the effects of chronic androgen excess, alone or in combination with an obesogenic diet, on metabolic and hepatic profiles at 15, 18 and 23 weeks of androgen exposure. By week 15, androgen excess significantly increased body weight, impaired insulin sensitivity and serum parameters, and promoted hepatic steatosis and collagen deposition. Interestingly, combination of hyperandrogenism and high-fat diet (HFD) consumption markedly worsened metabolic and hepatic outcomes. Longitudinal monitoring revealed a time-dependent aggravation of both metabolic and histological derangements at the 18 and 23-week timepoints.

Notably, LARKO mice exposed to chronic hyperandrogenism (LARKO PWA) exhibited partial protection against hepatic injury. While their metabolic profiles were similar to those of the hyperandrogenized controls (PWA), LARKO PWA mice showed a significant reduction in liver fat, collagen accumulation and hepatic inflammation, as well as a marked decrease in circulating transaminases and lipid levels. Notably, this protective effect was even more pronounced when mice were fed a HFD.

Our findings demonstrate that chronic hyperandrogenism is a major factor for MASLD progression in PCOS, especially when concurrent with obesity, via hepatic androgen receptor activation. Liver AR signaling may be considered a primary driver of (and eventual therapeutic target for) hepatic pathology in PCOS, independent of systemic metabolic dysfunction.

Abstract citation ID: lvag096.099

OC4.5 - ECE_2984 - Early pregnancy maternal progesterone supplementation alters fetal frontal cortex gene expression in male fetuses

Katarzyna Siemienowicz[1], Anna Sherriffs[1], Mick Rae[1] and Colin Duncan[2]

[1]School of Applied Sciences, Edinburgh Napier University, Edinburgh, United Kingdom; [2]Centre for Reproductive Health, The University of Edinburgh, Edinburgh, United Kingdom

Prenatal fetal exposure to steroids is a “Goldilocks phenomenon”, where too much or too little hormone is detrimental. Progesterone is critical to support and maintain pregnancy. Maternal progesterone supplementation is commonly used during assisted reproduction and as a treatment for increased risk of miscarriage, up to 16 weeks’ gestation. Progesterone and its metabolites are neuroactive steroids necessary for brain development. Effects of increased prenatal exposure to progesterone on fetal brain development are poorly understood. We previously reported that maternal progesterone administration increased male, but not female, fetal progesterone concentrations and disturbed normal hypothalamic-pituitary function in d75 sheep male fetuses (equivalent to 15 weeks of human gestation). We hypothesised that maternal progesterone supplementation in early pregnancy would alter gene expression in the fetal male frontal cortex.

Pregnant ewes received either 200 mg of intramuscular progesterone (P) or vehicle (C) twice weekly from day 20 until sacrifice at day 75 of gestation. These doses and timings were clinically realistic. Fetal frontal cortex was collected from males ($C = 10$; $P = 7$), RNA extracted, and gene expression measured by RNA sequencing (RNAseq) and qPCR. Data was further contextualised using Ingenuity Pathway Analysis (IPA).

There was no difference in the expression of genes encoding steroid receptors (AR, ESR1, ESR2 and PGR) and steroid metabolising enzymes (CYP17, HSD17B, CYP19 and AKR1C2), except for increased expression of SRD5A1 ($P < .05$), an enzyme that metabolises progesterone to 5α-dihydroprogesterone and testosterone to dihydrotestosterone, in the fetal male frontal cortex from progesterone-treated pregnancies. RNAseq revealed that there were 437 nominally differentially expressed genes (DEGs) in response to progesterone supplementation. IPA analysis indicated dysregulations of numerous pathways ($P < .05$, absolute Z score>2), including increased iron uptake and transport, cyclophilin signalling pathway, and decreased CREB and reelin signalling in neurons, calcium signalling, FAK signalling and G-protein coupled signalling, all with potential impact on brain development.

Progesterone is known to cross the placental barrier, entering the fetal circulation, reaching the developing brain and regulating key events in neural development. Progesterone may also be metabolised to different steroid classes locally within the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

developing brain. There is evidence in humans for increased fetal steroidogenic activity in autism, with oestradiol, oestrone and progesterone showing the largest effects on autism likelihood. Identified pathways and individual DEGs have links to neurological disorders and cognitive impairment. Whilst we cannot predict long-term consequences of these temporal gene expression shifts during fetal life, we demonstrated perturbed gene expression during development that warrants further investigation.

Abstract citation ID: lvag096.100

OC4.6 - ECE_3281 - Clinical determinants and evolution of bone health in an adult population with Turner syndrome: insights from a monocentric study

Laura Rotolo[1,2], Matteo Malagrinò[1,2], Carolina Cecchetti[2,3], Paola Dionese[1,2], Elisabetta Belardinelli[1,2], Beatrice Solmi[1,2], Guido Zavatta[1,2], Uberto Pagotto[1,2] and Alessandra Gambineri[1,2]

[1]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [2]Bologna, Italy; [3]Endocrinology Unit, Ospedale Morgagni-Pierantoni, Forlì, Italy

Background: Early-onset low bone mineral density(BMD) is a hallmark of Turner syndrome(TS); however, its pathogenesis and specific risk factors remain poorly understood.

Aim: To investigate low BMD and fragility fractures (FF) prevalence and determinants, and longitudinal BMD trend in a large population of adult TS patients attending a tertiary hospital with a structured transition program.

Methods: Cross-sectional and longitudinal analyses were conducted on 174 TS patients (median age: 37.5 yrs; range: 15.3-70.7 yrs) at the time of their most recent dual-energy X-ray absorptiometry (DXA). We evaluated anthropometrics, bone metabolism markers, karyotype, typical comorbidities, details about prior/current estrogen replacement treatment (ERT) and rhGH treatment (rhGHT). Metabolic bone disease (MBD) was defined as low BMD/osteoporosis (Z-score≤−2 if spontaneous menstruation/current ERT, T-score≤−2.5 if post-menopausal/stopped ERT), and/or FF occurrence.

Results: Most patients displayed 45,X0 karyotype and primary amenorrhea ($n=71$;41.0% and $n=136$;79.1%, respectively). ERT was started at a median age of 16.0 yrs (IQR: 14.0-18.0), lasting 19.0yrs (IQR: 12.0-26.0). rhGHT was administered in 119 patients (69.6%).

MBD was identified in 74 (42.5%) patients, 12 of them experiencing FF, and 10 currently receiving antifracturative treatment. Multiple regression analysis identified later age at spontaneous/induced menarche (OR = +1.19, $P=.042$), higher levels of bone alkaline phosphatase (BAP; OR = +1.07, $P=.013$) and larger aortic size index (OR = +4.44, $P=.034$) as independent predictors of MBD prevalence.

Clinical FF occurred mostly at vertebral and wrist sites, with an early onset (mean age 36.2 ± 15.5 yrs). Notably, five patients with normal BMD experienced FF; nonetheless, DXA diagnosis of low BMD/osteoporosis remained a reliable predictor of FF (OR = +7.2; $P=.004$). Multiple regression analysis showed that later age at menarche (OR = +1.37; $P=.071$) and nephropathy (OR = +8.28; $P=.021$) were independently associated with the presence of FF. Age, karyotype, rhGHT, prior/current ERT analysed as daily dose, type of estrogen, route of administration and duration, were not related to MBD or FF occurrence.

Linear mixed models ($n=147$) showed substantial overall stability of lumbar BMD over time (0.003 g/cm^2/y; $P=.002$). However, patients with primary amenorrhea and later age at menarche maintained lower values over time (−0.052 g/cm^2/y; $P=.001$, −0.008 g/cm^2/y; $P=.001$, respectively). Finally, a negative relationship was found between bone turnover markers and lumbar BMD trends (BAP: −0.002 g/cm^2/y; $P=.019$, cross-laps: −0.072 g/cm^2/y; $P=.002$). Karyotype, rhGHT and ERT showed no significant impact on lumbar BMD over time.

Conclusions: MBD in TS patient has a multifactorial pathogenesis. As modifiable factor, early ERT initiation is probably paramount to obtain and maintain adequate BMD for TS patients, and prevent the occurrence of FF. Continuous, lifelong monitoring of bone health is essential for all TS patients.

Abstract citation ID: lvag096.101

OC5.1 - ECE_2788 - Sex differences in clinical presentation, management and outcome in hospitalized patients with hyponatremia

Angelique Savelberg[1], Laura Potasso[2,3], Romy van der Groef[1,4], Sebastian Neggers[1], Mirjam Christ-Crain[2,3], Ewout Hoorn[5] and Julie Celine Refardt[1,2,3]

[1]Department of Internal Medicine, Division of Endocrinology, Erasmus Medical Center, University Medical Center Rotterdam, Rotterdam, The Netherlands; [2]Department of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland; [3]Department of Clinical Research, University of Basel, Basel, Switzerland; [4]Erasmus Medical Center, Rotterdam, The Netherlands; [5]Division of Nephrology and Transplantation, Erasmus Medical Center, University Medical Center Rotterdam, Internal Medicine, Rotterdam, The Netherlands

Introduction: Hyponatremia is the most common electrolyte disorder in hospitalized patients. Observational studies show a higher prevalence of hyponatremia in hospitalized female patients, but other sex-related differences in hyponatremia among hospitalized patients remain largely unknown.

Aim: To explore the impact of sex on the clinical presentation, management and outcomes of hyponatremia in hospitalized patients.

Methods: Predefined secondary analysis of a large European multi-center trial that randomized hospitalized patients with hyponatremia (plasma sodium <130 mmol/L) to targeted correction or standard of care, aiming to evaluate the effects on mortality and rehospitalization. Sodium trajectories were modelled using multivariable linear mixed models adjusted for age, sex and etiology with patient-specific random effects. The effect of sex on mortality and rehospitalization was analyzed with a multivariate cox proportional hazard model adjusting for age, hyponatremia etiology, treatment received, baseline plasma sodium, and Charlson Comorbidity Index. The difference in the likelihood of receiving treatment was assessed using the chi-square test. Subgroup analyses were performed for both the standard of care group and the targeted therapy group.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: 2173 patients (52.2% female, median age 73 years, median baseline plasma sodium of 127 mmol/L) were analyzed. Female patients more frequently had diuretic-induced hyponatremia (RR 1.51, 95%CI 1.13-2.03), and less often hypervolemic hyponatremia (RR 0.77, 95%CI 0.63-0.93). Female patients more often reported symptoms at baseline (RR 1.10, 95% CI 1.06-1.13) and were more likely to receive treatment when randomized to the standard of care group (RR 1.16, 95%CI 1.06-1.27). Additionally, female patients had a slightly lower plasma sodium over the entire trajectory of hospitalization (−0.4 mmol/L, $P = .003$). Female sex was independently associated with a lower 30-day mortality (HR 0.59, 95%CI 0.43-0.81) and 30-day rehospitalization (HR 0.76, 95%CI 0.60-0.68) rate. These sex differences persisted when adjusting for hyponatremia etiology.

Conclusions: While having lower plasma sodium levels and more frequently reporting symptoms, hospitalized female patients with hyponatremia had a lower hazard for 30-day mortality and rehospitalization. This raises the question of whether sex-specific mechanisms underlie differences in hyponatremia symptomatology and outcomes.

Abstract citation ID: lvag096.102

OC5.2 - ECE_1983 - Diagnosing vasopressin deficiency using mannitol-stimulated copeptin

Sven Lustenberger[1], Friederike Riehle[1], Talitha Hildebrandt[1], Cemile Bathelt[1], Joseph Verbalis[2], Cihan Atila[1] and Mirjam Christ-Crain[3]

[1]Department of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland; [2]Georgetown-Howard Universities Center for Clinical and Translational Science, Georgetown University, Washington, United States; [3]Basel, Switzerland

Background: The differential diagnosis between arginine vasopressin (AVP) deficiency (formerly known as central diabetes insipidus) and primary polydipsia remains challenging. To date, the method with the highest diagnostic accuracy is osmotically-stimulated copeptin—a surrogate marker of AVP—measured during hypertonic saline infusion. However, this method is often limited to experienced hospitals, requires close monitoring, and is contraindicated in some patients. An alternative simpler osmotic stimulation test would be highly desirable. Intravenous mannitol has been shown to increase plasma osmolality and stimulate AVP release. In this study, we investigated the effects of mannitol infusion on copeptin and its potential as a diagnostic tool in diagnosing AVP-deficiency.

Methods: In part 1 we conducted a randomized double-blind placebo-controlled cross-over trial to investigate the effect of mannitol infusion on copeptin in 22 healthy adults. Participants presented for two visits, each receiving either mannitol infusion (1 g/kg in 30 minutes, maximum 80 g) or placebo (normal saline) in random order. Serum copeptin was measured at baseline and at 30, 45, 60, 90, and 150 minutes. In part 2 we included 10 patients with AVP-deficiency and 10 patients with primary polydipsia. Participants presented for one visit, receiving open label mannitol infusion (1.5 g/kg in 30 minutes, maximum 120 g), and blood samples were taken at baseline, 30 and 90 minutes. The primary endpoint was copeptin levels after infusion of mannitol versus placebo (part 1) and in patients with AVP-deficiency versus patients with primary polydipsia (part 2).

Results: In healthy adults, median [IQR] baseline copeptin was 4.5 pmol/L [<2.7, 7.0] before mannitol infusion and 4.4 pmol/L [3.1, 6.7] before placebo infusion. Mannitol infusion was associated with a significant treatment effect, increasing copeptin at 30 minutes by +9.3 pmol/L compared to placebo (95% CI: +7.8, +10.8; $P < .001$).

In patients, baseline copeptin was <2.7 pmol/L [<2.7, <2.7] in primary polydipsia and <2.7 pmol/L [<2.7, <2.7] in AVP deficiency. After 30 minutes, the treatment effect on copeptin was +9.0 pmol/L in primary polydipsia (95% CI: +5.6, +12.3; $P < .001$) compared to AVP-deficiency. The best cutoff for differentiating AVP-deficiency from primary polydipsia was at 5.5 pmol/L with 100% sensitivity and 100% specificity.

Conclusions: Mannitol infusion represents a promising new approach for differentiating AVP deficiency from primary polydipsia. Its short test duration, straightforward dosing, minimal monitoring requirements and no relevant side effects make it accessible, cost-effective and safe, with the potential to become the new diagnostic standard of care.

Abstract citation ID: lvag096.103

OC5.3 - ECE_3463 - Foxl2 in establishing the gonadotrope lineage via a Fshb distal super-enhancer

Philippa Melamed[1], Tal Refael[1], Gil Golan[1], Daniella Darsa[1], Lilach Pnueli[1] and Karine Rizzoti[2]

[1]Haifa, Israel; [2]The Francis Crick Institute, London, United Kingdom

Follicle-stimulating hormone (FSH) levels are regulated by activin whose actions at the *Fshb* proximal promoter have been well-characterized. However, distal regulatory elements that confer its cell-specific expression and hormonal responsiveness are less clear. Analysis of scATAC-seq data revealed an extensive region in a gene-desert ~59-123 kb upstream of the mouse *Fshb* gene that contains several sites of gonadotrope-specific open chromatin, suggesting regulatory functions. The two most proximal sites (−59 kb and −67 kb) were seen in chromatin conformation capture (3C) to form distinct interactions with *Fshb* and *Kcna4*, located 230 kb upstream of *Fshb*. The region is transcribed abundantly into chromatin-associated lncRNAs which, like *Fshb* and *Kcna4*, are also upregulated by activin. Chromatin immunoprecipitation (ChIP) revealed that the −67 kb locus is bound by the lineage-specific transcription factor (TF), Foxl2, as well as chromatin architectural proteins, Brd4 and Med1, while Ctcf was enriched further upstream, at −123 kb; the binding of all increased following activin exposure. Brd4 and Med1 characterize “super-enhancers” and the expression of both *Fshb* and *Kcna4* was strongly inhibited by the BET inhibitor JQ-1, indicating super-enhancer regulation of both genes. Moreover, targeting CRISPR interference to each of the two more proximal peaks confirmed their differential effects on *Fshb* and *Kcna4* expression. Taken together with the 3C data, these results demonstrate that the −67 kb locus mediates basal and activin-stimulated *Fshb* expression, while the site at −59 kb contributes to activin-stimulation of both genes.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Single-cell multiomics revealed that the −67 kb locus is partially accessible in pituitary stem cells and throughout gonadotrope differentiation, preceding opening of the *Fshb* promoter, although it is closed in other differentiated cell types. Given that Foxl2 was found to bind this element, we hypothesized that this TF might keep the chromatin open at the locus. We thus characterized its protein interactome and investigated effects of its knockout (KO) in a gonadotrope cell line. The Foxl2 KO resulted in significantly elevated histone H3 levels across the −67 kb site, indicating more compact chromatin. Its protein interactors included Supt16h, a component of the FACT histone chaperone complex, which we show also binds this locus, and whose association was significantly reduced after Foxl2 deletion. Our findings have thus uncovered novel mechanisms governing gonadotrope differentiation and function, highlighting a distal "super-enhancer" in the regulation of *Fshb* expression, coordination with *Kcna4*, and a role for Foxl2 at this distal site during early establishment of the gonadotrope lineage.

Abstract citation ID: lvag096.104

OC5.4 - ECE_3532 - Constitutive active expression of ZFP36L1 in anterior pituitary SOX2+ stem cells results in pituitary hypoplasia and a failure of terminal differentiation via a non-cell autonomous mechanism

Olivia Sherwin[1,2], Saba Manshaei[3], Thea Willis[1], Hiba Hamdi[3], Yasmine Kemkem[1], Miriam Vazquez Segoviano[1], Bence Kover[1], James Kaufman-Cook[1], Shermin Mak[3], Dominic Withers[4], Jesus Gil[4], Juan Pedro Martínez-Barbera[3] and Cynthia Andoniadou[1]

[1]King's College London Guy's Campus, London, United Kingdom; [2]Technische Universität Dresden Medizinische Fakultät, Dresden, Germany; [3]London, United Kingdom; [4]Imperial College London, London, United Kingdom

SOX2+ pituitary stem cells (PSCs) are a critical source of signalling cues during pituitary development, yet the molecular orchestrators of this paracrine environment remain poorly defined. In this study, we identify ZFP36L1 as a key regulator of secreted factor expression within the PSC niche and demonstrate that its precise control is essential for terminal differentiation during pituitary organogenesis.

Using a *Sox2-CreERT2* model to induce constitutive active ZFP36L1 (ZFP36L1-CA) in PSCs from E12.5, we observed severe pituitary hypoplasia and a profound lack of terminal differentiation across POU1F1+ and NR5A1+ hormone-producing lineages by E18.5. To determine the nature of this developmental arrest, we performed mosaic lineage tracing via tamoxifen titration. Notably, wild-type cells neighbouring ZFP36L1-CA cells also failed to undergo hormone commitment, establishing a non-cell autonomous defect and suggesting a disruption of the extrinsic signalling environment.

This requirement for regulated ZFP36L1 expression was further validated using a *Hesx1-Cre* model, where early developmental ZFP36L1-CA expression resulted in dwarfism, perinatal lethality, and failure of POU1F1+ and NR5A1+ endocrine cell commitment. Crucially, this differentiation defect was rescued when *Hesx1-Cre* mutant pituitaries were co-cultured with normal PSCs, providing functional confirmation that the phenotype is driven by the loss of essential stem-cell-derived paracrine signals.

Mechanistic interrogation through scRNA-seq and mRNA *in situ* hybridisation identified secreted factors regulated by ZFP36L1 that co-localise with PSCs *in vivo*. ELISAs confirmed that these factors are actively secreted by PSCs and are significantly downregulated upon ZFP36L1-CA expression.

Collectively, these findings establish that ZFP36L1 regulation in PSCs is indispensable for pituitary organogenesis. These experiments identify specific paracrine mediators required for terminal differentiation in the anterior pituitary, offering new molecular targets for efficient regenerative approaches.

Abstract citation ID: lvag096.105

OC5.5 - ECE_2183 - Soluble alpha klotho in acquired adult-onset, and congenital growth hormone deficiency

Viviane Almeida[1], Martin Bidlingmaier[2], Manuel H. Aguiar Oliveira[3], Katharina Schilbach[2,4], Carla R. P. Oliveira[1], Angela Leal[1,5], Enaldo Melo[1], Keila R. Villar-Gouy[1], Roberto Salvatori[6], Jan Frystyk[7], Kevin C. J. Yuen[8], Michael Haenelt[2], Isabel Stüfchen[2], Friederike Völter[2], Elisabeth Nowak[2], Martin Reincke[2] and Júnia R.O.L. Schweizer[2]

[1]Endocrinology, Federal University of Sergipe, Aracaju, Brazil; [2]Department of Medicine IV, LMU Munich, LMU University Hospital, Munich, Germany; [3]Federal University of Sergipe, Aracaju, Brazil; [4]Deggendorf Institute of Technology, Deggendorf, Germany; [5]Medicine, Federal University of Sergipe Campus São Cristóvão, Aracaju, Brazil; [6]Johns Hopkins University, Baltimore, United States; [7]University of Southern Denmark, Odense, Denmark; [8]University of Arizona College of Medicine and Creighton University School of Medicine, Phoenix, United States

Background: Soluble alpha Klotho (sαKL) is an anti-aging protein with multiple functions in ion-regulation, antioxidative stress and energy metabolism. We previously demonstrated markedly elevated sαKL concentrations in active acromegaly (approximately 4-8x upper limit of normality), suggesting a role of growth hormone (GH)/insulin-like growth factor I (IGF-I) excess in its regulation. However, it appears that most patients with acquired adult-onset GH deficiency (AoGHD) exhibit sαKL concentrations within the lower reference interval for normal subjects. This indicates that factors other than GH/IGF-I signaling may be involved in the regulation of sαKL. This may be insulin, as in vitro studies have suggested that insulin stimulates sαKL secretion.

AoGHD and childhood onset GH deficiency (CoGHD) are distinct entities with differences in etiology, quality of life, insulin sensitivity, and possibly in longevity.

Objective: The purpose of this work was to assess sαKL concentrations in AoGHD (associated to insulin resistance) and CoGHD, by studying the Itabaianinha cohort, a congenital isolated GH deficiency (IGHD), due to the homozygous GHRH-R mutation (c.57 + 1G→A). These subjects exhibit severe short stature associated with low serum concentrations of IGF-I and IGFBP-3, increased secretion of glucagon-like peptide-1, favorable miRNA and stanniocalcin-PAPPA-system profiles, increased insulin sensitivity, and normal longevity.

Methods: We measured concentrations of sαKL, IGF-I and IGFBP-3 in 78 AoGHD, 23 IGHD subjects and 11 proven normal homozygous. All measurements were performed at the LMU University. The results are presented in median (interquartile range).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: In comparison to normal homozygous, IGF-I (µg/L) and IGFBP-3 (µg/L) (158.5 (128.2-189.7), 3433 (2817-3622), respectively) were reduced in both AoGHD (IGF-I: 38.5 (29.2-51.7), IGFBP-3: 1814 (1275-2722)) and IGHD (IGF-I: 11.5 810-21.9), IGFBP-3: 596 (479-707), respectively), more markedly in IGHD ($P < .001$ for all). sαKL concentrations (pg/mL) were similar in IGHD and normal homozygous (1052 (782-1349) and 993 (921-1301), respectively, $P > .05$). In contrast, sαKL was significantly lower in AoGHD 617 (468-793) pg/mL compared to IGHD ($P < .001$).

Conclusions: Patients with AoGHD exhibit sαKL concentrations within the lower normal reference interval, confirming the influence of the GH/IGF-I axis on sαKL regulation. However, individuals with IGHD have normal concentrations of sαKL, probably contributing to their normal longevity. Thus, increased insulin sensitivity, a hallmark of IGHD, may contribute to the maintenance of sαKL concentrations in this specific cohort.

Abstract citation ID: lvag096.106

OC5.6 - ECE_2863 - Defining the YAP/TEAD–SOX2–NFI network underlying pituitary stem cell maintenance and differentiation

Miriam Vazquez Segoviano[1], Bence Kover[1], Emily Lodge[2], James Kaufman-Cook[1], Yasmine Kemkem[1], Olivia Sherwin[1], Marika Charalambous[1,3], Stuart Sealfon[4], Frederique Ruf-Zamojski[5] and Cynthia Andoniadou[1,6]
[1]King's College London Guy's Campus, London, Northern Ireland; [2]University College London, London, United Kingdom; [3]The Francis Crick Institute, London, Northern Ireland; [4]Icahn School of Medicine at Mount Sinai, New York, United States; [5]Cedars-Sinai Medical Center, Los Angeles, United States; [6]Technische Universität Dresden Medizinische Fakultät, Dresden, Germany

Resident stem cells in the anterior pituitary contribute to all hormone-secreting cell types throughout life and are essential for maintaining proper gland function. While pituitary stem cells (PSCs) are highly active during early postnatal stages, they become largely quiescent in adulthood, underscoring the requirement for tightly controlled transcriptional programs to balance stem cell maintenance and lineage commitment. Disruption of this balance can lead to pituitary dysfunction and disease; however, the molecular mechanisms governing pituitary stem cell fate decisions remain poorly understood.

The transcriptional co-activator YAP, acting through TEAD transcription factors (TFs), has been established as a central regulator of PSC fate, promoting SOX2$^+$ stem cell self-renewal and proliferation while repressing differentiation. Using an inducible YAP overexpression model combined with single-nuclei multiomic analyses, we have previously identified members of the Nuclear Factor I (NFI) family as candidate core regulators of PSC function. However, how NFIs influence PSC behaviour and how they integrate within the YAP/TEAD and SOX2 regulatory framework remains unclear.

Here, we generated doxycycline-inducible SOX2 and NFI overexpression cell lines, alone and in combination, in pituitary-derived GH3 and LβT2 cells. Integration of RNA-seq and ATAC-seq analyses, complemented by immunofluorescence, revealed transcriptional and chromatin accessibility changes associated with pituitary lineage commitment. We show that SOX2 overexpression alone is sufficient to repress lineage-associated transcription factor programs at the transcript, chromatin and protein levels, whereas NFIs exert both shared and lineage-specific regulatory effects. Moreover, our data support a model in which YAP acts upstream to induce SOX2 expression, while NFIs function downstream of SOX2 to fine-tune lineage commitment.

Together, these findings identify the YAP/TEAD–SOX2–NFI axis as a core regulatory network controlling the balance between PSC maintenance and differentiation. This axis provides a framework to better understand PSC regulation, with potential implications for regenerative and therapeutic strategies in the pituitary.

Abstract citation ID: lvag096.107

OC6.1 - ECE_1021 - FOS and JUN regulate oxidative stress and steroidogenesis in human aldosterone-producing adenomas

Jia Wei[1], Eleonora Duregon[2], Mauro Papotti[2], Thomas Knoesel[3], Martin Bidlingmaier[1], Silviu Sbiera[4], Martin Reincke[1] and Tracy Williams[1]
[1]Medizinische Klinik und Poliklinik IV, Ludwig-Maximilians-Universität (LMU) München, Klinikum der Universität München, Munich, Germany; [2]Division of Pathology, Department of Oncology, University of Turin, Turin, Italy; [3]Institute of Pathology, Ludwig-Maximilians-Universität (LMU) München, Munich, Germany; [4]Department of Internal Medicine I, Division of Endocrinology and Diabetes, University Würzburg, University Hospital, Würzburg, Germany

Aldosterone-producing adenomas (APAs) are a major cause of primary aldosteronism (PA). While oxidative stress and steroidogenesis are intricately linked in adrenal disorders, their interplay and mechanistic basis in APA pathogenesis remain to be fully elucidated. Here, by integrating RNA sequencing of oxidative stress-exposed human adrenocortical cells with spatially-resolved transcriptomic profiling of human adrenal sections, we uncover a previously unrecognized role for the activator protein-1 (AP-1) transcription factors FOS and JUN as key mediators linking oxidative stress to steroidogenesis in PA. Their expression and activation are spatially restricted, coinciding with regions of elevated oxidative stress. Phosphorylated FOS and JUN were exclusively detected in the adrenal cortex adjacent to functional adenomas (APAs and cortisol-producing adenomas), with negligible levels in cortex adjacent to non-functional adenomas and in normal adrenal cortex. In vitro, oxidative stress induced the upregulation and activation of FOS and JUN. Conversely, co-overexpression of FOS and JUN suppressed key steroidogenic genes (*StAR*, *CYP11B1*, *CYP11B2*), reduced aldosterone and cortisol secretion, and increased reactive oxygen species accumulation. Together, this work demonstrates that FOS and JUN are central to coordinating the redox-steroidogenesis axis, linking molecular changes in the peritumoral cortex to tumor function and microenvironmental remodeling.

Abstract citation ID: lvag096.108

OC6.2 - ECE_3237 - Role of the mineralocorticoid receptor in the physiology of the adrenal cortex and the development of aldosterone producing adenomas

May Fayad[1,2], Rami M. El Zein[1], Nicolo Faedda[1], Rita Chamoun[3], Parisa Rezvanisanijouybari[2], Ourida Koual[1], Linghui Kong[1], Isabelle Giscos-Douriez[1], Oliver Domenig[4], Marko Poglitsch[4], Stephanie Baron[5], Fabio Fernandes-Rosa[1], Eleanor Davies[2], Sheerazed Boulkroun[1] and Maria-Christina Zennaro[1,6]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]PARCC, Université Paris Cité—Inserm U970, Paris, France; [2]School of Cardiovascular and Metabolic Health, BHF Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow, United Kingdom; [3]Maastricht University Medical Center, Maastricht Limburg, The Netherlands; [4]Attoquant Diagnostics, Vienna, Austria; [5]Assistance Publique-Hôpitaux de Paris, Service de physiologie, Hôpital Européen Georges Pompidou, Paris, France; [6]Assistance Publique-Hôpitaux de Paris, Service de génétique, Hôpital Européen Georges Pompidou, Paris, France

Background: Primary aldosteronism (PA) is a major cause of secondary arterial hypertension, characterized by autonomous aldosterone production. The mineralocorticoid receptor (MR) binds aldosterone and is expressed in the adrenal cortex specifically in the zona glomerulosa (ZG) and in aldosterone-producing adenomas. Given the role of MR in tissue remodeling and its expression in aldosterone-producing cells, we hypothesized that MR could be involved in the pathophysiology of PA through autocrine-paracrine mechanisms.

Objectives: To define the cell-autonomous roles of MR in aldosterone-producing cells using ZG-specific MR knockout mice combined with single-nucleus transcriptomics.

Methods: We generated Cyp11b2-Cre-driven MR knockout (MRKOAd) mice and performed morphological, hormonal and molecular phenotyping under standard and low-salt diets. Single-nucleus RNA sequencing (snRNAseq) across four conditions was analyzed to define population-specific MR functions and plasticity mechanisms.

Results: MR deletion reduced Cyp11b2 and aldosterone synthase (AS) expression in the adrenal cortex, with sex-specific effects on ZG architecture, but no change in basal aldosterone levels. This was associated with reduced proliferation and PKA activation, without modification of Wnt/β-catenin signaling. Under low salt diet, increased aldosterone production was accompanied by ZG expansion and increased AS expression in wild type mice, which was abolished in MRKOAd mice of both sexes. snRNAseq analysis revealed three mechanistically distinct plasticity programs following LSD: (1) ZG maintained identity through MR-dependent proliferation; (2) ZG_ZF transition zone showed robust plasticity driven by environmental signals (10% MR-dependent); and (3) zona fasciculata resolved into two subpopulations - ZF1 underwent authentic MR-dependent ZG transdifferentiation supported by constitutive metabolic priming, while ZF2 showed Cyp11b2 induction without acquiring ZG identity. MR-dependent genes, representing 28% of plasticity genes, accounted for 69% of functional ZG signature changes and converged on metabolic pathways (oxidative phosphorylation, ATP synthesis, steroid biosynthesis), establishing MR as an orchestrator of metabolic reprogramming.

Conclusions: MR plays distinct, cell-population-specific roles across the adrenal cortex. MR maintains ZG function in an autocrine-paracrine loop under basal conditions and regulates proliferative capacity, ZG architecture sex-specifically, and orchestrates metabolic transformation required for adrenal cortex plasticity following a salt challenge.

Abstract citation ID: lvag096.109

OC6.3 - ECE_3218 - Noninvasive [11C]-Metomidate PET/CT versus adrenal vein sampling for subtyping primary aldosteronism: a prospective multi-centre trial

Hieu T. N. Tran[1,2,3], Ismail Bin Osman[1], Ada Teo[4,5], Aaron Tong[6], Colin Jingxian Tan[7], Michael Chien Sheng Tan[8], Kang Min Wong[9], Wei Rui Goh[2], Tar Choon Aw[8], Prasanna Sivanath Tirukonda[10], Elvin Lim Yuan[10], Shi Ling Ng[11,12], Daryl Hee[2,13], Yi Ting Tan[13], Chin Meng Khoo[4], Hoi Yin Loi[14], Peng Chin Kek[15], Du Soon Swee[15], Matthew Chuah[16], Wei Lin Tay[16], Szemen Yee[17], Kurumbian Chandran[17], Wai Kit Alvin Tan[18], Seyed Ehsan Saffari[2], Julie Zhu[19], Guo Liang[19], Luming Shi[19], Pek-Lan Khong[20], Roger Foo[11,12,21] and Troy H. Puar[1,2]

[1]Endocrinology, Changi General Hospital, Singapore, Singapore; [2]Duke-Nus Medical School, Singapore, Singapore; [3]Endocrinology, University Medical Center, Ho Chi Minh City, Vietnam; [4]Division of Endocrinology, Department of Medicine, National University Health System, Singapore, Singapore; [5]Singapore, Singapore; [6]Nuclear Medicine and Molecular Imaging, Singapore General Hospital, Singapore, Singapore; [7]Radiology, ParkwayHealth, Singapore, Singapore; [8]Laboratory Medicine, Changi General Hospital, Singapore, Singapore; [9]Radiology, Changi General Hospital, Singapore, Singapore; [10]Interventional Radiology, Changi General Hospital, Singapore, Singapore; [11]Yong Loo Lin School of Medicine, National University of Singapore, Cardiovascular Research Institute, Singapore, Singapore; [12]Cardiovascular Metabolic Disease Translational Research Programme, National University Health Systems, Singapore, Singapore; [13]Shimadzu-Changi General Hospital Clinomics Centre, Singapore, Singapore; [14]Diagnostic Imaging, National University Health, Singapore, Singapore; [15]Endocrinology, Singapore General Hospital, Singapore, Singapore; [16]Endocrinology, Sengkang General Hospital, Singapore, Singapore; [17]Endocrinology, Ng Teng Fong General Hospital, Singapore, Singapore; [18]Endocrinology, Tan Tock Seng Hospital, Singapore, Singapore; [19]Singapore Clinical Research Institute, Singapore, Singapore; [20]Clinical Imaging Research Centre, Singapore, Singapore; [21]Agency for Science Technology & Research, Institute of Molecular and Cell Biology, Singapore, Singapore

Introduction: Primary aldosteronism (PA) is a common cause of secondary hypertension. Adrenal vein sampling (AVS) remains the reference method for PA subtyping, but it is invasive and technically challenging, limiting patients access to curable adrenalectomy. We evaluated the accuracy of non-invasive ^{11}C-Metomidate (MTO) PET/CT compared with AVS for guiding treatment.

Methods: We conducted a prospective, within-patient, multicentre trial enrolling patients with confirmed PA. All participants underwent both AVS and MTO PET/CT. Subtyping results were reviewed in a multidisciplinary meeting to recommend medical or surgery therapy. Unilateral adrenalectomy was offered when lateralization was demonstrated by AVS (lateralization index ≥4 times using aldosterone-to-cortisol ratios of the dominant to non-dominant adrenal veins) and/or MTO PET/CT (SUVmax in adrenal adenoma >1.25 times of the SUVmax of contralateral adrenal). The primary endpoint was complete biochemical success more than six months post-surgery, assessed by PA surgical outcome (PASO) criteria. The study was powered to test for non-inferiority of MTO PET/CT versus AVS (margin

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

−17%; 90% power; α = .01). Secondary endpoints included prediction of classical unilateral PA using HISTALDO criteria with CYP11B2-immunohistochemistry staining, characterization of somatic driver mutations (Sanger and whole-exome sequencing), and evaluation of hybrid hormones (18-oxocortisol and 18-hydroxycortisol) as markers of *KCNJ5*-mutant unilateral PA. (ClinicalTrials.gov: NCT06100367)

Results: A total of 106 patients completed both subtyping tests (mean age 48.4 ± 10.1 years; 71% male), and 101 had at least 6 months post-treatment follow-up. Unilateral PA was identified by both tests in 30 patients, by PET/CT only in 17, and by AVS only in 18. Five patients with bilateral PA opted for surgery, and 1 with unilateral PA was lost to follow-up. Surgery was performed in 69 patients; 64 (92.8%) achieved complete biochemical success, 4 (5.8%) had absent biochemical success, and 1 pending final evaluation. CYP11B2-immunohistochemistry was available in 52 surgical specimens and showed classical unilateral PA in 46 (88.5%). MTO PET/CT and AVS correctly identified classical unilateral PA in 32 (69.6%) and 31 (67.4%) cases, respectively. Somatic mutation analysis ($n = 34$) detected PA driver mutations in 33 (97.1%): *KCNJ5* (52.9%), *CACNA1D* (14.3%), *ATP1A1* (6.1%), *ATP2B2* (2.0%) and *CTNNB1* (2.0%). Hybrid hormones levels were significantly higher in patients with *KCNJ5*-mutant versus patients with non-*KCNJ5*-mutant tumours and offers an opportunity to identify unilateral *KCNJ5*-mutant PA.

Conclusions: Subtyping using MTO PET/CT is non-inferior to AVS and identifies patients with surgically curable unilateral PA not identified with AVS. Molecular imaging with MTO PET/CT offers an alternative first-line subtyping approach when available.

Abstract citation ID: lvag096.110

OC6.4 - ECE_2050 - Multi-center validation of a circulating microRNA combination with machine learning for the lateralization of primary aldosteronism

Bálint Vékony[1,2,3], Gábor Nyirő[1,2,4], Zoltan Herold[1,5], Bálint Szeredás[1,2], Markus Kroiss[6], Chiara Grasselli[7], Sven Gruber[8], Tomaz Kocjan[9], Piotr Kmieć[10,11], Renata Świątkowska-Stodulska[10,11], Michal Hoffmann[12,13], Piotr Glinicki[14], Alicja Duquenne[14], Nikolette Szücs[1,2], Judit Tőke[1,2], Vanessa Fell[15], Bahaa Salama[15], Ismail Bin Osman[16], Troy Hai Kiat Puar[16,17], Irina Bancos[15], Felix Beuschlein[6,8,18], Martin Reincke[6] and Peter Igaz[1,2]

[1]Department of Internal Medicine and Oncology, Semmelweis University, Budapest, Hungary; [2]Department of Endocrinology, Semmelweis University, Budapest, Hungary; [3]Department of Molecular Genetics and National Tumor Biology Laboratory, National Institute of Oncology, Budapest, Hungary; [4]Department of Laboratory Medicine, Semmelweis University, Budapest, Hungary; [5]National Institute of Oncology, Budapest, Hungary; [6]Medizinische Klinik und Poliklinik IV, LMU Hospital, Ludwig Maximilien University, Munich, Germany; [7]Hypertension Unit of Second Internal Cardiovascular Medicine, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Reggio Emilia, Italy; [8]Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich (USZ) and University of Zurich (UZH), Zurich, Switzerland; [9]Department of Endocrinology, Diabetes and Metabolic Diseases, University Medical Center Ljubljana, Ljubljana, Slovenia; [10]Department of Endocrinology and Internal Diseases, Medical University of Gdańsk, Gdańsk, Poland; [11]Department of Endocrinology and Internal Medicine, University Clinical Center, Gdańsk, Poland; [12]Department of Hypertension and Diabetology, Medical University of Gdańsk, Gdańsk, Poland; [13]Department of Hypertension and Diabetology, University Clinical Center, Gdańsk, Poland; [14]EndoLab Laboratory, Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland; [15]Division of Endocrinology, Diabetes, Metabolism and Nutrition, Department of Internal Medicine, Mayo Clinic, Rochester, United States; [16]DUKE-NUS Medical School, Singapore, Singapore; [17]Changi General Hospital, Singapore, Singapore; [18]The LOOP Zurich—Medical Research Center, Zurich, Switzerland

Background: Distinguishing unilateral primary aldosteronism (UPA/APA) from bilateral adrenal hyperplasia (BAH) is essential for treatment selection, yet the gold standard, adrenal venous sampling (AVS) is invasive, technically demanding and its availability remains limited. We previously identified a 6-miRNA combination (miR-146a-5p, miR-24-3p, miR-130b-3p, miR-99b-5p, miR-151a-3p, miR-199a-3p) capable of distinguishing APA from BAH using a neural network and deep learning approach. External validation remains the critical bottleneck for clinical translation of such biomarker panels.

Aim: To validate our previous 6-miRNA combination on a larger, independent multi-center dataset.

Methods: Peripheral plasma samples from 205 patients with AVS-confirmed PA were collected from nine centers and combined with our original discovery cohort ($n = 108$), yielding a total of 313 samples. MiRNA expression was quantified utilizing RT-qPCR with cel-miR-39 as spike-in and let-7d-5p as endogenous controls. Initial cross-center analysis revealed significant batch effects possibly attributable to inter-plate, inter-time and/or inter-center variability. To address this, we implemented plate-wise Z-score normalization, calculating miRNA-specific Z-scores within each plate to harmonize measurements. We expanded our analytical framework to six machine learning algorithms: KERAS deep neural network, Random Forest, XGBoost, Support Vector Machine, Logistic Regression, and Naive Bayes. Core clinical parameters (age, sex, plasma aldosterone, renin, imaging findings) were integrated as additional features. Ensemble predictions were generated via soft and hard voting. Model performance was assessed using 5-fold cross-validation.

Results: Using models trained on the original ($n = 108$) dataset, the validation performance matched training performance, confirming generalizability. On the harmonized 313-sample dataset, Random Forest achieved the highest individual performance (AUC 0.828), with XGBoost (0.809) and Keras (0.805) performing comparably. Soft voting ensemble yielded an AUC 0.815, a balanced accuracy of 72.9%, and an overall F1-score of 0.725. For BAH identification, the positive predictive value reached 80.0% and specificity was 84.3%.

Conclusions: This multi-center study validates circulating miRNAs for non-invasive PA lateralization and establishes a harmonization framework enabling cross-population application. The 80% positive predictive value for BAH suggests clinical utility in identifying patients whose pharmacological treatment could begin much sooner, leaving further lateralization procedures for only UPA cases. Additional cohort expansion and prospective validation are warranted to confirm the clinical utility of the approach.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.111

OC6.5 - ECE_3441 - Transcriptome signatures associated with response to treatment in advanced adrenocortical carcinoma

Anne Jouinot[1], Francois Bouvard[1], Margot Lombard[1], Florian Violon[1], Maria Francesca Birtolo[1], Karine Perlemoine[1], Martin Gaillard[1], Fidéline Bonnet-Serrano[1], Victor Gravrand[1], Fabio Bioletto[1], Nesrine Benanteur[1], Yoann Martin[1], Lucie Adoux[1], Anna Angelousi[2], Patricia Vaduva[3], Ante Mandic[4], Darko Kastelan[4], Maria Elena Aloini[5], Antonio Stigliano[5], Anna Aurora Dedonno[6], Michaela Luconi[6], Anna Babińska[7,8], Renata Świątkowska-Stodulska[7,8], Felicia Alexandra Hanzu[9], Maite Rodrigo[9], Otilia Kimpel[10], Martin Fassnacht[10], Rossella Libe[1], Jérôme Bertherat[1] and Guillaume Assié[1]

[1]Université Paris-Cité, Institut Cochin, INSERM U-1016, CNRS UMR-8104, Paris, France; [2]First Department of Internal Medicine, Unit of Endocrinology, European Reference Network on Rare Endocrine Conditions (ENDO-ERN), Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece; [3]Department of Endocrinology, Diabetes and Nutrition, Rennes University Hospital, Rennes, France; [4]Endocrinology Department, University Hospital Centre Zagreb, Kispaticeva 12, Zagreb, Croatia; [5]Endocrinology, Department of Clinical and Molecular Medicine, Sant'Andrea University Hospital, Sapienza University of Rome, Rome, Italy; [6]Department of Experimental and Clinical Biomedical Sciences, University of Florence, Florence, Italy; [7]Department of Endocrinology and Internal Medicine, Faculty of Medicine, Medical University of Gdansk; [8]Department of Endocrinology and Internal Medicine, University Clinical Center, Gdansk, Poland; [9]Endocrinology Department, Hospital Clínic, Barcelona, Spain; [10]Division of Endocrinology and Diabetes, Department of Medicine, University Hospital, University of Würzburg, Würzburg, Germany

Background: Adrenocortical carcinoma (ACC) is a rare aggressive malignancy with a poor prognosis. Standard treatments, including mitotane, platinum-based chemotherapy, and immune checkpoint inhibitors (ICI), show limited efficacy, with response rates below 25%, although exceptional and durable responses are occasionally observed. This study aimed to identify transcriptomic signatures associated with treatment response in advanced ACC.

Methods: A total of 133 patients with metastatic ACC treated with mitotane monotherapy, platinum-based chemotherapy, or ICI were recruited from eight European centers. The primary endpoint was the best objective response according to RECIST radiological criteria. The cohort was intentionally enriched for complete or prolonged responses lasting more than 12 months.

Transcriptomes were generated from tumor RNA extracted from frozen or paraffin samples, using 3' RNA-sequencing (QuantSeq, Lexogen). Transcriptomic analyses included unsupervised clustering, differential gene expression analyses (DESeq2 and GSEA) comparing responders and non-responders, and estimation of immune and stromal cell populations (MCP-counter).

Results: Among the 84 patients with available clinical data (69% female, median age 49 y), mitotane was administered to 60 patients, with 11 responses (18%; 7 partial responses [PR] and 4 complete responses [CR]), 11 stable disease (SD, 18%) and 38 progressive disease (PD, 63%). Platinum-based chemotherapy was administered to 62 patients, with 20 responses (32%, 14 PR and 6 CR), 14 SD (23%) and 28 PD (45%). ICI were administered to 13 patients, with 4 responses (30%, all PR), 1 SD (8%) and 8 PD (62%).

Unsupervised clustering identified 4 main transcriptomic clusters. One cluster was enriched in ICI responders (3/4, 75% vs 1/9, 11% in other clusters; $P = .05$) and was characterized by enrichment in immune-related pathways (lymphocyte mediated immunity, immune response regulation, adaptative immune response) and by a higher proportion of T cells ($P = .0006$), and myeloid cells ($P < 10^{-5}$, $<10^{-6}$ and 0.0003 for monocytes/macrophages, dendritic cells and neutrophils respectively).

Differential expression analyses identified 104, 17, and 192 genes associated with response to mitotane, platinum-based chemotherapy, and ICI, respectively. Mitotane response was associated with higher expression of *PON3*, encoding a paraoxonase involved in redox signaling. Platinum response was associated with higher expression of *ACSM2A* and *ACSM2B*, encoding acyl-coA synthetase. In addition to immune pathway activation, response to ICI was associated with downregulation of Wnt signaling.

Conclusions: Transcriptomic profiling reveals distinct molecular signatures associated with treatment response in advanced ACC. These findings warrant validation in independent cohorts and may contribute to improved patient stratification in the future.

Abstract citation ID: lvag096.112

OC6.6 - ECE_1967 - Integrated liquid biopsy approach for detection of recurrences in adrenocortical carcinoma

David S. Tourigny[1], Lorenzo Tucci[2], Balqees Shabaan[3,4], Meng Jie Xu[5,6], Joshua Bain[5], Kassiani Skordilis[7], Miriam Felicitas Asia[8], Alessandro Prete[5,9], Ana Crastin[5], Fozia Shaheen[5], Ezra Leander Onesimu[5], Jan Idkowiak[5,10], Angela Taylor[5], Vasileios Chortis[5] and Cristina L. Ronchi[5,8]

[1]School of Mathematics, University of Birmingham, Birmingham, United Kingdom; [2]Medical and Surgical Sciences Department, Alma Mater Studiorum University of Bologna, Bologna, Italy; [3]University of Birmingham, Birmingham, United Kingdom; [4]Bahrain National Genome Center, Manama, Bahrain; [5]Department of Metabolism and Systems Science, University of Birmingham, Birmingham, United Kingdom; [6]Taihe Hospital, Hubei University of Medicine, Shiyan, China; [7]Birmingham, United Kingdom; [8]Department of Endocrinology, Queen Elizabeth Hospital Birmingham NHS Trust, Birmingham, United Kingdom; [9]National Institute for Health and Care Research (NIHR) Birmingham Biomedical Research Centre, University of Birmingham, Birmingham, United Kingdom; [10]Department of Endocrinology and Diabetes, Birmingham Women's and Children's NHS FT, Birmingham, United Kingdom

Background: Adrenocortical carcinoma (ACC) is a rare and aggressive malignancy with high rates of post-operative recurrence. Current surveillance relies on frequent imaging, which is costly, exposes patients to cumulative radiation, and may miss early relapse. Liquid biopsy approaches offer a non-invasive alternative, but their comparative and combined utility in ACC remains unclear.

Methods: In this prospective pilot study, we evaluated three liquid biopsy modalities for ACC monitoring: 1. circulating cell-free DNA (ccfDNA) targeted next-generation sequencing (NGS) for

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

somatic mutations in ACC-specific genes, 2. low-pass whole-genome sequencing (lpWGS) for copy number calling and circulating tumour DNA detection, and 3. urinary steroid metabolomics (USM) by gas chromatography/mass spectrometry (32 adrenocortical steroid metabolites). USM profiles were assessed by three clinicians and three mass-spectrometry experts. Ten patients with histologically confirmed ACC (9F/1M, median age 37.5 yrs, one atypical case) were followed longitudinally from diagnosis through post-operative surveillance, ie, 6-8 weeks (early post-OP), 3 and 6 months. Tumour tissue, baseline and serial plasma and 24-hour urine samples were analysed and compared with standard radiological assessments. The diagnostic performance of individual and integrated liquid biopsy approaches was assessed.

Results: Somatic single-nucleotide variants (SNVs) were identified in 70% of primary tumours and detected in baseline ccfDNA in 50% of patients, while lpWGS identified CNVs in 100% of tumour samples and a non-zero tumour fraction in 60% of baseline ccfDNA samples. During follow-up, four patients developed disease recurrence at standard imaging. ccfDNA sequencing detected recurrence in 2/4 patients, including one case identified exclusively by lpWGS. Post-operative USM profiles were available for 7 patients (urine samples being not available for the other 3 cases) and identified recurrence in both cases with radiology relapse – but with variable sensitivity depending on expert consensus criteria. An integrated approach combining ccfDNA targeted NGS, lpWGS, and USM achieved the highest diagnostic performance, with a sensitivity of 75% and specificity of 80% for recurrence detection.

Conclusions: Each liquid biopsy modality captures complementary biological features of ACC and presents specific strengths or weaknesses. An integrated, multimodal liquid biopsy strategy improves detection of disease recurrence compared with any single approach and represents a promising non-invasive adjunct to imaging for ACC surveillance. Larger prospective studies are warranted to validate these findings and refine clinical implementation.

Abstract citation ID: lvag096.113

OC7.1 - ECE_2484 - Pancreatic neuroendocrine neoplasms share germline DNA repair gene predisposition with breast, ovarian and colorectal cancer syndromes (BRCA2, CHEK2 and MMR)

Beata Jurecka-Lubieniecka[1], Malgorzata Ros-Mazurczyk[1], Aleksandra Sygula[1], Alexander Cortez[1], Marcela Krzempek[1], Anna Barbara Tuleja[2], Agnieszka Kotecka-Blicharz[1], Malgorzata Oczko-Wojciechowska[1] and Daria Handkiewicz-Junak[1]

[1]*Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie Państwowy Instytut Badawczy Oddział w Gliwicach, Gliwice, Poland;* [2]*Uniwersytet Medyczny Imienia Piastów Śląskich, Wrocław, Poland*

Mutations in DNA repair genes are major drivers of both hereditary and sporadic malignancies, including breast, ovarian, prostate, colorectal adenocarcinoma, and pancreatic cancer. Familial tumors are typically associated with earlier onset and a more aggressive clinical phenotype. Advances in diagnostics and therapies targeting defective DNA repair pathways provide opportunities to improve outcomes and quality of life. Current recommendations from the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO) support germline genetic testing patients with these malignancies.

In pancreatic neuroendocrine neoplasms (pNENs), germline alterations in DNA repair genes have recently emerged as significant contributors to tumorigenesis. Large-scale genomic studies conducted by the International Cancer Genome Consortium (ICGC) identified pathogenic germline variants in approximately 11% of 102 patients with pNENs, including alterations in BRCA1/2 and CHEK2—well-established predisposition genes for breast and ovarian cancers—as well as MUTYH, which is associated with colorectal cancer susceptibility. Comparable results have been reported in US cohorts, in which pathogenic germline variants were detected in 14% of pNEN cases. Notably, these variants were frequently identified in patients with apparently sporadic disease and without a family history suggestive of hereditary cancer syndromes.

In the present study, germline DNA from 57 Polish patients diagnosed with pNENs was analyzed using targeted next-generation sequencing of a panel of DNA repair genes. Germline variants were identified in 14 patients (24.6%), including individuals both with and without a positive family history of malignancy. Pathogenic variants in BRCA2 and CHEK2 were detected in two cases. In addition, variants of uncertain significance (VUS) were identified in mismatch repair (MMR) genes in seven patients, raising concern for a potential predisposition to colorectal cancer syndromes, similar to that observed in association with MUTYH alterations.

Our findings are consistent with previous genomic studies and indicate that the germline landscape of pNENs includes clinically meaningful alterations in DNA repair pathways, similar to those observed in other solid tumors. These results support routine germline testing in patients with clinically sporadic pNENs, along with testing of relatives when pathogenic variants are confirmed, as already reflected in NCCN recommendations for patients with pNENs. Such variants may serve as biomarkers with potential therapeutic implications, and affected patients require appropriate oncologic surveillance focused on hereditary cancer risks.

Integrating germline diagnostics with genetically informed therapies may represent an important step toward precision medicine in pNENs. However, larger multicenter studies are needed to validate these observations and optimize clinical implementation.

Abstract citation ID: lvag096.114

OC7.2 - ECE_1828 - Safety of biopsy in pheochromocytoma/paraganglioma: a multicentre cohort study

Liang Zhang[1], Gautier Tisserand[2], Yanting Shen[3], Mahdi Salehi[4], Laurence Amar[5,6], Yunying Cui[7], Renata Świątkowska-Stodulska[8,9], Sophie Moog[2], Jun Liu[3], Sriram Gubbi[10], Henrik Falhammar[11,12], Tomaz Kocjan[13,14], Peter Igaz[15,16], Julien Hadoux[2], William Young[4], Hanna Remde[17], Anna Babińska[8,9], Valeria de Miguel[18], Felix Beuschlein[19,20,21], Longfei Liu[22], Serena Palmieri[23], Jingjing Jiang[3], Alessa Fischer[19], Jeena Varghese[24], Ana Carreira[25,26], Mirko Parasiliti Caprino[27], Svenja Noelting[19,21], Yue Zhou[7], Tamara Prodanov[10],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Irina Bancos[4], Martin Fassnacht[17], Camilo Jimenez[24], Hussam Alkaissi[10], Anli Tong[7], Karel Pacak[28,29,30] and Joakim Crona[1]

[1]Department of Medical Sciences, Uppsala University, Uppsala, Sweden; [2]Service d'Oncologie Endocrinienne, Département d'Imagerie, Institut Gustave Roussy, Villejuif, France; [3]Department of Endocrinology and Metabolism, Zhongshan Hospital Fudan University, Shanghai, China; [4]Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Mayo Clinic, Rochester, Minnesota, United States; [5]Assistance Publique-Hôpitaux de Paris (AP-HP) Centre, Hôpital Européen Georges Pompidou, Unité Fonctionnelle d'Hypertension Artérielle, Centre de référence des maladies de la surrénale, Université Paris Cité, Paris F-75015, France; [6]Inserm, équipe labellisée Ligue contre le cancer, centre de recherche des Cordeliers, université Paris-Cité, Sorbonne université, Paris 75006, France; [7]Department of Endocrinology, Key Laboratory of Endocrinology, National Health Commission of the People's Republic of China, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing 100730, China; [8]Department of Endocrinology and Internal Medicine, Faculty of Medicine, Medical University of Gdańsk, Poland and University Clinical Centre, Gdańsk, Poland; [9]Department of Endocrinology and Internal Medicine, University Clinical Centre, Gdańsk, Poland; [10]National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892, United States; [11]Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm SE-171 76, Sweden; [12]Department of Endocrinology, Karolinska University Hospital, Stockholm SE-171 76, Sweden; [13]Department of Endocrinology, Diabetes and Metabolic Diseases, University Medical Centre Ljubljana, Ljubljana, Slovenia; [14]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia; [15]Department of Endocrinology, Faculty of Medicine, Semmelweis University, Korányi Str. 2/a, Budapest 1083, Hungary; [16]Department of Internal Medicine and Oncology, Faculty of Medicine, Semmelweis University, Korányi Str. 2/a, Budapest 1083, Hungary; [17]Department of Medicine, Division of Endocrinology and Diabetes, University Hospital Würzburg, University of Wuerzburg, Oberdürrbacherstrasse 6, Wuerzburg 97080, Germany; [18]Servicio de Endocrinología, Hospital Italiano de Buenos Aires, Ciudad de Buenos Aires, Argentina; [19]Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich (USZ), and University of Zurich (UZH), Zurich CH-8091, Switzerland; [20]The LOOP Zurich—Medical Research Center, Zurich, Switzerland; [21]Department of Medicine IV, LMU University Hospital, LMU Munich, Munich 80336, Germany; [22]Department of Urology, Xiangya Hospital, Central South University, 87 Xiangya Road, Changsha 410008, Hunan, China; [23]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan 20122, Italy; [24]Department of Endocrine Neoplasia and Hormonal Disorders, The University of Texas MD Anderson Cancer Center, 1400 Pressler Street, Houston TX 77030, United States; [25]Unité Hypertension Artérielle, Centre de références en maladies rares de la surrénale, Université Paris Cité, AP-HP, Hôpital Européen Georges Pompidou, DMU Carte, Paris, France; [26]Department of Endocrinology, Diabetes and Metabolism, Hospitais da Universidade de Coimbra, Unidade Local de Saúde de Coimbra, Coimbra 3004-561, Portugal; [27]Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [28]Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, United States; [29]Faculty of Medicine, 5th Department of Medicine, Commenius University, Bratislava, Slovakia; [30]AKESO, Centre of Adrenal Endocrine Tumours, Prague, Czech Republic

Background: Biopsy of phaeochromocytomas and paragangliomas (PPGLs) is discouraged due to the perceived risk of catecholamine-related complications. However, a recent systematic review showed that this recommendation is primarily supported by case reports.

Methods: This multicentre retrospective cohort study included patients with PPGLs who underwent percutaneous biopsy. The predefined primary outcome was biopsy-related mortality rate (95% confidence interval [CI]) for biopsies performed at participating centres, since fatal cases elsewhere would be unlikely to be referred. Secondary outcomes included the incidence (95% CI) of serious catecholamine-related and non-catecholamine-related complications among all included patients.

Findings: Across 19 centres, 222 patients underwent 234 biopsies. Among these, 67% (136/203) had elevated epinephrine/norepinephrine (or metabolites) and 12·7% (29/229) received alpha-adrenoceptor blockade before biopsy. One death, due to biopsy-related infection, was reported. The mortality rate was 0·9% (1/106, 0·02-5·1%) among patients whose biopsies were performed at participating centres. Serious catecholamine-related complications occurred after four biopsies (1·7% [4/233, 0·5-4·3%]) and included tachyarrhythmia, hypertensive crisis, and/or cardiogenic shock. No serious catecholamine-related complications occurred in patients without catecholamine excess ($n = 67$) or following biopsy of metastatic lesions ($n = 120$). Serious non-catecholamine-related complications occurred after ten biopsies (4·3% [10/233, 2·1-7·8%]), mainly bleeding and infection.

Interpretation: Percutaneous biopsy of PPGLs was associated with a 0·9% mortality-rate. Serious complications occurred in 6·0%, of which most were not catecholamine-related. These findings challenge current recommendations that biopsy should be avoided in suspected or confirmed PPGL, and support a personalised, risk-benefit-based approach to the procedure.

Abstract citation ID: lvag096.115

OC7.3 - ECE_1415 - Glucocorticoid inhibition enables mono- and bispecific CAR-T cells to overcome immunotherapeutic resistance in adrenocortical carcinoma

Marc Philipp Schauer[1,2], Weber Justus[2], Laura Sophie Landwehr[1], Andrea Stabile[2], Peter Spieler[2], Barbara Altieri[1], Silviu Sbiera[1], Hermann Einsele[2], Martin Fassnacht[1] and Hudecek Michael[2,3]

[1]Würzburg, Germany; [2]Department of Internal Medicine II, Chair for Cellular Immunotherapy, University Hospital Würzburg, Würzburg, Germany; [3]Branch Site Cellular Immunotherapy, Fraunhofer Institute for Cell Therapy and Immunology (IZI), Würzburg, Germany

Glucocorticoids (GC) are secreted by ~60% of adrenocortical carcinoma (ACC) lesions and negatively affect immune-recognition and -therapy. Despite our previous observation that ROR1 expression is tightly linked to and triggered by GC secretion in ACC, GC inhibition induced a significant reduction of ROR1 making combinatorial CAR-T cell therapies with clinically relevant GC inhibitors obsolete.

Hence in this study, we applied transcriptomic and proteomic target screens to identify new potential CAR targets to overcome this ACC-intrinsic antigen-modulating resistance mechanism. In our screens, we identified B7-H3 - an immunomodulatory CAR

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

target - to be significantly upregulated in a large ACC patient cohort ($n = 135$) while being strongly associated with worse clinical outcome and poor overall survival. We observed B7-H3 to be inversely regulated to ROR1. Molecular analyses revealed a strong increase of B7-H3 upon GC inhibition driven by improved intratumoral STING pathway signaling that is usually abrogated upon glucocorticoid receptor (GR) signaling and ROR1 upregulation. We show that GCs induce ROR1 driven cancer proliferation, while GC inhibition upregulates B7-H3 by disrupting GR/NF-κB complex tethering enabling nuclear translocation of Stat3 and NF-κB. Phosphoproteomic analyses confirmed a direct link to B7-H3 induction and target modulation through pStat3 and pNF-κB. To further utilize this GC-related antigen interplay and to overcome antigen-mediated resistance, we developed different mono- and dual targeting CAR-T cells that showed potent antitumor efficacy alone and in combination with GC inhibitors. However, single transcriptomic data indicated B7-H3 expression in some healthy tissues increasing the risk of on-target off-tumor toxicity. Hence, we exploited the role of co-opted intracellular proximal T cell signaling molecules that can be repurposed into T cell surface receptors to engineer a synthetic logic gate CAR-T cell platform. By switching target binding domains, we were able to generate an asymmetric Functionally Layered and Unequal eXpression (FLUX)-CAR system which enables gradient-level AND-gating through spatially defined adaptor placement. When testing FLUX-CAR-T cells alone and together with GC inhibitors, we could selectively eliminate high antigen expressing ACC while obviating CAR-T cell killing in low single antigen positive tissues and inducing complete and persistent ACC tumor eradication in preclinical models.

Taken together this study provides a new ACC-specific GC-related therapy resistance mechanism as well as a safe and broadly applicable new CAR-T cell platform to overcome antigen-dependent therapeutic failure in GC secreting ACC.

Abstract citation ID: lvag096.116

OC7.4 - ECE_1921 - Sex-specific determinants of treatment response and progression in neuroendocrine tumours: a multicentre gender-based analysis of SSAs and PRRT

Camilla Mancini[1,2], Virginia Zamponi[1,2], Roberta Modica[3], Manuela Albertelli[4], Mariapia Brizzi[5], Giulia Puliani[6], Andrea Lania[7], Elisa Giannetta[8], Maria Chiara Zatelli[9], Erika Grossrubatscher[10], Antongiulio Faggiano[11] and Rosaria Maddalena Ruggeri[12]

[1]Endocrinology Unit, Sant'Andrea Hospital, Department of Clinical and Molecular Medicine and Department of Molecular Medicine, Sapienza University of Rome, ENETS Center of Excellence, Rome, Italy; [2]Department of Molecular Medicine, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy; [3]Endocrinology, Diabetology and Andrology Unit, Department of Clinical Medicine and Surgery, Federico II University of Naples, Naples, Italy; [4]Endocrinology Unit, Department of Internal Medicine and Medical Specialties (DIMI), University of Genova, Genoa 16132, Italy, Genoa, Italy; [5]Department of Oncology, University Hospital San Luigi Gonzaga, University of Turin, Orbassano, Italy; [6]CIAMPINO, Italy; [7]Endocrinology, Diabetology and Andrology Unit, IRCCS Humanitas Research Hospital, Rozzano 20089, Italy; [8]Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy; [9]Section of Endocrinology, Geriatrics and Internal Medicine, Department of Medical Sciences, University of Ferrara, Ferrara, Italy; [10]Endocrine Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [11]Endocrinology Unit, Department of Clinical and Molecular Medicine, Sant'Andrea Hospital, Sapienza University of Rome, ENETS Center of Excellence, Rome, Italy; [12]Endocrinology Unit, Department of Human Pathology of Adulthood and Childhood DETEV, University of Messina, Messina 98125, Italy

Background: Sex- and gender-based medicine is gaining relevance in oncology, highlighting how biological sex and gender-related factors may influence cancer outcomes. However, data on sex-related differences in prognosis, treatment efficacy, and tolerability in neuroendocrine tumours(NETs) remain limited.

Aim: To evaluate the impact of sex on clinical characteristics, treatment patterns, efficacy, and tolerability of somatostatin analogues (SSAs) and peptide-receptor-radionuclide-therapy (PRRT) in patients with gastroenteropancreatic neuroendocrine tumours (GEP-NETs).

Materials & Methods: This was a retrospective multicentre study including patients with GEP-NETs from 16 Italian centres participating in the NIKE project. Demographic data, disease characteristics, comorbidities, lifestyle factors, and treatment-related efficacy and safety outcomes for SSAs and PRRT were collected and analysed.

Results: A total of 500 patients were included (267 men, 233 women), with a median follow-up of 69 months. Mean age at diagnosis was significantly higher in men than in women (59.09 $\pm$ 13.8 vs 56.06 $\pm$ 14.4 years, $P = .018$). Men more frequently presented with advanced-stage disease ($P < .05$) and metastatic disease at diagnosis (67.4% vs 53.0%, $P < .001$).

Men also showed a higher prevalence of comorbidities (diabetes: 33.1% vs 19.0%, $P < .001$; hypertension: 49.6% vs 39.7%, $P = .026$) and unhealthy lifestyle factors, including alcohol consumption and smoking ($P < .001$).

PRRT was more frequently administered in men than in women (40.8% vs 28.9%, $P < .001$).

Although no sex differences were observed in the proportion of patients treated with SSAs, women showed a significantly longer duration of response to SSAs compared with men ($P = .003$). Progression-free survival (PFS) was longer in women treated with SSAs (median 108 vs 84 months in men) and with PRRT (60 vs 48 months), although the latter difference did not reach statistical significance ($P = .333$).

Regarding tolerability, no significant sex differences were observed in overall adverse events related to SSAs or PRRT. However, when stratifying patients by median year of diagnosis, women developed SSA-related adverse events earlier than men (mean time: 6.00 $\pm$ 7.21 vs 16.82 $\pm$ 25.49 months, $P = .030$), whereas men experienced a higher incidence of PRRT-related nephrotoxicity ($P = .034$).

Multivariable Cox regression analysis for PFS in SSA-treated patients showed that alcohol consumption was the only independent predictor of disease progression in the overall cohort ($P = .005$), regardless of sex. Sex-stratified analyses revealed distinct risk profiles: in women, advanced stage at diagnosis was the only significant predictor of progression (HR = 6.2, $P = .034$), while in men alcohol consumption was significantly associated with progression (HR = 2.09, $P = .01$), with metastatic disease at diagnosis showing a borderline association ($P = .051$).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: Sex influences the natural history of NETs, treatment allocation, and response to SSAs and PRRT. Although not an independent predictor of progression, sex modulates the effect of key prognostic factors, including alcohol consumption and disease stage. A gender-informed approach may support more personalised management of NET patients.

Abstract citation ID: lvag096.117

OC7.5 - ECE_3450 - Intraoperative hypotension versus hypertension in patients with pheochromocytoma and paraganglioma: a multicenter Chinese study of 998 cases

Minghao Li[1], Ndikuriyo Herve Pasteur[1], Junjie Chen[1], Yong Wang[2], Danlei Chen[3], Jingjing Jiang[4] and Longfei Liu[1]
[1]*Xiangya Hospital, Central South University, Changsha, China;* [2]*The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, Guangdong, China;* [3]*The First People's Hospital of Yunnan Province, Kunming, Yunnan, China;* [4]*Zhongshan Hospital, Fudan University, Shanghai, China*

Background: Pheochromocytomas and paragangliomas (PPGLs) are neuroendocrine tumors characterized by excessive catecholamine production, which predisposes patients to intraoperative hypertensive crises (IHC) and/or hypotension (IOH). This study aims to investigate the perioperative characteristics and identify risk factors associated with different hemodynamic profiles during PPGL surgery.

Methods: We conducted a retrospective analysis of patients with pathologically confirmed PPGL who underwent surgical resection between January 2010 and December 2024 across four tertiary medical centers in China. Data collected included demographic, clinical, tumor-related, genetic, and perioperative variables. IOH was defined as mean arterial pressure (MAP) <65 mmHg, and IHC as systolic blood pressure ≥180 mmHg. Patients were stratified into four hemodynamic groups: no IOH/IHC, IHC only, IOH only, and both IOH/IHC. Multivariable logistic regression was employed to identify independent predictors for each hemodynamic category.

Results: Among the 998 patients analyzed, 324 had no IOH/IHC, 306 had IHC only, 181 had IOH only, and 187 experienced both IOH and IHC. Postoperative intensive care unit (ICU) admission was highest in the combined IOH/IHC group (56.5%, 105/186), compared to the IOH-only (38.7%, 70/181), IHC-only (24.3%, 74/305), and no-instability groups (17.6%, 57/324). In multivariable analysis, older age (OR 4.931, 95% CI 1.523-15.965), presence of pre-surgical hypertension (OR 0.554, 95% CI 0.366-0.839), and preoperative α-blocker use (OR 2.006, 95% CI 1.225-3.487) were independent predictors of IOH only. Laparoscopic surgery (OR 1.483, 95% CI 1.001-2.197) and kinase-signaling pathway gene variants (OR 2.561, 95% CI 1.749-3.751) were predictors of IHC only. For combined IOH/IHC, independent predictors included older age (OR 5.319, 95% CI 2.077-13.623), tumor diameter ≤4.05 cm (OR 0.513, 95% CI 0.339-0.777), and kinase-signaling gene variants (OR 2.681, 95% CI 1.701-4.224).

Conclusions: Patients with PPGL exhibit distinct hemodynamic profiles during surgery, each associated with specific risk factors. Perioperative strategies—including surgical approach selection and α-blocker administration—should be tailored based on age, tumor size, pre-surgical hypertension, and genetic background to optimize intraoperative hemodynamic stability.

Abstract citation ID: lvag096.118

OC7.6 - ECE_2870 - SOX2-positive cells in pheochromocytoma and paraganglioma: implications for tumour initiation and maintenance

Yasmine Kemkem[1], Mark Quinn[2], Bence Kover[1], Alice Santambrogio[1,3], James Kaufman-Cook[1], Olivia Sherwin[1,3], Dimitria Brempou[2], Miriam Vazquez Segoviano[1], Paul Carroll[4], Louise Izatt[5], Paul Chapple[6], Stefan Bornstein[1,3], Nicole Bechmann[3], Charlotte Steenblock[3], Rebecca Oakey[2] and Cynthia Andoniadou[1,3]
[1]*Centre for Craniofacial and Regenerative Biology, King's College London, London, United Kingdom;* [2]*Department of Medical and Molecular Genetics, King's College London, London, United Kingdom;* [3]*Department of Internal Medicine III, University Hospital Carl Gustav Carus, Technische Universität, Dresden, Germany;* [4]*Guy's & St. Thomas' NHS Foundation Trust, London, United Kingdom;* [5]*Department of Clinical Genetics, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom;* [6]*Faculty of Medicine and Dentistry, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom*

Pheochromocytomas (PCCs) and paragangliomas (PGLs) are rare neuroendocrine tumours which arise from neural crest–derived chromaffin cells of the adrenal medulla and extra-adrenal paraganglia, respectively. Metastatic disease occurs in up to 40% of PPGLs and is associated with a median overall survival of seven years. Despite advances in the molecular characterisation of PPGLs, progress in prognostic stratification and the development of targeted therapies remains limited, reflecting an incomplete understanding of the cellular mechanisms underlying tumour initiation and progression. In several malignancies, tumour growth and dissemination are sustained by cells with stem-like properties, due to their ability to self-renew and give rise to differentiated cells. We have recently shown that, in the human adrenal, a subset of sustentacular cells are postnatal adrenomedullary stem cells expressing the stem cell transcription factor SOX2, specified along the neural crest migratory trajectory. In this study, we investigated whether SOX2-positive cells in PCCs and PGLs display features consistent with a tumour-initiating cell population.

Using transcriptomic profiling of 10 published and 3 new tumour datasets and expression analyses of an additional cohort of 19 tumours, we demonstrate the presence of SOX2-expressing cells across a broad range of PPGLs independent of tumour location, aggressiveness, or underlying genetic mutation. Transcriptomic analyses reveal a highly proliferative cell population co-expressing SOX2 and chromaffin cell markers. To determine whether expression of SOX2 is sufficient to promote proliferation, we overexpressed *Sox2* in PC12 cells, a well-characterised rat pheochromocytoma cell line. Cell cycle analysis showed that *Sox2* expression does not confer a proliferative advantage, supporting its role in PPGL as a stem cell hallmark. However, PPGLs enriched in SOX2+ cells showed differential expression of several genes encoding pro-tumourigenic paracrine

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

factors. Ligand-receptor analysis further confirmed signalling from tumour chromaffin cells to other cell populations. In summary, *in silico* analyses support that tumours enriched in proliferative SOX2+ chromaffin tumour cells have distinct oncogenic gene expression and a secretory signature consistent with cancer promotion. This suggests both a direct contribution and an indirect paracrine role of SOX2+ tumour chromaffin cells in PPGL tumour maintenance.

Isolation of SOX2-positive PPGL cells under stem cell–promoting conditions, followed by xenotransplantation onto the chicken chorioallantoic membrane, demonstrated their capacity for expansion and metastatic behaviour *in ovo*, confirming their tumour-initiating potential.

This study redefines the cellular origins of PPGLs by identifying SOX2-positive tumour cells with tumour-initiating potential. These findings may inform improved PPGL tumour stratification and offer new avenues for therapy.

Abstract citation ID: lvag096.119

OC8.1 - ECE_3665 - CheckED—EU Real-World endocrine-disrupting chemicals (EDCs) profiling enables exposure-informed prevention counselling and tracks reductions in exposure proxy indices across everyday settings.

Aleksandra Rutkowska[1,2], Szymon Graczyk[1], Aleksandra Olsson[1] and Heidrun Fammler[3]
[1]*DetoxED LTC, Gdańsk, Poland;* [2]*Division of Community Nursing & Health Promotion, Medical University of Gdansk, Gdańsk, Poland;* [3]*Baltic Environmental Forum Germany, Hamburg, Germany*

Endocrine-disrupting chemicals (EDCs) are ubiquitous environmental exposures and preventable upstream drivers of endocrine and metabolic disorders, including obesity, insulin resistance, thyroid dysfunction and reproductive disease. Yet European endocrinology lacks scalable real-world systems to quantify EDC multi-class exposure burden, identify modifiable sources, and demonstrate achievable exposure reduction supporting prevention and clinical counselling. This gap is critical for women of reproductive age, as pregnancy is a sensitive window shaping maternal metabolic adaptation, placental signalling and foetal endocrine development (DOHaD).

To quantify EU-wide EDC multi-class exposure burden in real-world settings, and determine whether feasible micro-habit changes can measurably reduce exposure burden relevant to endocrine prevention.

Data were collected using the CheckED mobile application developed within LIFE ChemBee and Interreg NonHazCity 3. The app prospectively captured anonymised, free-of-charge structured data on demographics, anthropometry, housing indicators, plastic/food-contact behaviours, and exposure-relevant routines across 15 EU countries. Exposure to bisphenols, phthalates, alkylphenols and brominated flame retardants (BFRs) was estimated using algorithm-derived class-specific composite exposure proxy indices (continuous scores) based on exposure-source databases implemented in the application. The study included 7061 women (260 pregnant) and 2102 men; 9988 participants completed one assessment and 1370 repeated assessments enabling within-person longitudinal comparisons.

Over 99% of participants had non-zero exposure proxy indices for at least one EDC class. Men showed higher bisphenol, phthalate and alkylphenol proxy indices than women (all $P \leq .00001$). Pregnancy was not associated with lower exposure proxy indices compared with non-pregnant women ($P = .38$). Higher BMI showed small but consistent correlations with exposure proxy indices across classes (Spearman $\rho \approx 0.14$-0.17). Among repeated users, bisphenol proxy scores decreased following micro-habit changes in lifestyle ($P = .006$) and the home environment ($P = .001$). Phthalates and alkylphenols did not change significantly in lifestyle ($P = .11$; $P = .15$), but decreased significantly in the home environment ($P = .0006$; $P = .001$).

EU real-world exposure profiling reveals consistent sex-specific EDC multi-class exposure burdens and demonstrates that pregnancy is not associated with lower exposure proxy indices, highlighting an urgent prevention gap in reproductive endocrinology. BMI-associated higher exposure proxy burden supports the clinical relevance of EDC exposure in metabolic risk stratification. Importantly, feasible micro-habits produced measurable reductions in exposure proxy indices, indicating prevention is implementable beyond awareness campaigns. CheckED provides a scalable digital support tool for endocrinologists to deliver exposure-informed counselling. These findings position endocrine disruption as a preventable driver of chronic endocrine disease risk in Europe and support integrating source-targeted prevention into endocrine care and EU public health strategies.

Abstract citation ID: lvag096.120

OC8.2 - ECE_2234 - Exposure to endocrine-disrupting chemicals (EDCs) in breast milk (BM) and infant urine samples: findings from the LIFE-MILCH project

Maria Street[1], Anna-Mariia Shulhai[1], Annalisa Pelosi[1], Francesca Alberghi[2], Marta Fontana[2], Silvia Paterlini[1], Maria Maddalena Brambilla[1], Cecilia Catellani[2], Emanuela Davolio[2], Francesca Nuti[3], Feliciana Real Fernandez[3], Chiara Scopa[1], Cecilia Rotteglia[2], Beatrice Righi[2], Chiara Sartori[2], Alessandro De Fanti[2], Vassilios Fanos[4], Anna Maria Papini[3] and Paola Palanza[1]
[1]*Medicine and Surgery, University of Parma, Pediatric Clinic, Parma, Italy;* [2]*AUSL Reggio Emilia, Reggio nell'Emilia, Italy;* [3]*University of Florence, Florence, Italy;* [4]*University of Cagliari, Cagliari, Italy*

Introduction: The LIFE-MILCH project (www.lifemilch.eu) investigates exposure to EDCs in mother-infant pairs. Analyzing EDCs in BM and in mothers' and infants' urine samples (IU), with occupational and lifestyle exposure data, the study explores associations of exposure with growth, adiposity, pubertal stages, anogenital distances and neurodevelopment. We present data on exposure to EDCs in BM and IU during the first year of life.

Methods: 689 mother-infant pairs were enrolled in Parma,Reggio Emilia and Cagliari, Italy. Healthy mothers with uncomplicated pregnancies were enrolled at 36-41weeks of gestational age. We present data on 336 BM and IU samples collected at 1(T1), 3(T2), and 6(T3) months after delivery. EDCs were measured by UPLC-MS/MS[4 different bisphenols,11 polycyclic aromatic hydrocarbons(PAHs),14 phthalates and metabolites(PHTHs),7parabens,3polar pesticides,2 pyrethroids].

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: Among bisphenols, BPA had the highest detection rate in BM (51.2% at T1 and 49.8% at T3), while it was in 32.9% of IU samples at birth and in 67.6% at T3. BPS was found in 10.7% of BM samples at T1 and in 18.3% at T3;in 22.4% IU samples at T0 and in 41.2% at T3. BPFDGE was almost undetectable in BM but was found in IU. PAHs, except indeno(1,2,3-cd)pyrene and dibenz(a,h)anthracene at T1, were scarcely detectable in BM but were stable in IU samples(up to 27.7%). Among parabens,MePB and EtPB were the most prevalent. In BM, MePB was in 51.2% at T1 and in 56.2% at T3;EtPB was in 42.3% at T1 and in 52.6% at T3. In IU, MePB was in 52.6% at T0 and in 82.4% at T3;EtPB was in 27.6% at T0 and 41.2% at T3. Glufosinate was in 27.4% of BM samples at T1 and in 31.9% at T3; in 44.7% IU samples at T0 and in 38.2% at T3. In all BM and urine samples, high levels of PHTHs were detected. DBP was in 90.2% of BM samples at T1 and in 86.5% at T3;in 30.3% IU samples at T0 and in 79.4% at T3. MBP,DEP,MEP,BBP,MnOP,MEOHP, were similarly detectable at different % over time in both BM and IU.DEHP,DnOP were subtly detectable.Overall,detectable EDCs were above the LOQ in approximately 50% of samples. EDCs in BM increased the probability of finding the same chemicals in IUs,but other sources contributed over time. Relationships with mothers' nutrition were investigated,yielding interesting findings.

Conclusions: Findings confirm BM as a vehicle of environmental contamination. As infancy represents a critical window of exposure, this calls for better biomonitoring, awareness, prevention campaigns and actions to reduce exposure.

Abstract citation ID: lvag096.121

OC8.3 - ECE_3540 - Mapping the European regulatory landscape of endocrine-disrupting plastic chemicals

Olwenn Martin[1,2]
[1]*Plastic Waste Innovation Hub, UCL Arts and Sciences, London, United Kingdom;* [2]*Plastic Waste Innovation Hub, UCL Arts and Sciences, University College London, London, United Kingdom*

Background: A wide variety of chemical additives,, some of which are known endocrine disrupters are intentionally added to plastics to enhance their performance or appearance. As most are not covalently bound to the polymeric matrix, they can readily migrate from materials or micro- and nanoplastic particles (MNPs) during and after the often very short useful life of the product. Due to the ubiquity and multitude of uses of plastic materials, releases of plastic additives to their surrounding environment across their lifecycle are regulated across regulatory silos in multiple pieces of legislation. Common plastic additives were mapped against regulatory requirements for various uses at different lifecycle stages.

Methods: Through a bottom-up approach, the 417 high production volume, common, additives listed under ECHA's plastic additive initiative (PlasI), their function and the type of polymers in which they are typically used were mapped against the regulations listed in the European Chemical Agency chemical legislation database (EUCLEF). The text of all legislations within EUCLEF was reviewed for articles relevant to chemicals generally, plastic additives and those addressing endocrine disrupting properties of substances specifically.

Results: Only 3 PlasI additives have been listed in the REACH candidate list of substances of very high concern (SVHC) due to their ED properties; the plasticisers dibutylphthalate (DBP) and diethylhexylphthalate (DEHP), and the flame retardant triphenyl phosphate (TPP), while 7 are currently being assessed for their ED properties. The protection of workers and the safety of products will only cover ED additives that are also carcinogens, mutagens or reproductive (CMR) toxicants or have been identified as SVHCs. DBP and DEHP are currently still authorised for use in food contact materials and for the supply of drinking water. For cosmetics, 10 SVHC PlasI additives (including TPP and decabromodiphenyl ether) are neither prohibited, restricted or listed as allowed colourants, preservatives or UV filters. In medical devices, endocrine disrupting substances are only allowed in invasive devices above 0.1% by weight if no suitable alternative is available.

Discussion: This exercise demonstrated that only a handful of plastic additives with potential ED properties are currently covered by EU regulation. In addition to exemptions and derogations, there are also uses for which known ED plastic additives are authorised. There are encouraging legislative developments, such as a new hazard class for ED properties or digital product passports, but without requirements to routinely test for ED properties using new approach methodologies, these may have only limited impact.

Abstract citation ID: lvag096.122

OC8.5 - ECE_3147 - Bone mineral density (BMD) evaluated using REMS is associated during the first year of life with early life exposure to endocrine-disrupting chemicals (EDCs)

Anna-Mariia Shulhai[1], Virginia Beretta[1], Letteria Anna Morabito[2], Francesca Nuti[3], Michele Casoria[3], Federica Grassi[1], Tommaso Aversa[2], Domenico Corica[2], Giorgia Pepe[2], Andrea Dall'asta[1], Anna Maria Papini[3], Serafina Perrone[1], Malgorzata Wasniewska[2] and Maria Street[1]
[1]*Medicine and Surgery, University of Parma, Pediatric Clinic, Parma, Italy;* [2]*University of Messina, Messina, Italy;* [3]*University of Florence, Florence, Italy*

Background: Human data on early exposure to EDCs and bone outcomes remain limited. This study-clinical trial*(NCT06750523)* evaluated bone status from intrauterine life and investigated factors affecting BMD in infants. We present data on early-life exposure to EDCs and BMD from birth to 12 months of age.

Materials and methods: This prospective, longitudinal cohort study analyzed urinary concentrations of EDCs in 88 full-term, healthy AGA infants at 1month of age. 52 compounds were analyzed, including bisphenols(BPA,BPS,BPF,BPFDGE), phthalates(DBP,BBP, DEHP,DEP,DMP,DnOP,MBP,MBzP,MEHP,MEHHP,MEOHP,MEP,MMP, MnOP), parabens(EtPB,MePB,PrPB,iBuPB,iPrPB) and per- and polyfluoroalkyl substances (PFAS:11Cl- PF3OUdS,4-2_FTS,8-2_FTS,6-2_FTS,9Cl-PF3ONS,ADONA,FBSA,FOSA,GenX_HFPO-DA,PFBA,PFBS, PFDA, PFDS, PFDoDA, PFHpS, PFHxS, PFNA, PFNS, PFOA, PFOS, PFPHpA,PFPHxA, PFPeA, PFPeS, PFTrDA,PFTreDA, PFUnDA) by UPLC-MS/MS. BMD was assessed usingRadiofrequency Echographic Multi Spectrometry(REMS), and BMD z-scores were defined at 48hours after birth(V0),at 1(V1),3(V3),6(V6) and 12 months of life(V12). Associations between urinary EDC concentrations and BMD z-scores across time points were evaluated by correlation and principal component(PCA) analyses.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: At V0 BMD z-score was 1.31 ± 0.87; −0.09 + 0.61 at V1; −0.06 ± 0.99 at V3; −0.03 ± 0.97 at V6, and -0.04 ± 1.01 at V12. At birth, BMD z-scores were different in males and females (*P*:.028),but this disappeared thereafter. In the infant's urine, BPA was detected in 62.5% of samples, BPS in 19.3%;EtPB in 1.1%, MePB in 21.6%,PrPB in 9.1%. Among PFAS,6-2_FTS was detected in 73.9% of samples, PFBA in 70.5%,PFDA in 3.4%,PGHxS in 29.5%,PFNA in 15.9%,PFOA in 69.3%,PFOS in 76.1%, PFPHpA in 78.4%, PFPHxA in 63.6%. DBP was detected in 2.3%, MBP in 100%, MBzP in 22.7%, MEHHP in 62.5%, MEHP in 1.1%, MEOHP in 42.0% and MEP in 98.9%. BPA and PFDA were associated with BMD z-score at V0(r: −0.31, *P*:.025 and r:0.99, *P*:.038, respectively). MePB was associated with BMD z-scores at V6 and V12(r:−0.52,*P*:.044 and r:−0.738,*P*:.009).PFHxS, PFNA and PFOS presented associations with BMD z-scores at V6(r: −0.49, *P*:.015; r:−0.615, *P*:.037; r:−0.287,*P*:.030). Phthalates showed the most consistent associations with BMD at both V6 and V12. DEP showed a linear association with BMD z-scores at 6(r:−0.557, *P*:.039) and 12(r:−0.703, *P*:.035) months. MBP,MBzP and MEOHP were associated with BMD z-scores at V12(r:−0.346, *P*:.015; r: −0.654,*P*:.040; r:−0.501, *P*:.021). Notably, PCA found a cluster (19%) of BPA and phthalates(MBzP, MBP, MEOHP) with BMD z-score at V12, suggesting that higher exposure is associated with lower BMD at 1 year of age. Additionally, PFHxS contributed to BMD z-scores at V1, V3 and V6 (13.4%).

Conclusions: Early-life exposure to EDCs may be associated with lower BMD during the first year of life. This emphasizes that infancy is a vulnerable window for environmental exposure and skeletal development, highlighting the need to reduce EDC exposure for better bone health.

Abstract citation ID: lvag096.123

OC8.6 - ECE_2842 - Association of gestational exposure to a mixture of endocrine disrupting chemicals with placental function

Rutuja Dhamale[1], Tim Korevaar[1], Hans Krabbe[2], Robin Peeters[1] and Arash Derakhshan[1]
[1]*Rotterdam, The Netherlands;* [2]*Department of Clinical Chemistry and Laboratory Medicine, Medisch Spectrum Twente, Enschede, The Netherlands*

Introduction: Endocrine disrupting chemicals (EDCs) interfere with the endocrine system and the function of affiliated organs. The placenta regulates the maternal-fetal interface and is a major endocrine organ producing human chorionic gonadotropin (hCG). However, the potential of EDCs to interfere with placental function remains unclear.

Aim: To study the association of gestational exposure to a mixture of 22 EDCs (phthalates, bisphenols, perchlorate, thiocyanate, nitrate and pesticides) with placental function.

Methods: We investigated the association of the mixture with gestational age adjusted serum hCG concentrations, placental function markers (placental growth factor [PlGF], soluble fms-like tyrosine kinase [sFlt-1]) during early and mid-pregnancy, and placental weight at birth using Bayesian Kernal Machine Regression in women with uncomplicated pregnancies participating in Generation R cohort.

Results: In 1496 included women, higher exposure to EDCs during early pregnancy was associated with a lower hCG and placental weight. We identified fetal-sex specific effects, with more pronounced associations in women carrying a female fetus. The common drivers of these associations were mono-methyl, mono-isobutyl, mono-butyl and mono-2-heptyl phthalates (mMP, mIBP mBP, mHpP with posterior inclusion probabilities >0.40). Higher concentrations of mBzP was associated with higher hCG in women carrying female fetus and lower hCG in women carrying male fetus. We did not identify any association of the EDC mixture with placental function markers.

Discussion: Higher exposure to EDCs was associated with lower hCG concentrations and lower placental weight in a fetal sex-specific manner. Our results highlight the need for further experimental studies to elucidate underlying sex-specific modes of action of EDCs and to investigate the risk of pregnancy complications as a result of placental disruption by EDCs.

Abstract citation ID: lvag096.124

OC9.1 - ECE_3866 - Unravelling the sexually dimorphic role of adrenocapsular progenitor cells during stress adaptation of the adult adrenal gland

Panagiota Siatra[1], Diana Leuker-Cozma[1], Timothé Benoit[2], Yasmine Neirijnck[2], Stefan Bornstein[1], Andreas Schedl[2] and Charlotte Steenblock[1]
[1]*Department of Internal Medicine III, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany;* [2]*Université Côte d'Azur, Inserm, CNRS, Institut de Biologie Valrose, Nice, France*

Chronic stress is a pervasive concern in the modern society. The HPA axis dysregulation in chronic stress and psychiatric disorders is tightly linked with hypertrophy and hyperplasia of the adrenal gland. These stress-induced cellular adaptations may involve capsular progenitor behaviour. However, little is known about the contribution of resident progenitor cells to these stress-induced cellular changes. To address this, we used single-cell RNA-seq to investigate the regulation of adrenocapsular progenitors during restraint stress. We analyzed UMAP representations of the stressed and non-stressed mouse adrenal cortex, generated for the first time for both sexes, revealing sex-specific features. Within the adrenal capsule cluster, we observed a stress-induced shift in capsular progenitor populations in both sexes. More specifically, in the male adrenal capsule, the capsular markers *Nr2f2* and *Rspo3*, a signalling molecule involved in the control of cell renewal in the tissue, were enriched under stress. In contrast, the distribution of capsular markers remained unchanged in the female adrenal capsule between stressed and non-stressed condition. This sex-differential capsular response was further confirmed by qPCR analysis. To determine whether the observed shifts reflect altered recruitment or differentiation of capsular cells, we performed lineage tracing of *Gli1*$^{+}$ adrenocortical progenitors during restraint stress using a tamoxifen-inducible *Gli1:CreERT2/R26R:eYFP* mouse line and both sexes. In stressed males, migratory patches of *Gli1*$^{+}$ spindle-like cells appeared in the zona glomerulosa, resembling previously described adrenocortical neoplasms and expressing GATA4, a marker of the adrenogonadal primordium. In females, where *Gli1*$^{+}$ cells normally contribute to homeostatic tissue renewal, preliminary results suggest that the subcapsular patches of *Gli1*$^{+}$-derived cells are rather reduced under stress. Overall, this

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

may suggest that in female mice the process of capsular progenitor cell recruitment is reduced when the need for increased steroid production occurs. Collectively, these findings confirm a sexually dimorphic capsular response during restraint stress. Further analysis of differentially expressed genes in these capsular populations and shifts may reveal molecular candidates mediating remodeling and paracrine signaling between the capsule and adrenal cortex during stress. These factors could directly or indirectly modulate stress response and the steroid production, highlighting the capsule as an active regulator of adrenal stress physiology.

Abstract citation ID: lvag096.125

OC9.2 - ECE_1670 - Single-cell transcriptomic profiling reveals divergent endocrine, immune, and angiogenic programs between ACTH/CRH-secreting and non-secreting pheochromocytomas

Wan Su[1], Shiwei Chen[2], Jinghua Liu[1], Di Zhang[1], Zheng Zhang[2] and Lin Lu[1]
[1]*Endocrinology, Peking Union Medical College Hospital, Beijing, China;* [2]*Peking University First Hospital, Beijing, China*

Background: Ectopic ACTH and/or CRH-secreting pheochromocytomas are rare catecholamine-secreting tumors originating from adrenal medulla, which could also secrete ectopic adrenocorticotropic hormone (ACTH) and corticotrophin-releasing hormone (CRH), mimicking Cushing syndrome and complicating the diagnosis clinically. The extremely low incidence limits the comprehensive understanding and management for specific individuals accompanied with this kind of tumor. Furthermore, mechanisms of tumorigenesis and ectopic ACTH secretion in pheochromocytomas are unknown. Studying this rare type of tumor will help tailor therapies to the specifically molecular and metabolic characteristics of pheochromocytomas.

Methods and Materials: Fresh tumor and peritumoral specimens were collected from three ACTH + &CRH+ pheochromocytoma patients and three ACTH-&CRH- pheochromocytoma patients, and then were digested and sent to construct single-cell library as well as sequencing. Subsequent analysis and immunohistochemical staining were conducted to explore the difference of ACTH + &CRH+ pheochromocytomas from the ACTH-&CRH- ones and normal tissues.

Results: We constructed the linear trajectory of 2 types of pheochromocytomas. The cluster of intermediate cells that differentiated into mature ACTH + &CRH+ pheochromocytomas showing high expression of CEBPB, and the immunohistochemical staining revealed that CEBPB was higher in ACTH + &CRH+ ones. Besides, Higher expression of POMC and PNMT was observed in ACTH + &CRH+ pheochromocytomas compared with ACTH-&CRH- ones, being in accordance with the clinical information that three ACTH + &CRH+ pheochromocytoma patients had relatively higher catecholamine levels. T cells in ACTH + &CRH+ pheochromocytomas were activated by signals, like HLA-B, promoting their cytotoxic functions, while T cells in ACTH-&CRH- ones were subject to inhibitory signals, especially from M2 macrophages. What's more, a population of endothelial cells marked by SELE was identified in ACTH + &CRH+ pheochromocytomas, showing strong interaction with CD8+ T cells and facilitating lymphocyte infiltration, particularly the $GZMK^{+}IL7R^{+}$ T cells. While ACTH-&CRH- pheochromocytomas were enriched in glycolysis and HIF signaling pathways, and characterized by lacking T cell infiltration, with macrophages being the dominant immune cells.

Conclusions: CEBPB plays a significant role in the fate transition of pheochromocytomas and may drive ACTH secretion. In addition, ACTH + &CRH+ pheochromocytomas are considerated as relatively immunologically "hot" tumors but poor in angiogenesis. In contrast, ACTH-&CRH- pheochromocytomas lack immune infiltration while exhibiting extensive angiogenesis. Immunotherapies may be effective for the former, and the latter may benefit from anti-angiogenic therapies.

Abstract citation ID: lvag096.126

OC9.3 - ECE_2794 - Insulin and adiponectin regulate adrenal steroidogenesis in obesity by shaping cholesterol availability and lipid droplet dynamics

Diana Leuker-Cozma[1,2,3], Panagiota Siatra[1,2], Stefan Bornstein[1,2,3], Cynthia Andoniadou[1,2,3] and Charlotte Steenblock[1,2]
[1]*Department of Internal Medicine III, Molecular Endocrinology, Technische Universität Dresden Medizinische Fakultät, Dresden, Germany;* [2]*Department of Internal Medicine III, University Hospital Carl Gustav Carus Dresden, MK3-L03, Dresden, Germany;* [3]*King's College London Guy's Campus/Guy's Hospital, London, United Kingdom*

Metabolic diseases are highly prevalent worldwide and are frequently associated with increased glucocorticoid (GC) output as a result of hyperactivation of the hypothalamus-pituitary-adrenal gland axis. Current studies highlight that metabolic disturbances can directly influence adrenocortical function, but direct mechanistic explanations remain scarce. Here, we investigated these molecular mechanisms using complementary *in vivo* mouse models of diet-induced obesity and *in vitro* studies of adrenocortical cell responses to metabolic cues. Using a high-fat diet (HFD)-induced obesity model, we characterized the temporal onset of adrenal steroidogenesis over a 16-week period and correlated adrenal output with metabolic parameters. We observed a delayed onset of increased plasma corticosterone at 16 weeks of HFD, coinciding with transcriptional and morphological changes in the adrenal gland, and impaired glucose and insulin tolerance. Increased GC output was preceded by hyperleptinemia and hyperinsulinemia and coincided with decreased adiponectin expression in the perirenal adipose tissue, while circulating plasma ACTH levels remained unchanged. To dissect the direct effects of these metabolic cues, we treated primary spheroids derived from mouse adrenocortical cells with insulin, adiponectin and leptin. Insulin increased and adiponectin decreased spheroid diameter and steroidogenic gene expression, while leptin affected these to a lesser extent. Integration of bulk RNA sequencing data revealed insulin-responsive gene networks regulating cholesterol metabolism at multiple levels, influencing lipid droplet storage, lysosomal accumulation and inhibition of lipophagy. We confirmed the *in vivo* relevance of these mechanisms by demonstrating that altered lipid droplet distribution and altered lipophagy gene expression coincided with increased GC output at 16 weeks of HFD. Together, our data indicates that obesity-associated corticosterone elevation could be due to chronic effects from metabolic disturbances

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

rather than early HPA axis activation. Early hyperinsulinemia and adiponectin-mediated suppression of adrenal steroidogenesis promote lipid storage and prime the cells for increased cholesterol availability while limiting lipophagy. At later disease stages, sustained hyperinsulinemia, insulin resistance, lipotoxicity and reduced adiponectin could cause a switch in lipophagy, subsequently increasing glucocorticoid production. Overall, our findings identify insulin and adiponectin as key regulators of adrenal cholesterol metabolism, lipid storage and lipophagy, and suggest that their dysregulation drives maladaptive steroidogenesis in obesity, metabolic syndrome and adrenal-related diseases. These results further highlight local adipose tissue–adrenal gland crosstalk as a central mechanism in adrenal adaptation to metabolic stress.

Abstract citation ID: lvag096.127

OC9.4 - ECE_3373 - A multicentre real-world crossover study of once-daily prednisolone versus hydrocortisone in adrenal insufficiency

Katharine Lazarus[1,2], Zin Htut[1,2], Kavita Narula[1], Cara Go[1,2], Angelica Sharma[1,2], Sirazum Choudhury[1,2] and Karim Meeran[1,2]

[1]Imperial College Healthcare NHS Trust, London, United Kingdom; [2]Imperial College London, London, United Kingdom

Background: Adrenal insufficiency (AI) requires lifelong glucocorticoid (GC) replacement to maintain metabolic, cardiovascular, and immune homeostasis. Standard hydrocortisone therapy, usually given three times daily, has a short half-life and produces fluctuating, non-physiological cortisol exposure. This may contribute to persistent symptoms, reduced quality of life, and increased cardiometabolic risk. Once-daily low-dose prednisolone, with its longer biological half-life and greater GC receptor affinity, may provide more stable daytime GC exposure and a more physiological and convenient replacement option.

Methods: This prospective, multicentre, open-label crossover observational study included adults aged 18-85 years with primary or secondary AI receiving stable GC replacement for at least 4 months. Participants were assessed on their usual regimen and then switched to the alternative GC with at least 4 months' follow-up. Outcomes included cardiometabolic measures, routine biochemical markers, bone turnover markers, and quality of life assessed using a modified SF-36 questionnaire, analysed using within-participant comparisons.

Results: A total of 213 participants completed both study visits (mean age 56.3 years; 63% female; 27% primary AI). Among those treated with prednisolone, the median daily dose was 4 mg (IQR 3-4 mg). Switching from hydrocortisone to prednisolone ($n = 194$) was associated with significant improvements in cardiometabolic outcomes, including reductions in body weight (−2.01 kg; $P < .001$), body mass index (−0.51 kg/m^2; $P = .005$), systolic blood pressure (−5.32 mmHg; $P < .001$), diastolic blood pressure (−2.52 mmHg; $P = .002$), and HbA1c (−0.79 mmol/mol; $P = .001$). The total cholesterol–HDL ratio decreased by 0.18 ($P = .006$). No significant changes were observed in renal, electrolyte, inflammatory, or bone turnover markers. Patient-reported outcomes improved, with significant increases in SF-36 scores for general health (+4.5; $P = .031$), energy (+9.2; $P < .001$), and well-being (+4.6; $P = .017$), while nausea scores showed no significant change (+2.4; $P = .13$). In contrast, participants switching from prednisolone to hydrocortisone ($n = 19$) experienced weight gain (+2.15 kg; $P = .005$), increased triglycerides (+0.68 mmol/L; $P = .037$), and reduced HDL cholesterol (−0.19 mmol/L; $P = .003$), while other parameters remained unchanged.

Conclusions: Low-dose once-daily prednisolone was associated with more favourable cardiometabolic outcomes and improved patient-reported wellbeing compared with hydrocortisone, supporting its use as an effective and potentially preferable GC replacement option in adults with AI.

Abstract citation ID: lvag096.128

OC9.5 - ECE_2036 - Adults with classic congenital adrenal hyperplasia taking crinecerfont demonstrated sustained decreases in glucocorticoid doses: 2-year results from the CAHtalyst™ adult study

Irina Bancos[1], Oksana Hamidi[2], Florian Kiefer[3], Rosario Pivonello[4], Aled Rees[5], Mabel Yau[6], Jacques Young[7], Jean Chan[8], Andrea Hartzell[8], Sanjay Keswani[8], Vivian Lin[8], Eiry Roberts[8], Julia Sturgeon[8] and Richard Auchus[9]

[1]Mayo Clinic College of Medicine, Rochester, United States; [2]University of Texas Southwestern Medical Center, Dallas, United States; [3]Medical University of Vienna, Vienna, Austria; [4]Federico II University, Naples, Italy; [5]Cardiff University, Cardiff, United Kingdom; [6]Icahn School of Medicine at Mount Sinai, New York, United States; [7]Bicêtre Hospital, AP-HP, Université Paris-Saclay, Paris, France; [8]Neurocrine Biosciences, Inc., San Diego, United States; [9]University of Michigan Medical School, Ann Arbor, United States

Background: Crinecerfont is a novel corticotropin releasing factor type 1 receptor (CRF_1) antagonist that is FDA-approved as an adjunct to glucocorticoid (GC) replacement to control androgens in patients (≥4 years) with classic congenital adrenal hyperplasia (CAH). This study evaluated changes in GC doses in adults who received up to 2 years of crinecerfont in the phase 3 CAHtalyst™ Adult trial (NCT04490915).

Methods: Participants who completed the double-blind placebo-controlled and open-label periods (Month 12 [M12]) continued on crinecerfont in an open-label extension. Mean % change from baseline (BL) in GC dose (at M12, M18, M24) and % achieving ≤11 mg/m^2/d (at M24) were assessed while androstenedione (A4) was maintained/improved relative to BL with decrease in GC dose set to 0 if A4 was not ≤120% of BL or ≤upper limit of normal. These outcomes were also assessed based on observed GC dose (ie, without imputation based on A4) at M18 and M24, when GC doses could be adjusted without reference to BL A4.

Results: At BL, mean ± SD daily GC dose was 17.6 ± 4.9 mg/m^2/d [32.3 ± 9.3 mg/d] and mean A4 after the morning GC dose was 12.2 ± 14.3 nmol/L. Mean ± SEM % changes from BL in GC dose while maintaining/improving A4 relative to BL were: M12, -26 ± 1.6%; M18, −28 ± 1.7%; M24, −25 ± 1.8%. Moreover, 45% (67/149) of participants achieved a physiologic GC dose (≤11 mg/m^2/d) while maintaining/improving A4 at M24. Observed mean ± SEM % decreases from BL in GC dose (without imputation based on A4) were -38 ± 1.2% at M18 and −38 ± 1.2% at M24, with observed mean GC doses of 10.6 ± 0.2 mg/m^2/d [19.4 ± 0.5 mg/d] at M18 and 10.6 ± 0.2 mg/m^2/d [19.4 ± 0.5 mg/d] at M24. In addition, 71% (114/161) and 69% (103/149) of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

participants achieved a physiologic GC dose at M18 and M24, respectively, without imputation based on A4. Despite decreased GC doses, mean changes from BL in A4 were −0.4 ± 1.1 nmol/L at M18 and +2.0 ± 1.0 nmol/L at M24. Crinecerfont was overall well-tolerated; no new safety signals were observed during long-term treatment.

Conclusions: Adults with CAH taking crinecerfont, a novel CRF_1 antagonist recently approved for androgen control in patients with both salt-wasting and simple virilizing forms of CAH, had substantial reductions in GC doses that were maintained for up to 2 years, with over two-thirds of participants achieving a GC dose in the physiologic range. Crinecerfont is a well-tolerated treatment option for patients with CAH to reduce chronic supraphysiologic GC exposure, which might improve long-term outcomes.

Abstract citation ID: lvag096.129

OC9.6 - ECE_2087 - Modified-release hydrocortisone rapidly normalizes reproductive hormone regulation in women with non-classic congenital adrenal hyperplasia

Matthias Auer, Lea Tschaidse, Orsela Dervishi, Kathrin Bayer, Ann-Christin Welp, Martin Bidlingmaier, Sonja Kunz, Hanna F. Nowotny and Nicole Reisch
Internal Medicine and Endocrinology, LMU Hospital Munich, Medical Clinic and Polyclinic IV, Munich, Germany

Introduction: Non-classic congenital adrenal hyperplasia (NCCAH) often necessitates glucocorticoid (GC) therapy to suppress adrenal androgen excess, which frequently underlies menstrual irregularities and subfertility. While conventional GCs are standard, their pharmacokinetic profiles often fail to mimic the physiological cortisol circadian rhythm, particularly the nocturnal surge required to suppress early-morning ACTH and subsequent androgen escape. Modified-release hydrocortisone (MR-HC; Efmody®) provides a superior pharmacokinetic profile, but its efficacy in NCCAH remains insufficiently characterized.

Methods: In this retrospective observational cohort study conducted between September 2021 and November 2025, 30 women with NCCAH were evaluated (median follow-up 22.5 months). At baseline, 15 patients presented with irregular menses or secondary amenorrhea, and 16 expressed a desire to conceive. Participants were either treatment-naive ($n = 10$) or transitioned from conventional GCs ($n = 20$). The primary endpoints were biochemical androgen control (salivary 17-OHP, serum testosterone), restoration of the regularity of the menstrual cycle, and time to conception.

Results: Fifteen women presented with irregular menses or secondary amenorrhea. Thirteen of fourteen evaluable women (92.6%) demonstrated restoration of ovulatory function, defined as return of a regular menstrual cycle or conception within six months. One woman with hypothalamic hypogonadism remained amenorrheic and initiated hormone replacement therapy. Cycle normalization occurred at a median MR-HC dose of 10 mg (IQR 10-15 mg); all but two women used a single bedtime dose. Among the 16 women seeking pregnancy, 10 conceived within 57.5 weeks (IQR 20.25-64) after treatment initiation. Transition to MR-HC, independent of prior glucocorticoid exposure, significantly reduced morning salivary 17-OHP and serum testosterone levels. Metabolic effects were minimal: body weight decreased slightly over time, and HbA1c showed a transient rise, primarily in treatment-naive women with normalization by the third visit. Blood pressure, fasting glucose, and lipid parameters remained largely unchanged.

Conclusions: Once-daily nightly MR-HC effectively suppresses the adrenocortical axis in women with NCCAH, facilitating rapid restoration of menstrual cyclicity and successful conception at lower total daily GC doses than conventional regimens. These findings suggest that MR-HC is a potent and metabolic-neutral therapeutic option for the reproductive management of NCCAH, potentially reducing the necessity for assisted reproductive techniques.

Abstract citation ID: lvag096.130

OC10.1 - ECE_3948 - Encaleret restores mineral homeostasis in Autosomal Dominant Hypocalcemia Type 1 (ADH1): primary results from the phase 3 CALIBRATE trial

Peter Kamenicky[1], Michael Mannstadt[2], Steven Ing[3], Andrea Giustina[4], Nobuaki Ito[5], Aliya Khan[6], Michael A. Levine[7], Tariq Ahmad[8], Erik Imel[9], Lars Rejnmark[10], Mark Warren[11], Robert Wermers[12], Filomena Cetani[13], Roderick Clifton-Bligh[14], Abishek Kansara[15], Syndia Lazarus[16], Lemoine Sandrine[17], Andrea Palermo[18], John Sayer[19], Vit Zikan[20], Nina S. Ma[21], Mishaela Rubin[22], Jeremy Turner[23,24], Evert Van Velsen[25], Maria Luisa Brandi[26], Alex Dmitrienko[27], Keiichi Ozono[28], Peter Tebben[29], Michael Collins[30], Mary Scott Roberts[31], Scott Adler[32] and Rachel Gafni[33]
[1]Service d'Endocrinologie et des Maladies de la Reproduction, Centre de Référence des Maladies Rares du Calcium et du Phosphate, Université Paris-Saclay, AP-HP, Hôpital Bicêtre, Le Kremlin-Bicêtre, France; [2]Massachusetts General Hospital, Boston, United States; [3]Ohio State University Wexner Medical Center, Columbus, United States; [4]IRCCS San Raffaele Hospital, Milan, Italy; [5]University of Tokyo Hospital, Tokyo, Japan; [6]McMaster University, Oakville, ON, Canada; [7]Children's Hospital of Philadelphia, Philadelphia, United States; [8]UCSF Benioff Children's Hospital, Oakland, United States; [9]Indiana University School of Medicine, Indianapolis, United States; [10]Aarhus University Hospital, Aarhus, Denmark; [11]Physicians East PA, Greenville, United States; [12]Mayo Clinic, Rochester, United States; [13]Department of Clinical and Experimental Medicine, Section of Endocrinology, Pisa, Italy; [14]Royal North Shore Hospital, Sydney, Australia; [15]Houston Methodist Hospital, Houston, United States; [16]Royal Brisbane and Women's Hospital, Brisbane, Australia; [17]HCL Hopital Edouard Herriot, Lyon, France; [18]Unit of Metabolic Bone and Thyroid Disorders, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy; [19]Freeman Hospital, Newcastle upon Tyne, United Kingdom; [20]General University Hospital in Prague, Prague, Czech Republic; [21]Children's Hospital Colorado, Aurora, United States; [22]Columbia University, New York, United States; [23]Norfolk and Norwich University Hospital, Norwich, United Kingdom; [24]Department of Diabetes and Endocrinology, Norfolk and Norwich University Hospital, Norwich, United Kingdom; [25]Erasmus MC—University Medical Center, Rotterdam, The Netherlands; [26]Fondazione Italiana di Ricerca sulle Malattie dell'Osso (FIRMO), Florence, Italy; [27]Mediana LLC, Carolina, Puerto Rico; [28]ISEIKAI International General Hospital, Osaka, Japan; [29]Yale University, New Haven, United States; [30]MT Collins Consulting, Washington, DC,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

United States; [31]BridgeBio Therapeutics, San Francisco, United States; [32]BridgeBio, San Francisco, United States; [33]NIDCR, NIH, Bethesda, United States

Autosomal dominant hypocalcemia type 1 (ADH1), due to gain-of-function variants in the calcium-sensing receptor gene (*CASR*), manifests as low parathyroid hormone (PTH), hypocalcemia, hypercalciuria, hyperphosphatemia and hypomagnesemia. Standard of care (SoC) treatment, calcium and active vitamin D, worsens hypercalciuria and can lead to renal morbidity. Encaleret, an investigational, oral, negative allosteric modulator of the CaSR, normalized mean albumin-corrected blood calcium (cCa) and 24-hour urine calcium excretion (UCa) in a Phase 2b study of ADH1.

CALIBRATE (NCT05680818) is a global, Phase 3, randomized, controlled, open-label trial of encaleret for ADH1. After screening, all participants entered Period 1 (P1), a 4-week (W) SoC maintenance period. Participants were then randomized 2:1 to encaleret or SoC in Period 2 (P2), a 20W dose titration period. SoC was stopped prior to encaleret initiation; encaleret dose was adjusted to achieve target cCa. Both treatment groups then entered Period 3 (P3), a 4W dose maintenance period, with the final visit at W24.

Sixty-seven participants (16-76 y) with ADH1 due to 46 distinct *CASR* variants were randomized; 66 completed P3W24. The composite primary endpoint assessed the proportion of those randomized to encaleret ($n = 45$) achieving target cCa (2.08-2.68 mmol/L) AND UCa (<7.0(M), <6.25(F) mmol/day) at P3W24 compared to themselves on SoC at P1W4. This endpoint was met in 75.6% of encaleret-treated participants at P3W24 compared to 4.4% at P1W4 ($P < .0001$). Encaleret increased mean cCa by P2Day3 and decreased mean UCa by P2W3, the first time after encaleret these analytes were measured, and were maintained through P3W24. Within the encaleret group, 91.1% had PTH ≥1.6 pmol/L (nl 1.6-6.9) at P3W24 compared with 6.7% at P1W4 ($P < .0001$); 91.1% achieved normal serum phosphate (0.81-1.55 mmol/L) at P3W24 compared with 55.6% at P1W4 ($P = .0002$). Additional analyses between groups assessed the proportion of those randomized to encaleret versus SoC who achieved these endpoints at P3W24. More participants randomized to encaleret (75.6%) had cCa and UCa within the target ranges compared to those randomized to SoC ($n = 21$) at P3W24 (19%; $P < .0001$). In the SoC group, 0% had PTH ≥1.6 pmol/L at P3W24 ($P < .0001$ compared to 91.1% on encaleret), and 52.4% had normal serum phosphate at P3W24 ($P = .0003$ compared to 91.1% on encaleret). Encaleret was well-tolerated with no discontinuations in the encaleret arm. Few serious adverse events (AE) were reported with frequency similar between treatment arms.

These results establish encaleret as a potential disease-specific therapy for ADH1 with clinically meaningful efficacy, safety, and tolerability.

Abstract citation ID: lvag096.131

OC10.2 - ECE_1406 - Five-year data report from the phase 2 PaTH forward trial of palopegteriparatide for adults with hypoparathyroidism

Andrea Palermo[1], Lars Rejnmark[2], Aliya Khan[3], Peter Schwarz[4], Lorenz Hofbauer[5], Filomena Cetani[6], Rajesh Jain[7], Bart L. Clarke[8], Carol Zhao[9], Mike Ominsky[9], Jenny Ukena[9], Christopher Sibley[9], Aimee Shu[9] and Mishaela Rubin[10]

[1]Campus Bio-Medico University, Rome, Italy; [2]Aarhus University Hospital, Aarhus, Denmark; [3]Endocrinology, Metabolism, and Geriatrics, McMaster University, Hamilton, Ontario, Canada; [4]Rigshospitalet, Copenhagen, Denmark; [5]Technische Universität Dresden, Dresden, Germany; [6]Department of Clinical and Experimental Medicine, Endocrine Unit, University of Pisa, Pisa, Italy; [7]University of Chicago, Chicago, United States; [8]Mayo Clinic, Rochester, United States; [9]Ascendis Pharma, Inc., Palo Alto, United States; [10]Columbia University, New York, United States

Introduction: Hypoparathyroidism is a rare endocrine disease, in which insufficient parathyroid hormone (PTH) can lead to systemic complications. Historically, conventional therapy for hypoparathyroidism (active vitamin D and calcium) aims to correct hypocalcemia but does not address underlying insufficient PTH. Palopegteriparatide is a prodrug of PTH (1-34), administered once daily and designed to provide active PTH within the physiological range for 24 hours/day. It is approved in multiple countries for the treatment of hypoparathyroidism. This analysis evaluated the safety and efficacy of palopegteriparatide throughout the phase 2 PaTH Forward trial.

Methods: PaTH Forward included a 4-week, double-blind, randomized, placebo-controlled period and a 262-week open-label extension (OLE). OLE efficacy endpoints included independence from conventional therapy (≤600 mg/day of elemental calcium and no vitamin D) and maintenance of normocalcemia (2.07-2.64 mmol/L). Bone turnover markers C-terminal telopeptide of type 1 collagen (CTx) and procollagen type 1 N-terminal propeptide (P1NP), and bone mineral density (BMD) measured by dual x-ray absorptiometry were assessed regularly. Renal function was assessed using estimated glomerular filtration rate (eGFR). Hypoparathyroidism-related symptoms and impact were measured using the Hypoparathyroidism Patient Experience Scales. Safety assessments included serum chemistries, 24-hour urine calcium, and treatment-emergent adverse events (TEAEs).

Results: Fifty-six of 59 participants (95%) completed the trial. Of those, 95% (53/56) were independent from therapeutic doses of calcium, 96% (54/56) were independent from active vitamin D, and 88% (49/56) were normocalcemic. Mean (SD) albumin-adjusted serum calcium was 2.25 (0.17) mmol/L at Week 266. Mean CTx and P1NP increased from the low end of normal at baseline, peaked by Week 26, and declined thereafter, remaining stable above baseline through Week 266. Mean BMD Z-scores trended towards age- and sex-matched norms at multiple regions, remaining above zero through Week 266. Mean (SD) eGFR was 78.01 (22.16) mL/min/1.73 m^2 at Week 266, reflecting a mean (SD) increase of 9.38 (14.08) mL/min/1.73 m^2. Hypoparathyroidism-related symptoms and impacts on physical functioning and daily life improved by Week 4 with palopegteriparatide treatment and were maintained through Week 266. Mean (SD) 24-hour urine calcium levels normalized with palopegteriparatide treatment and remained below the upper limit of normal (≤6.2 mmol/day) through Week 266 (mean 3.61 [2.01] mmol/day). Most TEAEs were mild-to-moderate; no TEAEs led to trial or study drug discontinuation.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: Palopegteriparatide demonstrated durable safety and efficacy in adults with hypoparathyroidism, enabling independence from conventional therapy and maintaining normocalcemia while providing sustained improvements in patient-reported outcomes for participants through Week 266.

Abstract citation ID: lvag096.132

OC10.3 - ECE_2879 - Dynamic postoperative PTH as a strong predictor of hypoparathyroidism after total thyroidectomy: a large cohort analysis

Miguel Paja[1,2,3], Leire Pérez de Azpeitia[2], Josune Rodríguez-Soto[3], Cristina Moreno[3], Eider Etxeberria[3], Javier Espiga Alzola[3], Ana Izuzquiza[3], Iñigo Hernando[2,3], María Ausín[3], Jon Portu[3], Jon Garai[3], Alejandra Santamaría[3], Amaya Exposito[2], Aitzol Lizarraga[2], Aitziber Ugalde[3], Amelia Oleaga[2] and Elena Cruz-Iglesias[3]
[1]*Endocrinology & Nutrition, Biobizkaia Health Research Institute, Bilbao, Spain;* [2]*EHU, Basque Country University, BIlbao, Spain;* [3]*Osakidetza, Basurto University Hospital, BIlbao, Spain*

Background: Postoperative hypoparathyroidism (poHypoPT) is a frequent complication of total thyroidectomy. Its early identification is clinically relevant, and postoperative PTH dynamics—particularly the 24-hour decline—have emerged as strong predictors. poHypoPT is best defined as an undetectable or inappropriately low postoperative PTH level in the presence of hypocalcaemia, with or without symptoms. This study evaluates its incidence and predictive factors in a large surgical cohort.

Methods: We retrospectively analysed patients who underwent total thyroidectomy, with or without central neck dissection (CND), between 2016 and 2022. poHypoPT was defined by at least one of the following: (a) corrected calcium (CorCa) <7.5 mg/dL; (b) CorCa <8.0 mg/dL with simultaneous PTH <15 pg/mL during postoperative admission; (c) hypocalcaemic symptoms resolving with oral or intravenous calcium during admission or after discharge; or (d) PTH <10 pg/mL at 24 hours. Variables included demographics, thyroid function, surgical characteristics, intraoperative parathyroid identification, and postoperative PTH dynamics (baseline, immediate, and 24-hour values).

Results: A total of 768 patients were included (79.7% women; median age 54 years). Hyperthyroidism (TSH <0.1) was present in 19.3%. CND was performed in 25%, and malignancy was suspected or confirmed preoperatively in 50%. poHypoPT occurred in 296 patients (38.5%). It was associated with younger age, lower BMI, female sex, surgery for suspected/confirmed malignancy, CND, greater immediate and 24-hour postoperative declines in PTH, total calcium and CorCa, and larger gland size by specimen weight. In multivariate analysis excluding calcium and PTH values (diagnostic criteria), age, sex, and postoperative PTH dynamics remained independent predictors. When PTH dynamics were excluded, CND was the strongest predictor (OR 3.58; IC_{95}: 2.49-5.18). PTH at 24 hours (PTH24H) showed the highest diagnostic accuracy (AUC 0.930). A PTH24h >17.5 pg/mL predicted a 93.3% probability of not developing poHypoPT, while a reduction <68.8% from baseline predicted its absence with 96.37% sensitivity and 80.9% specificity with a predictive negative value of 97.3%.

Conclusions: Using strict biochemical and clinical criteria, poHypoPT incidence reached 31.5%. Lower BMI and female sex were modest predictors. Postoperative PTH dynamics—particularly a 24-hour PTH >17.5 pg/mL or a decline <70% from baseline—demonstrated excellent negative predictive value and are reliable tools for early risk stratification after total thyroidectomy.

Abstract citation ID: lvag096.133

OC10.4 - ECE_2600 - Genetic testing of over 400 individuals with non-surgical hypoparathyroidism shows gain-of-function CASR variants as the most common genetic cause identified

Michael Mannstadt[1], Lyndsay Smith[2], Ananth Sridhar[2], Mary Scott Roberts[2], Scott Adler[2] and Arun Mathew[2]
[1]*Endocrine Unit, Massachusetts General Hospital and Harvard Medical School, Boston, United States;* [2]*BridgeBio Pharma, San Francisco, United States*

Hypoparathyroidism is a rare endocrine disorder characterized by low serum calcium with undetectable or inappropriately low parathyroid hormone levels, leading to disrupted mineral homeostasis. Hypoparathyroidism is most often caused by inadvertent injury to or removal of the parathyroid glands during neck surgery. Increasingly, genetic causes are being recognized as diagnostic testing expands and awareness for non-surgical etiologies grows. Genetic forms of hypoparathyroidism may present as isolated disease or as part of a broader syndrome, and include disorders affecting parathyroid gland development, parathyroid hormone synthesis or secretion, and autoimmune-mediated injury to the parathyroid glands.

Individuals with a clinical diagnosis of non-surgical hypoparathyroidism, a positive family history, or suspicion of a genetic etiology are eligible to enroll in a no-charge sponsored genetic testing program in the United States and Canada. The next-generation sequencing panel leveraging a whole-exome backbone includes 26 genes associated with hypoparathyroidism: *ACADM*, *AIRE*, *ATP1A1*, *CASR*, *CHD7*, *CLDN16*, *CLDN19*, *CNNM2*, *DHCR7*, *EGF*, *FAM111A*, *FXYD2*, *GATA3*, *GCM2*, *GNA11*, *HADHA*, *HADHB*, *KCNA1*, *NEBL*, *PTH*, *SEMA3E*, *SLC12A3*, *SOX3*, *TBCE*, *TBX1,* and *TRPM6*.

A total of 446 participants (mean age 29 years, range 0-83 years) were tested during 2020-2025. 294 pathogenic or likely pathogenic variants or variants of uncertain significance were identified across 222 individuals (50%). Among these 222 individuals, *CASR* was the most frequently affected (40%), followed by *AIRE* (18%), *GATA3* (10%), *TBX1* (10%), *GNA11* (6%), *DHCR7* (4%), *GCM2* (4%), *SLC12A3* (4%), *CHD7* (3%), *ACADM* (3%), *HADHA* (3%), *FAM111A* (2%), *SEMA3E* (2%), *HADHB* (2%), *CNNM2* (1%), *EGF* (1%), *NEBL* (1%), *CLDN19* (1%), *PTH* (1%), *TRPM6* (1%), and *CLDN16*, *FXYD2*, *KCNA1, SOX3*, and *TBCE* (each under 1%). Notably, 60 individuals had more than one variant identified, reflecting either multiple variants within a single gene or variants identified in multiple genes.

In non-surgical hypoparathyroidism without another clear cause, genetic testing and family evaluation are recommended by the current practice guidelines. Identification of genetic etiology can clarify the underlying defect, guide therapy selection, and prompt targeted evaluation and counseling, consistent with recent adult clinical-practice guidance and best practice

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

recommendations. In this cohort, the most common genetic form of hypoparathyroidism was autosomal dominant hypocalcemia type 1, caused by gain-of-function *CASR* variants (20% of the total population; 88/446). Overall, genetic testing offers a practical, high-yield pathway to establish definitive diagnoses in non-surgical hypoparathyroidism and, consistent with consensus guidance, may thus enable informed counseling for patients and families, better targeted evaluation, and more precise management.

Abstract citation ID: lvag096.134

OC10.5 - ECE_2799 - Bone and blood transcriptome profiles in postmenopausal osteoporotic vertebral fracture patients

Lucie Šedová[1], Josef Včelák[2], Adam Král[2], Blanka Chylíková[1] and Ondřej Šeda[1]

[1]*First Faculty of Medicine, Charles University, Institute of Biology and Medical Genetics, Prague, Czech Republic;* [2]*Prague, Czech Republic*

Osteoporotic vertebral fractures (OVF) represent a major cause of morbidity, yet Bone Mineral Density (BMD) often fails to accurately predict fracture risk. A significant proportion of fractures occur in individuals with BMD scores above the osteoporotic threshold, as BMD measures bone quantity rather than quality (microarchitecture and turnover). Consequently, there is a critical need to identify specific molecular profiles and biomarkers that reflect bone quality to improve risk stratification for OVF.

Methods: This study aimed to elucidate the distinct genomic and transcriptomic profiles associated with OVF vs non-osteoporotic controls. Intraoperative vertebral bone tissue and peripheral blood were collected from postmenopausal women undergoing surgery for OVF ($n = 67$) and patients undergoing elective thoracolumbar surgery without osteoporosis (Control, $n = 48$). RNA was extracted from intraoperative vertebral bone tissue and peripheral blood. RNA sequencing libraries were prepared using the NEBNext Ultra II Directional RNA Library Prep Kit for Illumina and sequenced using Illumina NovaSeq6000 as 150-bp paired-end reads. We performed differential expression and gene ontology and pathway analyses to compare osteoporotic and non-osteoporotic samples.

Results: The control and OVF groups were age-matched (73.3 ± 5.4 vs 73.9 ± 7.4 years in OVF, $P = .6$), with similar profiles regarding prevalence of concomitant cancer, hyperuricemia, dyslipidemia, hypertension, inflammation, thyreopathies, smoking status or medication (except for osteoporosis-specific medication). Control group showed slightly higher body mass index (28.9 ± 4.3 vs OVF 26.5 ± 4.2, $P = .004$) and prevalence type 2 diabetes. Transcriptomic analysis of bone tissue revealed 285 differentially expressed genes (FDR <0.05; >2-fold change), with 256 downregulated and 29 upregulated in OVF. Gene ontology and pathway analysis identified enrichment in extracellular matrix organization, collagen fibril organization and PI3K-Akt signalling pathways (all Bonferroni-corrected $P < 10^{-4}$). Transcriptomic analysis of blood revealed only 23 significantly differentially expressed genes with 6 downregulated and 17 upregulated in OVF. Interestingly, the most significantly downregulated gene in OVF blood was lactoferrin with known roles in bone formation, conversely, among the most upregulated genes in OVF were Syndecan 1, long non-coding RNA LINC00958 or myomesin-2, all previously linked to bone homeostasis.

Conclusions: This study identifies a distinct transcriptomic signature distinguishing OVF patients from controls, characterized by disrupted collagen and matrix organization pathways. Furthermore, the data suggests potential non-invasive biomarkers for assessing bone quality and fracture risk beyond standard BMD measurements.

Abstract citation ID: lvag096.135

OC10.6 - ECE_1238 - Real-world safety of romosozumab in high cardiovascular risk patients

Joshua Stokar[1,2,3] and Auryan Szalat[1,2]

[1]*Hadassah Medical Center, Jerusalem, Israel;* [2]*Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel;* [3]*Hadassah Medical Center, Endocrinology, Internal Medicine, Jerusalem, Israel*

Introduction: Use of Romosozumab for treatment of osteoporosis is hindered by a black box regulatory warning regarding an increased risk for major adverse cardiovascular (MACE). We previously demonstrated that romosozumab was not associated with increased MACE in patients without recent cardiovascular (CV) events; however, data on its safety in individuals with recent CV events remain limited.

Objective: To compare 1-year cardiovascular risk following initiation of romosozumab versus parathyroid hormone (PTH) analogues in patients with documented recent acute CV events prior to therapy.

Methods: Using TriNetX, a global federated electronic health record network, we identified adults who initiated romosozumab or a PTH analogue (abaloparatide or teriparatide) after experiencing an acute myocardial infarction or cerebral infarction within the preceding year. Propensity-score matching (PSM) generated 702 patients per cohort, balanced across 54 demographic, clinical, medication, and laboratory variables. Outcomes were assessed from day 1 to day 365 post-index. The primary endpoint was incident 3-point MACE (3P-MACE): acute myocardial infarction, acute stroke, or death. Secondary endpoints included myocardial infarction, cerebrovascular events, acute heart failure, and all-cause mortality. Hazard ratios (HRs) were calculated using Cox proportional hazards models.

Results: During 1-year follow-up, romosozumab was not associated with excess cardiovascular risk compared with PTH analogues. Event counts and hazard ratios (HR [95% CI]) for romosozumab vs PTH analogues were: 3P-MACE: 293 vs 321; HR 0.94 (0.80-1.10); Myocardial infarction: 72 vs 84; HR 0.88 (0.65-1.21); Acute heart failure: 31 vs 38; HR 0.84 (0.52-1.35); CVA or TIA: 222 vs 238; HR 0.97 (0.81-1.16); Death: 30 vs 44; HR 0.72 (0.45-1.14).

Conclusions: Among patients with recent major cardiovascular events, romosozumab was not associated with an increased risk of cardiovascular events or mortality compared with PTH analogues. These real-world findings support the cardiovascular safety of romosozumab even in patients at very high baseline cardiovascular risk, challenging the conclusions derived from the ARCH trial.

Abstract citation ID: lvag096.136

OC11.1 - ECE_1977 - A clinical plus genetic score to predict 5-year bariatric surgery efficacy: the OBEGEN project

Josep León Mengíbar[1,2], Marta Zorzano[3], Aaron Switzer[1], Andreea Ciudin[1], Assumpta Caixás[4], N. Vilarrasa[5],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Marta Bueno[6], Andres Cardona[1], Lourdes Gomez[1] and Albert Lecube[1]
[1]Hospital Universitari Vall d'Hebrón, Barcelona, Spain; [2]Vall d'Hebron University Hospital, Barcelona, Spain; [3]Hospital Universitario Araba, Vitoria-Gasteiz, Spain; [4]Parc Taulí, Sabadell, Spain; [5]Hospital de Bellvitge, L'Hospitalet de Llobregat, Spain; [6]Hospital Universitario Arnau de Vilanova, Lleida, Spain

Introduction: The modest durability of lifestyle-based weight management and, until recently, the limited access to safe and effective anti-obesity drugs have helped drive the growing uptake of bariatric surgery (BS). However, 25%-30% of individuals fail to attain clinically meaningful weight loss, and as many as 50% develop substantial weight regain beyond the second postoperative year. Obesity has a strong genetic component (heritability ~40%-75%), with more than 120 genes implicated. To support preoperative risk stratification, we developed the OBEGEN clinico-genetic score (range −4 to +4; cut-off 0.662), which combines 8 single-nucleotide polymorphisms with 3 clinical variables to classify BS candidates as "good" or "bad" weight-loss responders (J Pers Med. 2021;11:1040).

Methods: A total of 342 patients undergoing BS were analyzed and stratified according to the OBEGEN score. Outcomes included percentage total weight loss (%TWL), the proportion of patients achieving >20% TWL, and weight regain >30%. These outcomes were assessed at 6 months and annually from 1 to 5 years postoperatively. Continuous variables were compared using t-tests or ANOVA, and categorical variables using chi-square or Fisher's exact tests, as appropriate.

Results: Across follow-up, good responders consistently achieved greater %TWL than bad responders (1 year: 34.1% vs 29.6%, $P <$ .001; 5 years: 26.3% vs 22.9%, $P = .006$), with the greatest between-group difference observed at 3 years (30.5% vs 22.3%, $P < .001$). The proportion of patients achieving >20% TWL was significantly higher among good responders at 1 year (96.4% vs 86.9%, $P = .002$), 2 years (92.8% vs 78.3%, $P < .001$), and 4 years (78.7% vs 60.0%, $P = .001$). At 5 years, weight regain >30% was numerically more frequent among good responders, although this difference did not reach statistical significance (9.6% vs 4.1%, $P = .095$).

Conclusions: Clinical–genetic stratification using the OBEGEN score identifies distinct postoperative weight-loss trajectories following bariatric surgery. Differences between responder groups are most pronounced during the first three years and diminish by year five, coinciding with an apparent increase in weight regain among individuals initially classified as good responders. These findings highlight the potential value of incorporating genetic information into early postoperative risk stratification and follow-up planning, while underscoring the need for sustained long-term support in all patients undergoing BS.

Abstract citation ID: lvag096.137

OC11.2 - ECE_2967 - Metreleptin therapy in pediatric and adult patients with congenital leptin deficiency: a multicenter real-world experience

Selin Uzun Karaüzüm[1], Sevde Nur Firat[2], Funda Feryal Taş[3], Gökçen Güngör Semİz[4], Leyla Akın[5], Elif Özsu[6], Mehmet Nuri Özbek[7], Zafer Pekkolay[8], Hüseyin Onay[9], Elif Oral[10], Baris Akinci[11] and Samim Ozen[12]
[1]Department of Pediatric Endocrinology, Ege University Faculty of Medicine, Izmir, Türkiye; [2]Department of Endocrinology and Metabolism, University of Health Sciences Ankara Training and Research Hospital, Ankara, Türkiye; [3]Department of Pediatric Endocrinology, Diyarbakir Gazi Yasargil Training and Research Hospital, Diyarbakır, Türkiye; [4]Department of Endocrinology and Metabolism, Buca Seyfi Demirsoy Training and Research Hospital, Izmir, Türkiye; [5]Department of Pediatric Endocrinology, Ondokuz Mayıs University, Samsun, Türkiye; [6]Department of Pediatric Endocrinology, Ankara University Faculty of Medicine, Ankara, Türkiye; [7]Department of Pediatric Endocrinology, Mardin Artuklu University, Mardin, Türkiye; [8]Department of Endocrinology and Metabolism, Dicle University Faculty of Medicine, Diyarbakır, Türkiye; [9]Multigen Genetic Diseases Diagnosis Center, Medical Genetics, Izmir, Türkiye; [10]Metabolism, Endocrinology and Diabetes Department, Department of Internal Medicine, Caswell Diabetes Institute, North Campus Research Complex, University of Michigan, Ann Arbor, MI, United States; [11]DEPARK & Izmir Biomedicine and Genome Center, Izmir, Türkiye; [12]Department of Pediatric Endocrinology and Diabetes, Ege University Faculty of Medicine, Izmir, Türkiye

Background: Congenital leptin deficiency (CLD) is a rare monogenic cause of severe early-onset obesity and hyperphagia, with limited long-term real-world evidence on metreleptin therapy. In this study, we aimed to evaluate the long-term clinical outcomes and safety of metreleptin therapy in a large, multicenter cohort of pediatric and adult patients.

Methods: We conducted a multicenter, observational cohort study including 17 patients with CLD (10 pediatric, 7 adult) across 8 centers. Clinical characteristics, genetic findings, longitudinal anthropometric measurements, metabolic parameters, and total daily metreleptin doses were systematically evaluated. Pediatric and adult cohorts were analyzed separately to account for age- and growth-related trajectories. Repeated-measures analyses were performed in subgroups with complete longitudinal data. One patient who developed loss of efficacy due to neutralizing antibodies was presented separately.

Results: Obesity onset clustered within the first year of life in 87.5% of patients, and hyperphagia was present in all patients at baseline. Pathogenic or likely pathogenic *LEP* gene variants were identified in most cases; three individuals with ongoing genetic analyses were included based on markedly low leptin levels and a robust clinical response to metreleptin. Across the entire cohort, metreleptin induced a marked, time-dependent reduction in BMI (median −25.7% at month 6; −40.7% at month 18). In pediatric patients, BMI and BMI SDS decreased substantially (mean BMI SDS 5.52 ± 1.47 at baseline to 2.66 ± 1.37 by month 24) and remained stable long term; all children showed a net BMI SDS reduction at last follow-up. Linear growth was preserved, with stable height SDS and no evidence of growth attenuation. In adults, BMI decreased from 55.7 kg/m^2 at baseline to 29.9 kg/m^2 by month 18, with subsequent inter-individual variability but overall preservation of therapeutic gains. Glycemic and lipid parameters remained largely within reference ranges, no severe adverse events occurred, and total metreleptin doses remained stable without systematic escalation. A boy with a large deletion in the *LEP* gene started metreleptin at 24 months and initially lost 10 kg. By month 6, he began regaining weight and developed injection-site reactions. He tested strongly positive for neutralizing antibodies and was later treated with an investigational agent.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: This multicenter cohort is among the largest real-world series jointly evaluating pediatric and adult patients with congenital leptin deficiency. Metreleptin was effective and well-tolerated during long-term follow-up in routine clinical practice. Neutralizing antibody–associated loss of efficacy occurred in one patient; otherwise, responses were sustained without clinically relevant safety signals.

Abstract citation ID: lvag096.138

OC11.3 - ECE_1591 - Food-induced cortisol and short-term energy partitioning during overfeeding in healthy men: a randomized, placebo-controlled crossover study

Gabriele Cypaite[1], Jil Chevailler[1], Zanetti Lisa[1], Lorena Wyniger[1], Susanne Thierry[1], Michael Epstein[2] and Eleonora Seelig[1]
[1]*Division of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland;* [2]*Statistical Consulting, Letchworth, United Kingdom*

Background: Food intake elicits a small but measurable increase in circulating cortisol levels. The physiological relevance of this response remains uncertain.

Methods: In this randomized, placebo-controlled, crossover study, 20 healthy lean men were enrolled at the University Hospital Basel, Switzerland. Participants received either a block-and-replace regimen mimicking physiological cortisol rhythm (metyrapone plus hydrocortisone) or placebo (1:1 randomization). Each participant completed two 3-day overfeeding periods (4000-5000 kcal/day), once under each treatment condition. The block-and-replace regimen suppressed the postprandial cortisol rise. The primary outcome was insulin sensitivity assessed using a mixed-meal tolerance test. Secondary outcomes included body weight as well as lean and fat mass measured by body impedance analysis. Outcomes were analyzed using mixed-effects models.

Results: All 20 participants completed the study per protocol. There was no evidence for a treatment effect on insulin sensitivity (Matsuda Index estimate: −121.175; standard error: 148.217; $P = .424$) or total body weight (estimate: −0.502 kg; SE 0.317; $P = .131$). However, the block-and-replace treatment significantly reduced fat mass (estimate: −1.532 kg; SE 0.435; $P = .002$) and increased lean mass (estimate: 1.968 kg; SE 0.489; $P = .001$) compared with placebo.

Conclusions: Although the intervention did not affect the primary metabolic endpoint, suppression of the food-induced cortisol response was consistently associated with a shift towards lower fat mass and higher lean mass during short-term overfeeding. These findings point to a previously unrecognised role of postprandial cortisol in energy partitioning in humans and suggest that modulation of this response may represent a biologically relevant target for future investigation.

Abstract citation ID: lvag096.139

OC11.5 - ECE_1834 - Progesterone attenuates the metabolic benefits of estradiol in late-onset hormone replacement in ovariectomized mice

Alessandra Gonçalves da Cruz, Anne Raissa Melo Santos, Felipe Nunes de Camargo, Bruna Maria Fantini Trinca, Jessica Denielle Matos Dos Santos, José Francisco Turino Silva, Jorge Felipe Argenta Model, Sandro Leão Matos and João Paulo Camporez
Departamento de Fisiologia, Faculdade de Medicina de Ribeirão Preto—Universidade de São Paulo, Ribeirão Preto, Brazil

Hormone replacement therapy is considered a valuable strategy with protective effects against insulin resistance and obesity. However, data are limited on the metabolic effects of late-initiated treatment with estradiol (E2) combined with progesterone (P4).

Our aim was to assess the effects of late-onset combined E2 and P4 treatment on insulin resistance and lipid profile in high-fat-fed ovariectomized female mice.

Eight-week-old female C57BL/6J mice underwent bilateral ovariectomy and were allocated to four groups: OVX, E2, P4, E2 + P4. Hormone therapy was evaluated 12 weeks after ovariectomy to model advanced menopause. E2 and/or P4 were delivered via subcutaneous pellets for 4 weeks. All animals received a high-fat diet 45%. Body composition, glucose tolerance test (GTT), HOMA-IR, fasting insulin, total cholesterol, liver histology (Oil Red O), and hepatic and muscle triglycerides (TAG) levels were measured. Protein levels of estrogen receptor alpha (ERα) and sterol regulatory element-binding protein-1c (SREBP1c), related to fatty acid and TAG synthesis, were also analyzed (CEUA 1031/2021R1).

Even after a prolonged period following ovariectomy, E2 treatment alone improved the analyzed parameters compared with OVX, reducing body weight gain and fat mass and increasing lean mass percentage. Area under the curve (AUC) during GTT, fasting insulin, HOMA-IR, TAG content in liver and muscle (confirmed by histology), and cholesterol levels were also reduced after late E2 treatment. However, when E2 was combined with P4, E2 + P4 did not show the same improvements observed with E2 alone. Final body weight in E2 + P4 did not differ from P4 and OVX but was higher than in E2. Fat mass percentage in E2 + P4 was lower than in P4 and OVX but higher than in E2, whereas lean mass percentage was higher than in P4 and OVX but lower than in E2. AUC did not differ among E2 + P4, P4, and OVX, but was higher in E2 + P4 than in E2. E2 + P4 also showed higher tissue TAG than E2. Plasma cholesterol didn't differ among E2 + P4, P4, and E2, although all were lower than OVX. Fasting insulin and HOMA-IR were higher in E2 + P4 than in E2. Regarding protein content, E2 + P4 and E2 showed higher ERα levels than OVX, while SREBP1c was lower in E2 + P4 than in E2.

The simultaneous combination of E2 and P4 attenuated or abolished several of the protective effects observed with E2 alone, suggesting a modulatory role of P4 on E2-mediated metabolic actions and lipogenic signaling. Further studies are needed to identify the exact pathways involved in this mechanism.

Abstract citation ID: lvag096.140

OC11.6 - ECE_1916 - Linking growth patterns to metabolic risk in SGA children: insights into the FGF21/β klotho system and adiponectin

Giulia Rodari[1], Valeria Citterio[1], Deborah Mattinzoli[2], Masami Ikehata[2], Valentina Collini[3], Aurora Pedroli[3], Eriselda Profka[1,3], Carlo Alfieri[2,3], Giovanna Mantovani[1,3] and Claudia Giavoli[1,3]
[1]*Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy;* [2]*Department of Nephrology, Dialysis and Renal Transplantation, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy;* [3]*Department of Clinical*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Sciences and Community Health, Dipartimento di Eccellenza 2023-2027, University of Milan, Milan, Italy

Introduction: Children born small for gestational age (SGA) constitute a heterogeneous population with diverse growth and metabolic trajectories. Low birth length and/or weight increases the risk of impaired growth and metabolic dysfunction, the latter mainly in those exhibiting rapid postnatal catch-up. Among relevant cytokines, fibroblast growth factor 21 (FGF21), its co-receptor β-Klotho, and adiponectin (Adn) have emerged as biomarkers of insulin sensitivity and glucose homeostasis. FGF21 also interacts with the GH/IGF-I axis, influencing linear growth and contributing to GH resistance. Characterizing the FGF21/β-Klotho system and Adn may help elucidate the mechanisms linking growth patterns to metabolic risk in SGA children.

Aims: To investigate associations between anthropometric measures, metabolic parameters, and the FGF21/β-Klotho–Adn axis in SGA children, with particular focus on glycaemic control and lipid metabolism.

Methods: This cross-sectional study included 60 SGA children (birth weight and/or length <−2.0 SDS, INeS charts) aged 4-16 years, thirteen of whom (21.7%) receiving recombinant GH (rGH) therapy for short stature. Anthropometric data, body composition (TANITA BC-420MA), and metabolic markers—including fasting glucose, insulin, HbA1c, IGF-I SDS, lipid profile, FGF21, β-Klotho, and Adn—were collected. HOMA-IR and QUICKI indices were calculated.

Results: The cohort (35F/25M; mean age 9.5 ± 2.9 years) included 23.3% children with height <−2.0 SDS. Median concentrations were: FGF21 139.6 pg/ml, β-Klotho 720.2 pg/ml, and Adn 4.3 ng/ml. HbA1c showed a significant positive association with height gain ($P = .018$; $P = .023$ adjusted for Mid-parental height). FGF21 and β-Klotho were strongly correlated ($P < .001$), whereas Adn showed no relationship with either marker. Both FGF21 and β-Klotho were inversely associated with triglycerides ($P = .043$ and $P = .026$), and β-Klotho and Adn correlated positively with HDL cholesterol ($P = .029$ and $P = .024$). None of the biomarkers were associated with glycaemic indices and IGF-I SDS levels. In children receiving rGH, lipid-related associations disappeared, and FGF21–β-Klotho and Adn instead correlated with HbA1c ($P = .043$, $P = .036$, $P = .041$, respectively).

Conclusions: Our findings support a link between postnatal height catch-up growth and metabolic risk, as shown by the association between height and HbA1c—a marker predictive of future diabetes even in healthy paediatric populations. Unexpectedly, the FGF21–β Klotho system showed an inverse relationship only with triglycerides; however, these lipid-related associations were no longer present in children undergoing rGH therapy. In treated patients, FGF21–β-Klotho and adiponectin, instead, correlated with glycaemic markers, suggesting that rGH may alter the metabolic context in which FGF21 operates, shifting its associations from lipid to glucose metabolism.

Abstract citation ID: lvag096.141

OC12.1 - LBA_ECE_1384 - Integrating lncrnas expression with machine learning for accurate preoperative diagnosis of thyroid cancer

Melissa Borsa[1], Corrado Possieri[2], Valeria Pecci[1], Pietro Locantore[1], Antonella Farsetti[3], Alfredo Pontecorvi[1] and Simona Nanni[1]

[1]*Catholic University of the Sacred Heart of Rome, Rome, Italy;* [2]*University Tor Vergata of Rome, Rome, Italy;* [3]*CNR Iasi, Rome, Italy*

Background and Aim: Thyroid nodules are increasingly detected in clinical practice, poising a major clinical challenge in distinguishing benign from malignant lesions and often leading to unnecessary surgery. Indeed, only 25%-30% of TIR3B and 50%-80% of TIR4 nodules are confirmed as malignant on final histology, resulting in surgical overtreatment.

Recent evidence highlights the role of long non-coding RNAs (lncRNAs) in thyroid cancer, but their clinical application remains in the research phase.

In this context, the aim of this project is to develop a machine learning-driven lncRNAs level-based strategy to improve diagnostic accuracy enabling more personalized treatment strategies.

Methods: Patients were enrolled at the Endocrinology and Diabetes Center of Fondazione Policlinico Gemelli (Rome, Italy) and undergoing to fine-needle aspiration (FNA) biopsies for suspicious nodules ($n = 356$). Expression of selected lncRNAs (MALAT1, HOTAIR and PVT1) was evaluated by Droplet Digital PCR (ddPCR) in FNAs. The lncRNAs expression levels and cytological and histopathological data, from 161 patients, have been used to developed a "Decision Tree" based predictive model. Among these patients, 125 are inliers (38 benign and 87 malignant lesions), contain TIR3A ($n = 28$), TIR3B ($n = 37$) and TIR4 ($n = 60$). To prevent overfitting, the model was restricted to a maximum of 5 decision variables per split and 12 number of leaf nodes.

Results (overall cohort): The predictive model demonstrated an accuracy of 93% in benign/malignant classification, and 80% in 10-fold cross-validation. In the overall cohort, the "decision tree" strategy achieved 91% sensitivity and 97% specificity, with a positive predictive value (PPV) of 98% and a negative predictive value (NPV) of 82%. In addition, in TIR3A lesions, we obtained a sensitivity of 73% and a specificity of 100% with a PPV of 100% and NPV of 77%. While, in TIR3B lesions, sensitivity and specificity were 93% and 100%, respectively with a PPV of 100% and an NPV of 97%. Of note, the expression levels of lncRNAs in both thyroid nodule and lymph node analysis showed significantly higher MALAT1 and PVT1 expression in malignant samples.

Conclusions: Overall, these finding suggest that an integrated analysis of lncRNAs in FNA biopsies may serve as a reliable diagnostic tool to reduce unnecessary surgery and supporting personalized patient management.

Abstract citation ID: lvag096.142

OC12.2 - LBA_ECE_1287 - Preoperative TSH and risk of hypothyroidism after hemithyroidectomy: a nationwide matched cohort study

Nichlas Udholm[1], Diana Grove-Laugesen[2], Martin Almquist[3], Rasmus Reinke[1], Anna Vincent[4], Mathilde Seekjær[1], Sebastian Udholm[1], Christian Christiansen[4] and Lars Rolighed[1]

[1]*Department of Otorhinolaryngology, Head and Neck Surgery, Aarhus University Hospital, Aarhus, Denmark;* [2]*Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus, Denmark;* [3]*Section of Endocrine and Sarcoma Surgery, Department of Surgery, Skåne University Hospital, Lund, Sweden;* [4]*Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Hemithyroidectomy (HT) is the most frequently performed thyroid operation. Although part of the thyroid gland is preserved, postoperative hypothyroidism (hypoT) develops in a considerable proportion of patients. Identifying patients at increased risk of hypoT following HT may improve risk stratification and support surgical decision-making and postoperative surveillance. However, population-based data on the incidence of hypoT after HT and the predictive value of postoperative thyroid function remain limited.

Objective: To estimate the risk of hypoT following HT in a Danish population and evaluate preoperative thyroid-stimulating hormone (TSH) as predictor of postoperative hypoT.

Methods: We conducted a nationwide, population-based cohort study including all adult Danish patients undergoing HT from 1998 to 2024. We excluded patients <18 years or with preoperative medical treatment for hypoT or hyperthyroidism (hyperT), and patients having additional thyroid surgery after HT. The primary outcome was postoperative hypoT defined as initiation of thyroid hormone replacement therapy (TRT) following HT. We generated a matched cohort (1:10) from the general population based on sex and year of birth. Matching criteria included being alive at the time of HT, no treatment for hypoT or hyperT before HT, and no previous thyroid surgery. We estimated the cumulative incidence (risk) of hypoT using the Aalen–Johansen estimator with death as a competing risk and compared the risk between HT patients and the matched reference cohort. Subgroup analyses were performed according to preoperative TSH categories for the patients where these data were available.

Results: We identified 41 056 thyroid operations in 38 257 patients, of whom 29 423 met the inclusion criteria and were compared with a matched reference cohort of 294 230 individuals. Due to data availability, preoperative TSH measurements were only available for the period 2008-2024, including 16 136 patients (54, 8%). The 5-year risk of hypoT following HT was 21.0%, compared with 1.2% in the matched reference cohort. The risk of hypoT increased with higher preoperative TSH levels. The 5-year risk was 9.2% among patients with preoperative TSH <1 mIU/L, 19.5% for TSH 1-2 mIU/L, 42.8% for TSH 2-3 mIU/L, and 73.2% for TSH >3 mIU/L.

Conclusions: One out of five patients developed hypoT within five years after a HT. Higher preoperative TSH levels were strongly associated with an increased risk of postoperative hypoT. Preoperative TSH may therefore be a useful predictor for risk stratification and patient counselling when informing about the risk of postoperative hypoT.

Abstract citation ID: lvag096.143

OC12.3 - LBA_ECE_1123 - Tocilizumab and Sirolimus show higher response rates than methylprednisolone as first-line treatment for moderate-to-severe active Graves' Orbitopathy: a proof-of-concept study

Silvia Corrias, Giulia Faa, Federica Diana, Filippo Lixi, Giuseppe Giannaccare, Erica Ragno, Gianluigi Canu, Francesca Pigliaru, Stefano Mariotti, Francesco Boi and Giulia Lanzolla
Cagliari, Italy

Objective: Tocilizumab and sirolimus have emerged as potential therapeutic alternatives for moderate-to-severe active Graves' Orbitopathy (GO). This study aimed to compare the clinical efficacy and safety of tocilizumab, sirolimus, and ivGCs in patients with moderate-to-severe active GO.

Materials and Methods: Fifty-two consecutive patients with moderate-to-severe active GO were retrospectively evaluated: 14 treated with sirolimus (2 mg on day 1, followed by 1 mg/day for 12 weeks), 14 with tocilizumab (8 mg/kg once monthly for 4 months), and 24 with methylprednisolone (500 mg/weekly for 6 weeks, followed by 250 mg/weekly for 6 weeks), as first line treatment. Sirolimus and tocilizumab were administered when methylprednisolone was contraindicated. Clinical assessments were performed at baseline and 12 weeks after treatment completion. Primary endpoint: overall GO outcome based on a composite evaluation. Secondary endpoints: proportion of responders and the change from baseline in 1) quality of life, evaluated by GO-QoL questionnaire; 2) proptosis; 3) Clinical Activity Score (CAS); 4) ocular motility; 5) eyelid aperture.

Results: The overall response rate was significantly higher with tocilizumab (85%, OR 14.6, 95% CI 2.49-72.3; $P = .002$) and sirolimus (71%, OR 6.07, 95%CI: 1.39-21.2; $P = .018$) compared with methylprednisolone (29%). CAS response was significantly greater with tocilizumab (92%, OR 13.0, 95%CI: 1.94-148; $P = .012$) and sirolimus (71%) (OR 6.0, 95% CI 1.09-30.1; $P = .039$) versus methylprednisolone (50%). Proptosis response was significantly higher with tocilizumab (85%, OR 30.0, 95%CI: 4.27-153; $P < .0001$) and sirolimus (50%) (OR 6.67, 95%CI: 1.33-24.3; $P = 0.014$) versus methylprednisolone (16.6%). QoL response was significantly higher with tocilizumab (92%) (OR 18.0, 95%CI: 2.95-89.6; $P = .0005$) and sirolimus(65%) (OR 5.4, 95%CI: 1.24-22.7; $P = .037$) versus methylprednisolone (25%). Consistently, mean reductions in CAS, proptosis and QoL were significantly greater in both sirolimus ($P = .01$, .02 and .003 respectively) and tocilizumab groups (all $P < .0001$) compared to with methylprednisolone. Eyelid aperture and diplopia response rates did not differ significantly across groups. However, ocular ductions showed greater improvement in tocilizumab ($P = .009$) and sirolimus ($P = .01$) groups compared with methylprednisolone. No significant differences in adverse effects were observed across groups. On multivariate logistic regression, treatment with tocilizumab (OR 28.5,95% CI 3.1-64.1) and sirolimus (OR 7.35, 95%CI 1.33-53.5) were associated with a greater probability of response compared to methylprednisolone, regardless of baseline CAS, TRAb levels and smoking habit.

Conclusions: As novel therapies targeting precise molecular pathways are emerging in the treatment landscape of GO, both tocilizumab and sirolimus demonstrated significantly superior response rate compared to methylprednisolone, with comparable safety profiles and sustainable costs. If confirmed in randomized trials, these findings support the use of IL-6 inhibition and mTOR pathway modulation as first-line therapeutic strategies in GO.

Abstract citation ID: lvag096.144

OC12.4 - LBA_ECE_1141 - The safety and efficacy of eneboparatide, a parathyroid hormone 1 receptor agonist, in adults with chronic hypoparathyroidism: a phase 3, randomized, placebo-controlled study (CALYPSO)

Maria Luisa Brandi[1], Jeremy Turner[2,3], Steven Ing[4], Istvan Takacs[5], Aliya Khan[6], Lynn Kohlmeier[7],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Andrea Palermo[8,9], Lars Rejnmark[10], John Bilezikian[11], Natasha Appelman-Dijkstra[12], Lorenz Hofbauer[13], Manoj Rajadhyaksha[14], Julien Laffaire[15], Anna Petryk[16], Taha Ould Rouis[17], Soraya Allas[17] and Michael Mannstadt[18]
[1]FIRMO Italian Foundation for the Research on Bone Diseases, Florence, Italy; [2]Department of Diabetes and Endocrinology, Norfolk and Norwich University Hospital, Norwich, United Kingdom; [3]Faculty of Medicine and Health Sciences, Norwich Medical School, University of East Anglia, Norwich, United Kingdom; [4]Division of Endocrinology, Diabetes and Metabolism, The Ohio State University Wexner Medical Center and Arthur G. James Comprehensive Cancer Center, Columbus, OH, United States; [5]Department of Internal Medicine and Oncology, Semmelweis University, Budapest, Hungary; [6]Division of Endocrinology and Metabolism, McMaster University, Hamilton, ON, Canada; [7]Spokane Osteoporosis and Endocrinology, Arthritis Northwest Research, Spokane, WA, United States; [8]Unit of Metabolic Bone and Thyroid Disorders, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy; [9]Unit of Endocrinology and Diabetes, Campus Bio-Medico University, Rome, Italy; [10]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus, Denmark; [11]Department of Medicine, Vagelos College of Physicians and Surgeons, Columbia University, New York, NY, United States; [12]Department of Internal Medicine, Section Endocrinology, Leiden University Medical Center, Leiden, The Netherlands; [13]Division of Endocrinology and Bone Diseases, Department of Medicine III, University Center for Healthy Aging, Technische Universität Dresden, Dresden, Germany; [14]Immunogenicity Sciences, Alexion, AstraZeneca Rare Disease, Boston, MA, United States; [15]Quantitative Sciences, Alexion, AstraZeneca Rare Disease, Barcelona, Spain; [16]Global Medical Affairs, Alexion, AstraZeneca Rare Disease, Boston, MA, United States; [17]Clinical Development, Alexion, AstraZeneca Rare Disease, Ecully, France; [18]Endocrine Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States

Background: Chronic hypoparathyroidism (cHypoPT) is a rare endocrine disease caused by parathyroid hormone (PTH) deficiency, resulting in hypocalcemia, hypercalciuria, and low bone turnover. Despite conventional therapy (oral active vitamin D and/or calcium) and PTH replacement therapies, there is a need for additional treatments that stabilize calcium and provide control of symptoms and urinary calcium (uCa) excretion with balanced effects on bone. Eneboparatide is a long-acting, novel PTH 1 receptor agonist in development to meet these goals in patients with cHypoPT.

Objectives: To assess the efficacy and safety of daily subcutaneous (SC) eneboparatide for 24 weeks versus placebo in patients with cHypoPT, followed by a 28-week open-label extension (OLE).

Methods: Design: Phase 3, multicenter, randomized, double-blind, parallel, placebo-controlled, 24-week treatment, followed by an OLE (NCT05778071).

Participants: 200 adults (77% women; 154/200) aged 18-80 with cHypoPT were randomized 2:1 to eneboparatide or placebo. All patients who completed the 24-week period enrolled in the OLE ($n = 187/200$).

Intervention: After optimization to ensure albumin-adjusted serum calcium (ADsCa) was within 7.8-9 mg/dL (1.95-2.25 mmol/L), participants received a daily SC injection of eneboparatide or placebo. Conventional therapy was progressively reduced, and uptitration of eneboparatide was permitted according to a predefined protocol. Uptitration was not permitted in the last 4 weeks but was allowed again in the OLE.

Outcomes: The primary efficacy endpoint was the proportion of participants achieving independence from active vitamin D and therapeutic doses of oral calcium (ie, >600 mg/day) and normal ADsCa (8.3-10.6 mg/dL [2.07-2.64 mmol/L]). Key secondary endpoints included normalization of uCa excretion in participants with hypercalciuria at baseline and improvement in symptoms and physical functioning as assessed by disease-specific patient-reported outcomes (PROs). Safety parameters were evaluated, and bone safety measures included serum bone turnover biomarkers and bone mineral density (BMD).

Results: All primary and key secondary endpoints met statistical significance at week 24. A higher proportion of patients receiving eneboparatide achieved the primary endpoint versus placebo (31% [41/132] vs 6% [4/68] [$P < .0001$]). 57% (43/76) of hypercalciuric eneboparatide patients normalized uCa excretion versus 20% (9/45) of placebo patients ($P = .0001$). Through week 52, ADsCa was stable with conventional therapy and eneboparatide titration, and uCa excretion and PRO benefits persisted. Mild-to-moderate hypocalcemia was the most frequently reported adverse event. Changes in bone turnover biomarkers and BMD were consistent with balanced bone turnover.

Conclusions: Eneboparatide provides prolonged, positive results and clinical benefits for patients with cHypoPT with acceptable safety.

Abstract citation ID: lvag096.145

OC12.5 - LBA_ECE_1391 - Characterisation of tumour-associated macrophages across adrenocortical adenomas and carcinomas: evidence for cortisol-driven and sex-specific polarisation

Rosa Catalano[1], Cynthia Mendoza Pimentel[2], Mario Detomas[2], Otilia Kimpel[2], Giacomo Cristofolini[2], Ali Kerim Secener[3], Sarah Küppers[2], Sonja Steinhauer[2], Sabine Herterich[4], Stefan Kircher[5], Cristina L. Ronchi[6], Silviu Sbiera[2], Erika Peverelli[7], Giovanna Mantovani[7], Martin Fassnacht[2] and Barbara Altieri[8]
[1]Division of Endocrinology and Diabetes, Department of Internal Medicine I-Department of Clinical Sciences and Community Health, University Hospital, University of Würzburg-University of Milan, Würzburg, Germany; [2]Division of Endocrinology and Diabetes, Department of Internal Medicine I, University Hospital, University of Würzburg, Würzburg, Germany; [3]Max Delbrück Center for Molecular Medicine, Berlin, Germany; [4]Central Laboratory University Hospital Würzburg, Würzburg, Germany; [5]Institute of Pathology, University of Würzburg, Würzburg, Germany; [6]Department of Metabolism and System Science, University of Birmingham, Birmingham, United Kingdom; [7]Department of Clinical Sciences and Community Health-Endocrinology Unit, University of Milan-Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [8]Division of Endocrinology and Diabetes, Department of Internal Medicine I-Bavarian Cancer Research Center (BZKF), University Hospital, University of Würzburg, Würzburg, Germany

Background: Tumour-associated macrophages (TAM) are key regulators of the tumour microenvironment. Single-nucleus RNA data indicate that macrophage infiltration decreases from normal adrenal glands (NAG) to adrenocortical adenomas

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(ACA) and carcinomas (ACC). However, a comprehensive characterisation of TAM polarisation across adrenocortical tissues is still lacking.

Aim: To characterise TAM infiltration and polarisation in ACA and ACC compared with NAG, and to investigate associations with clinicopathological characteristics.

Methods: Immunohistochemistry for CD16 (immune-infiltration marker), CD68 (M1/M2-marker), and M2-like markers (CD163, CD206, CD204) was performed in a cohort of 250 adrenocortical tumours (102 ACA and 148 ACC, including 130 primary and 18 recurrent/metastatic cases) and 16 NAG. Immunostaining was quantified using QuPath (v0.5.1) and expressed as percentage of positive pixels. Associations with circulating white blood cell parameters and clinicopathological characteristics, including hormonal secretion and clinical outcomes, were analysed.

Results: In NAG, median CD68 expression (2.4%) was lower than other markers (CD16 = 10.3%, CD163 = 5.8%, CD206 = 7.4%, CD204 = 8.2%; $P < .001$). In ACA and ACC, CD68 (1.6% and 1.81%) and CD206 (1.6% and 0.33%) were lower than CD16 (6.2% and 5.24%), CD163 (6.6% and 2.97%), and CD204 (7.9% and 4.96%) (all $P < .001$). While CD68 expression remained stable across all tissues, CD206 was reduced in ACA compared with NAG. In ACC, all M2-like markers were significantly decreased compared with both NAG and ACA ($P < .001$), and CD16 was lower than in NAG ($P = .036$), indicating a global loss of macrophage infiltration in ACC. No differences were observed between primary and recurrent/metastatic ACC.

In endocrine inactive ACA (EIA), but not in cortisol-producing ACA (CPA), CD68, CD16 and CD204 inversely correlated with circulating lymphocyte-to-monocyte ratio (LMR) (all $P < .05$). In ACC, this pattern was reversed, with CD68 inversely correlating with LMR only in cortisol-secreting tumours ($P = .020$). Cortisol excess was associated with reduced macrophage infiltration (lower CD68 and CD16 in CPA vs EIA and inverse correlation between cortisol and CD16 in ACC) and with distinct polarisation profiles: $CD163^+/CD206^-$ in ACA and $CD163^+/CD206^-/CD204^-$ in ACC (all $P < .05$). These associations were observed in women but not in men, suggesting sex-specific immune modulation.

Advanced ENSAT tumour stage, Ki67>10%, Weiss score ≥ 7 were associated with a $CD204^+/CD163^-/CD206^-$ macrophage profile ($P < .05$). No marker correlated with overall or progression-free survival.

Conclusions: TAM exhibit distinct and dynamic polarisation patterns across adrenocortical tissues. Cortisol excess and sex shape TAM phenotypes, while aggressive ACC is characterised by a specific TAM profile. These findings highlight the complexity and heterogeneity of the immune microenvironment in adrenocortical tumours.

Rapid Communications

Abstract citation ID: lvag096.146

RC1.1 - ECE_3438 - Thyroid disease during pregnancy: pre-existing disease or pregnancy-specific abnormality?

Leonie Warringa, Joris Osinga, Arash Derakhshan, Vincent Jaddoe, Sjoerd Van Den Berg, Robin Peeters and Tim Korevaar
Academic Center for Thyroid Diseases, Erasmus MC, Internal Medicine, Rotterdam, The Netherlands

Background: Both overt and subclinical thyroid disease are associated with adverse pregnancy outcomes such as miscarriage, preterm birth and pre-eclampsia. It remains unclear if thyroid function test abnormalities that are first diagnosed during pregnancy, result from the changes in gestational thyroid physiology or if they were already present prior to pregnancy and only diagnosed for the first time during pregnancy. However, preconception thyroid function data of women with gestational thyroid disease is scarce.

Methods: This study included 2718 women of the Generation R Next study, a population-based prospective cohort from pregnancy planning through postpartum in Rotterdam. The prevalence of abnormalities in thyroid function tests during both the preconception and gestational periods was assessed using various reference ranges, and individual trajectories were illustrated with Sankey diagrams. For those women with thyroid function test abnormalities in pregnancy, the mean thyroid hormones concentrations of preconception were determined.

Results: A subgroup of 503 women had thyroid function measurement during preconception and subsequent pregnancy. The median interval between the thyroid function measurements was 4.2 months (95% range 0.9-13.0). The overall prevalence of thyroid function test abnormalities was largely consistent during preconception and pregnancy. However, when assay cutoffs are applied during pregnancy, prevalence of eg subclinical hyperthyroidism changed from 1.4% to 8%. Women with (subclinical) hypothyroidism or hypothyroxinemia during pregnancy had a higher preconception TSH than euthyroid pregnant women (3.08 mU/L, 3.83 mU/L and 2.25 mU/L vs 1.65 mU/L) and women with hyperthyroidism during pregnancy had a significant lower preconception TSH (0.53 mU/L vs 1.65 mU/L). Women with hypothyroxinemia during pregnancy had a lower preconception FT4 than euthyroid pregnant women (15.6 pmol/L vs 17.9 pmol/L).

Conclusions: This is the first study to show that thyroid function test abnormalities identified during pregnancy are predominantly likely to present pre-existing thyroid disease rather than a failure to adapt to gestational thyroid physiological changes.

Abstract citation ID: lvag096.147

RC1.2 - ECE_3230 - Ocular surface dysfunction in Graves' orbitopathy (GO): quantitative conjunctival hyperemia as a novel tool to identify active GO

Federica Diana, Alessandro Colleo, Laura Pinna, Filippo Lixi, Francesco Nannipieri, Francesca Saba, Sara Bernardi, Silvia Corrias, Giuseppe Giannaccare, Stefano Mariotti, Francesco Boi and Giulia Lanzolla
Quartu Sant'Elena, Italy

Introduction: Dry eye disease (DED) is a frequent but underrecognized feature of Graves' orbitopathy (GO), and the relationship between ocular surface alterations, GO activity and severity remains insufficiently characterized. The aims of this cross-sectional observational study were 1) to compare the prevalence of DED in GD without GO, mild GO, moderate-to-severe active GO, and healthy controls; 2) to evaluate the relationship between a)non-invasive break-up time (NIBUT), b)tear meniscus height (TMH), c)meiboscore, and d)quantitatively assessed conjunctival hyperemia and the clinical activity score (CAS).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Materials and Methods: A total of 138 consecutive patients with GD (F:101, M:37), including 109 with GO and 29 without GO, along with 67 age- and sex-matched healthy controls, were enrolled. DED was defined by the presence of symptoms (Ocular Surface Disease Index [OSDI] ≥33) and abnormalities in NIBUT and/or TMH, measured by Oculus Keratograph 5M.

Results: DED was diagnosed in 78/138 (56.5%) of GD patients with a significantly higher frequency compared with healthy controls (OR 6.2; 95% CI 3.01-13.27; $P < .0001$). Within the GD cohort, DED was more frequent in patients with GO compared with those without GO (OR 2.91; 95% CI 1.16-7.12; $P = .01$), with a significant difference between moderate-to-severe active GO and mild GO (OR 4.06; 95% CI 1.38-10.48; $P = .007$).

NIBUT was significantly reduced in patients with moderate-to-severe active GO compared with healthy controls ($P < .0001$), GD without GO ($P = .01$), and mild GO ($P = .013$). TMH was reduced in moderate-to-severe active GO compared with GD without GO ($P = .01$), mild GO ($P = .002$), and healthy controls ($P = .0005$). Meiboscore values were higher in GD patients without GO ($P = .01$), mild GO ($P < .0001$), and moderate-to-severe active GO ($P < .0001$) compared with healthy controls.

Quantitatively measured conjunctival hyperemia was significantly increased in moderate-to-severe active GO compared with mild GO ($P = .04$), GD without GO ($P = .003$), and healthy controls ($P < .0001$). Notably, conjunctival hyperemia showed a significant correlation with CAS ($P < .0001$, $r = 0.60$, 95% CI 0.45-0.71), which was confirmed in multivariate analysis ($P = .002$). Higher conjunctival hyperemia values were independently associated with active GO ($\chi^2 = 28.01$, $P < .0001$), with good discriminative ability (AUC = 0.76).

Conclusions: DED is highly prevalent in GD, particularly in patients with moderate-to-severe active GO. Among ocular surface parameters, quantitative conjunctival hyperemia is uniquely and independently associated with GO activity and may represent a useful tool to identify patients with active GO.

Abstract citation ID: lvag096.148

RC1.3 - ECE_1308 - Serum exosomes from patients with Graves' orbitopathy promote proliferation of orbital fibroblasts

Chia-Hung Lin[1] and Cheng-Yu Tsai[2]
[1]National Taiwan University Hospital, Zhongzheng District, Taiwan; [2]Taipei, Taiwan

Introduction: Graves' orbitopathy (GO) is characterized by orbital soft tissue expansion due to inflammation and adipogenesis. While the pathogenesis involves the activation of orbital fibroblasts (OFs), the specific intercellular signaling mechanisms remain incompletely understood. Exosomes are extracellular vesicles that facilitate cell-to-cell communication by transferring bioactive cargo, including proteins and nucleic acids, effectively protecting them from degradation in the systemic circulation. Previous research indicates that the protein and microRNA profiles within serum exosomes differ significantly among patients with GO, Graves' disease (GD), and healthy controls. However, the functional impact of these circulating extracellular vesicles on orbital tissue remains unclear. This study aimed to compare the effects of serum exosomes derived from patients with GO, GD without GO, and non-GD controls on the proliferation of OFs.

Methods: Serum exosomes were isolated from patients with GO, GD without GO, and non-GD controls. The exosomes were characterized by nanoparticle tracking analysis (NTA) and Western blotting for exosomal markers. Primary orbital fibroblast cell lines were established from orbital fat tissue obtained during surgery from both GO and non-GO subjects. OFs were co-cultured with serum exosomes (5 μg/well) from the distinct study groups. Cell proliferation was assessed using CCK8 and Crystal Violet assays up to 120 hours.

Results: A total of 12 participants (4 GO, 4 GD without GO, and 4 non-GD controls) were enrolled in this study for serum sample, while OFs were isolated from orbital fat obtained from 3 GO and 3 non-GO subjects. NTA and Western blot analysis confirmed the successful isolation of exosomes, showing typical size ranges and expression of exosomal markers. In cell proliferation experiments, both CCK-8 and Crystal Violet assays consistently demonstrated that treatment with serum exosomes from GO patients significantly promoted the proliferation of OFs compared to those treated with serum exosomes from GD without GO or non-GD controls (all $P < .05$). Notably, this pro-proliferative effect was universally observed regardless of whether the OFs derived from GO patients or non-GO subjects.

Conclusions: Our findings demonstrate that circulating serum exosomes in patients with Graves' orbitopathy possess the capacity to stimulate the proliferation of OFs, suggesting that serum exosomes may serve as an important mediator in the pathogenesis of GO. Ongoing studies are now focusing on the impact of these exosomes on myofibroblast differentiation, adipogenesis, and hyaluronan production, as well as identifying the specific protein or miRNA candidates within the exosomal cargo responsible for this effect.

Abstract citation ID: lvag096.149

RC1.4 - ECE_2209 - Gut microbiota in patients with Hashimoto's thyroiditis isolated or framed in polyautoimmunity

Marco Centanni, Ilaria Stramazzo, Anna Carretti and Camilla Virili
Endocrine Unit SM Goretti Hospital, Medical-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy

Background: The colonization of germ-free murine models with different bacterial species enlightened the role of gut microbiota in shaping immune response. A role for gut microbiota has been hypothesized in both the pathogenesis and clinical presentation of different autoimmune disorders, including thyroid autoimmunity. No data are available about gut microbiota composition in patients with Hashimoto's thyroiditis (HT) associated to further non-endocrine autoimmune disease and this was the aim of the this study.

Patients and Methods: We examined the fecal microbial composition of 58 euthyroid adult patients (50F/8M) with HT subdivided into three groups: A) 24 with isolated HT (iHT); B) 22 with HT and gastric atrophy (HT+GCA) and C) 12 with HT and vitiligo (HT+VIT). None of the enrolled patients followed unbalanced diets, had further disorders, or used interfering drugs or

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

supplements. Nineteen matched healthy subjects (HD) were used as an internal control group. Microbiota composition was determined via 16s rDNA sequencing of the hyper-variable region V3-4 on Illumina MiSeq; α- and β-diversity indices and all statistical analysis were computed in Qiime2.

Results: All autoimmune patients showed a significant increase in the relative abundance of Firmicutes spp. and Actinobacteria spp. ($P < .00001$) and a reduced relative abundance of Proteobacteria spp. and Bacteroidetes spp. compared to HD ($P < .001$). Firmicutes/Bacteroidetes ratio was significantly higher in groups iHT, HT+GCA and HT+VIT than in HD ($P < .0001$); to note, this ratio was higher in HT+VIT group than in iHT patients ($P = .046$). α-diversity analysis revealed that both the richness and phylogenetic diversity of microbial communities were higher in every study group than in HD ($P < .001$ and $P < .0001$, respectively). Upon β-diversity analysis, the phylogenetic distance was highly clusterized in all patient groups compared to HD in both the Unweighted ($P = .001$) and the Weighted ($P = .001$) UniFrac analyses. The LEfSe analysis, revealed that Lachnospiraceae, Peptostreptococcaceae and Bifidobacteriaceae, encompassing the bacterial species *Fusicatenibacter saccharivorans*, *Anaerostipes hadrus* and *Blautia massiliensis*, were significantly associated to patients with HT+VIT (group C). In contrast, patients with HT+CAG (group B) were strongly associated to Lachnospiraceae and Streptococcaceae, with the prevalence of *Streptococcus salivarius*, whereas patients with HT were mostly associated to *Blautia faecis*, in accordance to ANCOM results.

Conclusions: These results described the variations in relative taxa abundances as well as phylogenetic distances between the gut microbial communities in autoimmune patients and those in healthy controls. Specific signatures at family and species level characterized the different autoimmune disorders associated to HT.

Abstract citation ID: lvag096.150

RC1.5 - ECE_1492 - Patterns of amiodarone-related thyroid dysfunction and associated comorbidities: a nationwide study

Adnan Zaina[1] and Sameer Kassem[2]
[1]*The Azrieli Faculty of Medicine, Clalit Medical Health Care Services, Endocrinology, Bar-Ilan University, Safed, Israel;* [2]*Carmel Medical Center, Internal Medicine, Technion Israel Institute of Technology, Haifa, Israel*

Introduction: Amiodarone is the most commonly used antiarrhythmic medication in the Western world, with a multifaceted mechanism of action. It is highly effective in treating and preventing both atrial and ventricular tachyarrhythmias. Despite its efficacy, amiodarone use is associated with significant side effects, including thyroid dysfunction, pulmonary fibrosis, hepatic impairment, and cardiac rhythm disturbances.

Objective: This study evaluated amiodarone-induced thyroid dysfunction (AITD) in previously euthyroid individuals and assessed associated cardiovascular risks.

Methods: A retrospective cohort of patients prescribed amiodarone from 2010 to 2022 was studied. Patients with a history of thyroid disease were excluded. Eligible participants with normal TSH levels were included. Patients were followed for up to 5 years and categorized into four groups based on TSH levels: euthyroid ($0.5 < TSH < 4.5$), amiodarone-induced hypothyroidism (AIH; $TSH > 10$), subclinical AIH ($4.5 < TSH < 10$), and amiodarone-induced thyrotoxicosis (AIT; TSH <). The AIT group was further subdivided into two groups: those with $TSH < 0.1$ and those with subclinical AIT ($0.1 < TSH < 0.5$). Outcomes included mortality, heart failure (HF), acute coronary syndrome (ACS), atrial fibrillation (AF), and ischemic stroke (IS).

Results: Of 43 880 records, 13 444 patients met the inclusion criteria (mean age: 73.8 ± 10.7 years; 55.9% male). During follow-up, 65.6% maintained normal TSH, 23.4% developed subclinical AIH, 7.1% developed AIH, and 3.8% developed AIT; 1.8% had subclinical AIT and 2.1% had AIT. AIH patients were older than previously reported. AIT patients were younger (71.3 ± 10.9 years) and predominantly male. AIT was associated with a higher risk of mortality (OR = 1.64; 95% CI, 1.24-2.17), particularly in the subclinical group. An increased risk of HF was observed in both AIH (OR 1.61, 95% CI 1.23-2.12) and subclinical AIH (OR 1.3, 95% CI 1.11-1.51).

Conclusions: This extensive study underscores the importance of risk assessment and management in patients receiving amiodarone. The average age of patients who developed thyroid disorders was higher than previously reported, particularly among those with hypothyroidism. The study emphasizes the need for vigilance not only in symptomatic patients with overt thyroid dysfunction but also in those with subclinical hypo- and hyperthyroidism. Although the drug remains a key treatment for arrhythmias, its potential complications, particularly thyroid dysfunction and associated cardiovascular risks, require frequent monitoring for early detection. Further research is needed to explore strategies that balance the therapeutic benefits of amiodarone against its risks and to evaluate appropriate alternative treatment modalities.

Abstract citation ID: lvag096.151

RC1.6 - ECE_2341 - Initiation and cessation of levothyroxine therapy: results from a largepopulation based cohort

Adrian Heald[1], Mike Stedman[2], Peter Taylor[3], Suhani Bahl[4], Anish Patil[5], Lakdasa Premawardhana[4], David Halsall[6], Ian Halsall[6], Antonio Bianco[7], Anna Bloomfield[8], Onyebuchi Okosieme[4] and Colin Dayan[9]
[1]*Department of Diabetes and Endocrinology, Salford Royal Hospital, Salford, United Kingdom;* [2]*Res Consortium, Andover, United Kingdom;* [3]*Cardiff University, Cardiff, United Kingdom;* [4]*Cardiff University School of Medicine, Cardiff, United Kingdom;* [5]*Salford Royal Hospital, Salford, United Kingdom;* [6]*Addenbrooke's Hospital, Cambridge, United Kingdom;* [7]*Medicine-Endocrinology, University of Chicago, Chicago, United States;* [8]*University of Lancaster, Lancaster, United Kingdom;* [9]*University of Birmingham, Birmingham, United Kingdom*

Introduction: Community prescriptions for levothyroxine (LT4) increased from 9-million annually in 2000 to 30-million in 2024. Understanding the outcomes of patients discontinuing treatment, particularly those on low LT4 doses, may inform as to the causes of this increase.

Methods: This study utilised patient-level primary care data 2010-2024, encompassing 2.85 million patients with recorded thyroid function tests (TFTs) and LT4 prescriptions.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Cohort definition: Patients with prescriptions for LT4 were divided into two classes: those on medication at the start of the period (2010)(Class A) and those who started LT4 medication during the period 2011-2023 (Class B). Codes for other thyroid disorders, including Thyrotoxicosis, were excluded.

Dose classification: A cut-off of an average prescribed LT4 of 80 mcg/day was derived from the recommended 1.6 mcg/d/kg +BMI to distinguish between lower doses (<80 mcg/day) and higher doses (>=80 mcg/day).

Results: In the period 2011-2023 of the total 1 097 586 with recorded TFT-results, 106 117 received LT4.

Treatment growth: The number of patients prescribed LT4 in GMCR increased from 17.0/1000 population in 2011 to 28.3/1000 population in 2023, an Annual Average Rate of Increase (AARI) of 4.4%. The use of low doses (<80 mcg/day) grew faster (AARI = 7.9%) than higher doses (>=80 mcg/day, AARI = 2.2%). The largest increases were observed in the elderly (80+years) and males for both dose categories.

Cessation: Of 58 070 patients who started LT4 post-2010 (Class B), 5100 (Class B2) stopped medication and had subsequent thyroid function measurement. Patients who stopped (Class B2) had a significantly lower median dose (50 mcg/day (Interquartile Range (IQR) 43-57 mcg/day) compared to those continuing (Class B1: 76 mcg/day (IQR 68-84 mcg/day). Median age at diagnosis for those who stopped was 45-years vs those continuing at 49-years). The median duration on medication for low-dose patients who stopped was 12-months.

TFT outcomes post-cessation (low dose patients <80 mcg/day): For patients who stopped (Class B2, $n = 4646$), the median serum TSH 12-months after stopping (3.5 mIUL (IQR 3.2-3.miU/L)) was lower than the median TSH 3-months before starting LT4 (6.9 mIU/L (IQR 6.6-7.2 miU/L), $P = .005$). Similarly, median FT4 12-months after stopping (13.4 pmol/L (IQR 13.3-13.6 pmol/L)) was higher than before starting (12.9 pmol/L (IQR 12.7-13.1 pmol/L), $P = .02$). TSH after treatment for 55% of patients who had stopped LT4 remained within the reference range.

Conclusions: LT4 use has increased by two-thirds, notably those started on very low doses, older individuals and males. A significant subset of patients, those started on lower doses of LT4, successfully discontinued treatment and maintained euthyroid status. This suggests that initial elevation of serum TSH may have been transient.

Abstract citation ID: lvag096.152

RC2.1 - ECE_2511 - Impact of SGLT2 inhibitors on telomere length in type 2 diabetes patients with and without chronic kidney disease

Yanina Rebrova[1,2,3], Yanina Saienko[1], Kostiantyn Midlovets[1], Dmytro Krasnenkov[1] and Borys Mankovsky[1,3]
[1]*D. F. Chebotarev Institute of Gerontology of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine;* [2]*The Scientific and Practical Medical Center of Pediatric Cardiology and Cardiac Surgery of the Ministry of Health of Ukraine, Government Institution, Kyiv, Ukraine;* [3]*Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine*

Background and Aims: Telomeres are repetitive DNA–protein structures at chromosome ends that maintain genomic stability and serve as markers of biological aging. Accelerated telomere shortening is associated with cellular senescence and increased risk of chronic diseases. In type 2 diabetes mellitus (T2DM), telomere attrition is enhanced due to chronic hyperglycemia, oxidative stress, and inflammation. Chronic kidney disease (CKD) further aggravates these mechanisms, making telomere length a potential biomarker of biological age and prognosis. Sodium–glucose cotransporter-2 (SGLT2) inhibitors are established nephroprotective agents and may also modulate cellular aging by reducing oxidative stress and inflammation. However, their effect on telomere length in patients with T2DM with and without CKD remains insufficiently studied. This study aimed to evaluate the association between SGLT2 inhibitor therapy and telomere length in patients with T2DM stratified by CKD status.

Materials and Methods: The study included 100 patients with T2DM divided into two groups: with CKD ($n = 50$) and without CKD ($n = 50$). In each group, half of the patients received SGLT2 inhibitor therapy. Clinical and laboratory characteristics were assessed in all participants. Telomere length in whole blood leukocytes was measured using monochrome multiplex quantitative polymerase chain reaction and expressed as the telomere-to-single-copy gene ratio (T/S). Age-adjusted residual telomere length (ΔT/S) was calculated using linear regression. Pathologically short telomeres were defined as ΔT/S values with a Z-score < -1. Statistical analysis included Mann–Whitney U test, χ^2 test, Pearson correlation analysis, and multiple linear regression.

Results: Patients with CKD were older, had longer diabetes duration, higher HbA1c levels, lower estimated glomerular filtration rate, and higher albuminuria compared with patients without CKD. Body mass index was comparable between groups, while cardiovascular disease was more prevalent in the CKD group. Residual telomere length (ΔT/S) was significantly lower in patients with CKD ($P = .035$). Pathologically short telomeres were more frequent in CKD patients than in those without CKD (20.8% vs 2.1%, $P = .0076$). In both groups, SGLT2 inhibitor therapy was positively associated with longer telomere length (CKD: $r = 0.50$, $P < .01$; non-CKD: $r = 0.60$, $P < .01$). In multivariate analysis, SGLT2 inhibitor therapy was the only independent predictor of longer telomere length ($P < .001$; $R^2 = 0.51$).

Conclusions: CKD is associated with accelerated telomere shortening in patients with T2DM. SGLT2 inhibitor therapy is associated with longer residual telomere length regardless of CKD status, suggesting a potential slowing of cellular aging.

Abstract citation ID: lvag096.153

RC2.2 - ECE_1370 - Prevalence and outcomes of DKA in type 1 and type 2 DM patients treated and not treated with SGLT-2 inhibitors

Elena Chertok Shacham[1,2], Sireen Sharif[3] and Snait Ayalon[3]
[1]*Emek Medical Center, Internal Medicine B, Afula, Israel;* [2]*Medical Faculty, Technion, Israel Institute of Technology, Haifa, Israel;* [3]*Emek Medical Center, Research Authority, Afula, Israel*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Diabetic ketoacidosis (DKA) is a life-threatening complication occurring in people with type 1 (T1DM) and type 2 diabetes (T2DM). Sodium–glucose cotransporter-2 (SGLT2) inhibitors have raised concern for DKA risk.

Aim: To compare the clinical characteristics, biochemical presentation, and short- and long-term outcomes of DKA in hospitalized adults with T1DM and T2DM, including the impact of SGLT2 inhibitor therapy.

Methods: A retrospective cohort of 2283 adults (838 with T1DM; 1445 with T2DM) hospitalized with DKA between 2013 and 2023 across Clalit Health Services hospitals was analyzed. Patients were stratified by SGLT2 inhibitor use within 4 months before admission. Outcomes included AKI, 30-day mortality, 1-year mortality, and readmissions. One-year mortality was assessed using Cox proportional hazards regression, 30-day mortality using logistic regression, and recurrent readmissions using a negative binomial model.

Results: 2.3% ($N = 19$) of T1DM and 16% (235) of T2DM patients were treated with SGLT-2 inhibitors. A total of 115 patients from all cohorts presented with eu DKA, characterized by lower glucose and bicarbonate levels. In T2DM, the incidence of AKI was higher among SGLT2 users (26% vs 17%; $P = .030$), but lower in euDKA cases (9.6% vs 19%; $P = .020$).

In Cox regression analysis, treatment with SGLT2 inhibitors was independently associated with reduced 1-year mortality (HR 0.55, 95% CI 0.36-0.82; $P = .004$). Predictors of increased 1-year mortality included older age, higher HbA1c, cardiovascular disease, CKD, and insulin therapy. In the negative binomial model, higher readmission rates were independently associated with T1DM, higher HbA1c, higher BMI, CKD, and pre-admission insulin use, while SGLT2 inhibitor use was not linked to increased readmissions.

Conclusions: Pre-hospital SGLT2 inhibitor therapy in patients presenting with DKA was associated with improved long-term survival and no increase in short-term mortality, supporting their continued use with appropriate clinical monitoring.

Table 1 Cox proportional hazards model for 1-year mortality in T2DM.

Variable	Hazard ratio (HR)	95% Confidence interval	*P* value
HbA1c	0.85	0.80-0.90	<.001
Age (per year)	1.05	1.04-1.07	<.001
AKI	1.09	0.79-1.48	.062
BMI	0.98	0.96-1.00	.360
Congestive heart failure	1.01	0.91-1.48	.409
Chronic kidney disease	1.15	0.89-1.49	.013
Cardiovascular disease	1.14	0.85-1.51	.004
DPP-4 inhibitor	0.97	0.70-1.36	.866
Male sex	1.12	0.87-1.44	.378
GLP-1 receptor agonist	0.82	0.52-1.32	.215
Hypoglycemia (<70 mg/dL)	1.00	0.98-1.02	.308
Metformin	1.07	0.82-1.39	.230
Pre-hospital long-acting insulin	1.66	1.28-2.16	<.001
SGLT2 inhibitor	0.55	0.36-0.82	.004

Abstract citation ID: lvag096.154

RC2.3 - ECE_2061 - Liver Kiss1 is dispensable for systemic glucose homeostasis but essential for hepatic sex-biased transcriptomic patterns

Krisztina Kukoricza[1], Guillermo Martinez[1], Esperanza Uceda-@rodriguez[2], Suvi Ruohonen[1], Andreas Landin[3], Laura Mairinoja[1], Maria Vazquez[2], Claes Ohlsson[3], Marina Mora-Ortiz[2], Leena Strauss[1], Matti Poutanen[1] and Manuel Tena-Sempere[2]
[1]*University of Turku, Turku, Finland;* [2]*University of Córdoba, Córdoba, Spain;* [3]*Gothenburg University, Gothenburg, Sweden*

Kisspeptins, encoded by the *Kiss1* gene and originally identified as metastasis suppressors, are pivotal elements for reproductive regulation, but their expression in non-reproductive tissues, including the liver, suggests broader physiological functions. However, the physiological roles of liver-born kisspeptins remain largely unknown. We report here the generation and characterization of a liver-specific *Kiss1* knockout (LiKKO) mouse. Reproductive function was unaffected in LiKKO mice, that displayed also preserved glucose homeostasis in both sexes, despite previous reports suggesting a role of liver kisspeptin in insulin secretion and glycemic control. Conversely, ablation of hepatic *Kiss1,* expressed in hepatocytes, resulted in a clear sexually-dimorphic impact, as revealed by histological, expression and transcriptomic analyses. Female, but not male LiKKO mice displayed signs of low-grade, focal hepatic inflammation. In turn, qPCR analyses documented gene expression changes preferentially in LiKKO males, with altered mRNA levels of key factors for lipogenesis, beta-oxidation and metabolic sensing, despite consistent elevation of liver Ppar-γ expression in both sexes. In good agreement, RNA-seq transcriptomic analyses revealed a much larger number of differentially expressed genes in male vs female LiKKO mice (1.474 and 132, respectively), with divergent sex-dependent changes. Thus, while female LiKKO displayed deregulation of cancer-associated gene pathways and activation of pro-inflammatory genes, LiKKO males showed transcriptional alterations related to protein processing and the unfolded protein response, and induction of anti-inflammatory genes. Notably, loss of hepatic *Kiss1* markedly amplified the intrinsic sex differences in liver gene expression, suggesting a repressive role in the control of sex-biased transcriptional patterns. Pathway analysis of genes contributing to gained sex differences in the absence of *Kiss1* highlighted immune-related processes, rather than conventional metabolic pathways. Together, our findings indicate that liver-born kisspeptins are dispensable for systemic glucose homeostasis but play a major role in modulating key liver molecular pathways, including non-metabolic functions, in a sexually dimorphic manner.

Abstract citation ID: lvag096.155

RC2.4 - ECE_2045 - Association between GIPR p.E354Q and glycemic response to sulfonylureas in individuals with type 2 diabetes

Heejun Son[1], Jee-Soo Lee[2], Moon-Woo Seong[3], Sung Ok Lee[1], Eun Jin An[1], Min Seop Sim[1], Hyun Ah Kim[1] and Hye Seung Jung[1]
[1]*Internal Medicine, Seoul National University Hospital, Seoul, South Korea;* [2]*Laboratory Medicine, Seoul National University Hospital, Seoul, South Korea;* [3]*Seoul, South Korea*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Sulfonylureas (SUs) remain widely used in the treatment of type 2 diabetes (T2D), with substantial interindividual variability in glycemic response. A loss-of-function variant in the glucose-dependent insulinotropic polypeptide receptor (*GIPR*) has been identified among patients with T2D who rely on SUs for optimal glycemic control. We therefore aimed to investigate the association between *GIPR* functional variants and SU responsiveness.

Methods: Adults with T2D were enrolled from the Korea Biobank Network at Seoul National University Hospital, where comprehensive clinical data and buffy coat samples are available. Participants who had stably maintained SU treatment for at least 12 months were included. Whole-exome sequencing was performed to identify *GIPR* variants predicted to be deleterious *in silico*. The primary outcome was achievement of HbA1c < 7.0% in 1 year following SU therapy. The study was approved by the Institutional Review Board (No. H-2310-141-1479). To explore underlying mechanisms, *in vitro* experiments were conducted using insulin-secreting cell lines and human islets exposed to chronic glucolipotoxicity, assessing SU-stimulated insulin secretion following modulation of GIPR expression via RNA silencing.

Results: A total of 153 participants (mean age 60 ± 11 years, 58% male, BMI 25.5 ± 3.7 Kg/m^2, and baseline HbA1c 8.4% ± 0.9%) were enrolled. We identified a common but predicted significantly deleterious *GIPR* variant, p.E354Q (minor allele frequency ~0.2; CADD score 32). Fifty-seven participants (37.3%) carried p.E354Q, including nine homozygous individuals. In multivariable regression models adjusted for age, sex, BMI, diabetes duration, eGFR, and concomitant anti-diabetic medications, carriage of p.E354Q was independently associated with a higher likelihood of achieving HbA1c < 7.0% (OR 2.201, 95% CI 1.033-4.689; $P = .041$), and with greater HbA1c reduction (standardized $\beta = .146$; $P = .008$).

In vitro GIPR downregulation restored SU-stimulated insulin secretion under conditions of metabolic stress, but not under physiological culture conditions. Given that SU action depends on cellular ATP levels and that high-glucose reduces cellular ATP through *VDAC1* induction, we further examined these pathways. Consequently, *GIPR* silencing attenuated glucolipotoxicity-induced *VDAC1* expression and increased cellular ATP retention, supporting enhanced insulinotropic effects of SUs.

Conclusions: The functional *GIPR* variant p.E354Q contributes to a genetic predisposition to enhanced SU responsiveness in Korean individuals with T2D. The high prevalence of this variant suggests potential utility as a precision medicine marker for optimizing SU therapy.

Funding: NRF (2022R1A2C2004570)

Abstract citation ID: lvag096.156

RC2.5 - ECE_2773 - Safety and efficacy of DCCR in patients with Prader-Willi syndrome who have pre-diabetes or diabetes

Jennifer Miller[1], Neil Cowen[2], Julie Perry[2], Jing Gong[2], Michael Huang[2], Anish Bhatnagar[2] and Evelien Gevers[3]

[1]*University of Florida, Gainesville, United States;* [2]*Soleno Therapeutics Inc., Redwood City, California, United States;* [3]*Queen Mary University of London, Barts and The London Medical School, Centre for Endocrinology, William Harvey Research Institute, London, United Kingdom*

Introduction: Diazoxide choline extended-release (DCCR) is an oral, once-daily medication in development for the treatment of patients with Prader-Willi syndrome (PWS) who have hyperphagia. Here, we present an analysis of the safety and efficacy of DCCR in individuals with PWS who have evidence of prediabetes (PD) or diabetes (DM) at baseline, using data from the Phase 3 studies.

Methods: Participants were classified as having evidence at baseline of PD or DM based on their medical history, use of glucose-lowering concomitant medications, and clinical laboratory values (using the American Diabetes Association [ADA] criteria of baseline fasting plasma glucose [FPG] ≥ 100 mg/dL or HbA1c ≥ 5.7%). Efficacy outcomes included the Hyperphagia Questionnaire for Clinical Trials (HQ-CT). Safety was assessed based on hyperglycaemia-related laboratory values and adverse events (AEs).

Results: A total of 125 participants ≥4 years-old with genetically confirmed PWS who received DCCR were identified in the Phase 3 studies. Of these, 75 (60.0%) participants had evidence of PD or DM at baseline (PD/DM group). Discontinuation rates were low regardless of baseline PD/DM status, with 29.3% of participants discontinuing in the PD/DM group compared with 32.0% in the non-PD/DM group. At Week 156, both groups showed comparable, statistically significant reductions in HQ-CT score from baseline (mean [SD] reduction: 12 [9.4] and 12.9 [8.5] for the PD/DM and non-PD/DM groups, respectively; $P < .0001$ for both).

Mean (SD) HbA1c at Baseline and Week 156 was 5.7 (0.43) and 5.9 (1.18) vs 5.3 (0.24) and 5.4 (0.37), respectively, for participants with and without PD/DM. As expected, hyperglycaemia-related AEs were reported for more participants with than without PD/DM (42.7% vs 24.0%, respectively), but these events were generally manageable.

Conclusions: In the DCCR Phase 3 studies, more than half of participants with PWS had baseline evidence of PD or DM. The results of our analysis show that DCCR can be administered safely and effectively to individuals with PWS who have PD/DM, and that HQ-CT improvements are comparable between participants with and without PD/DM. Hyperglycaemia-related AEs were, as expected, reported in a greater proportion of participants with PD/DM. After 156 weeks of DCCR treatment, mean HbA1c remained in the prediabetes range for those with PD/DM, and below for those without PD/DM. Notably, DCCR-treated participants remained on study and had high treatment compliance, regardless of PD/DM status or occurrence of hyperglycaemia-related AEs.

Abstract citation ID: lvag096.157

RC2.6 - ECE_3164 - Predictive utility of OGTT-based insulin resistance and secretion indices for type 2 diabetes—a focus on HOMA-IR and ISSI-2

Huiwen Tan[1], Qingyue Zeng[2], Danting Li[2] and Nong Li[3]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Department of Endocrinology & Metabolism, West China Hospital Sichuan University, Chengdu, China; [2]Department of General Medicine, West China Hospital Sichuan University, Chengdu, China; [3]Department of Endocrinology and Metabolism, Karamay Hospital of Traditional Chinese and Western Medicine, Karamay, China

Objective: Insulin resistance (IR) and pancreatic β-cell secretion dysfunction are the core pathophysiological mechanisms underlying the development and progression of type 2 diabetes mellitus. Although multiple assessment indices are currently available in clinical practice, controversy remains regarding their predictive efficacy and optimal selection. This study aimed to identify optimal surrogate indices for IR and pancreatic β-cell function from oral glucose tolerance test (OGTT) data and evaluate their independent and combined value in predicting dysglycaemia and type 2 diabetes (T2D).

Methods: This cross-sectional analysis included 7588 participants in Karamay classified as normal glucose tolerance (NGT, $n = 992$), prediabetes (Pre-DM, $n = 4911$), or diabetes (DM, $n = 1685$). We evaluated eight IR indices (HOMA-IR, TyG index, TyG-BMI, METS-IR, VAI, CVAI, TG/HDL ratio, and Matsuda index) and ten secretion indices [basal secretion (HOMA-β, Fins/FPG ratio), early-phase secretion (IGI, CIR), overall secretion (AUC Ins/Glu ratio, 120-minute secretion index), and disposition indices (Insulin secretion-sensitivity index-2(ISSI-2), DI_Oral, DI_Basal, DI_TyG]. Relationships with three outcomes (DM vs non-DM; dysglycaemia vs NGT; DM vs Pre-DM) were analysed using restricted cubic splines (RCS). Diagnostic performance was assessed via ROC analysis, multivariable logistic regression, and incremental value (NRI/IDI).

Results: All metabolic indices differed significantly across groups (P-trend < .001), showing rising IR and a pattern of compensatory then failing secretion from NGT to DM. Restricted cubic spline analysis revealed significant nonlinear relationships with diabetes risk for most indices. Key inflection points were identified at 1.87 for HOMA-IR and 24.38 for ISSI-2. HOMA-IR and ISSI-2 were selected as optimal indices for resistance and secretion, respectively. For diabetes prediction, fully adjusted standardised odds ratios (ORs) were 2.04 (95% CI:1.92-2.18) for HOMA-IR and 0.07 (0.06-0.08) for ISSI-2, with AUCs of 0.71 and 0.11. The indices were negatively correlated (Spearman $r = -0.43$, $P < .001$). In combined models, ISSI-2 provided substantial incremental predictive value over HOMA-IR, increasing the AUC from 0.75 to 0.90 ($P < .001$). A significant multiplicative interaction was observed ($P < .001$). Stratification by median values created four pathophysiological subtypes with markedly different diabetes prevalence, ranging from 3.6% (low resistance/high secretion) to 44.5% (high resistance/low secretion) (P-trend<.001).

Conclusions: HOMA-IR and ISSI-2 are optimal indices for assessing IR and insulin secretion, exhibiting synergistic predictive value for identifying patients at the highest risk for developing diabetes. Their nonlinear relationships with diabetes risk offer early warning thresholds. A dual-index classification strategy provides a practical tool for risk stratification and precision prevention.

Keywords type 2 diabetes mellitus, insulin resistance, pancreatic β-cell function, HOMA-IR, insulin secretion-sensitivity index-2 (ISSI-2), prediction model

Abstract citation ID: lvag096.158

RC3.2 - ECE_1307 - Digital and intelligent pathology application in PitNETs

Nidan Qiao, Haixia Cheng and Yao Zhao
Shanghai, China

Background: The diagnosis, subtyping, and prognostic prediction of pituitary neuroendocrine tumors (PitNETs) primarily rely on hematoxylin and eosin (H&E)-based assessment and transcription factor (TF) immunohistochemical classification.

Purpose: This study aimed to develop and evaluate a foundation artificial intelligence (AI) model for improving diagnostic accuracy, subtyping, and recurrence prediction in PitNETs.

Methods: A novel AI model was constructed using a state-of-the-art pathology foundation model. It comprises three modules: 1) distinguishing PitNETs from other sellar region pathologies; 2) predicting TF expression from H&E slides and generating virtual TF-stained images; and 3) predicting post-surgical recurrence. The model was trained at a primary center and its performance was validated using multi-institutional data from nine external centers.

Results: This is a multicenter cohort study. We included four cohorts: 2146 patients with PitNETs (retrospectively recorded data), 1513 patients with PitNETs (prospectively recorded data), 1205 patients with PitNETs treated at nine external institutions (external data), and 1078 patients with other sellar region pathologies. Module 1 achieved high diagnostic accuracy, with 95.6% in the internal test set and 93.5% in external validation for differentiating PitNETs from other sellar region pathologies. It not only demonstrated diagnostic performance statistically comparable to senior pathologists ($P = .069$) and superior to intermediate/junior pathologists ($P = .001$ and $P < .001$, respectively), but also successfully learned pathologist-recognized morphological features. Module 2 generated virtual TF stains from H&E slides with high morphological concordance to ground-truth, maintaining 95.9% accuracy and reducing diagnostic workload of pathologists by 68.9% in external validation. Module 3 stratified PitNETs into three recurrence-risk profiles. In multivariable analysis, the high-risk versus low-risk profile showed a hazard ratio of 6.16 (95% CI 3.01-12.6, $P < .001$). Explainable analysis implicated stromal infiltration by fibroblasts, T cells, macrophages, and microvasculature in elevated recurrence risk. By integrating the three modules, a clinical web application was deployed to facilitate clinical implementation.

Conclusions: The application of digital and intelligent pathology for PitNETs enhances diagnostic precision, reduces pathologist workload, and provides robust prognostic stratification, supporting optimized clinical management.

Abstract citation ID: lvag096.159

RC3.3 - ECE_1030 - European primary analysis from the LINC 5 phase II study: pharmacokinetics, pharmacodynamics, efficacy and tolerability of osilodrostat in paediatric patients with Cushing's disease

Agnès Linglart[1], Jean De Schepper[2], Martinerie Laetitia[3], Michel Polak[4], Fausto Bogazzi[5], Andrea Piacentini[6],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Massimo Casi[6], Angela Pastore[6], Michal Sarnecki[7] and Marco Cappa[8]
[1]AP-HP, Paris Saclay University, Le Kremlin-Bicêtre, France; [2]University Hospital Brussels, Vrije Universiteit Brussel, Brussels, Belgium; [3]Robert Debré Hospital and Université Paris Cité, Paris, France; [4]Necker Hospital, Paris, France; [5]University of Pisa, Pisa, Italy; [6]Recordati SpA, Milan, Italy; [7]Recordati AG, Basel, Switzerland; [8]Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

Introduction: Cushing's disease (CD) is a rare disorder of cortisol excess associated with increased morbidity and mortality across all age groups. Available pharmacological treatments for paediatric CD are limited. LINC 5 (NCT03708900), an ongoing, open-label, non-comparative study, evaluates the pharmacokinetics, pharmacodynamics, efficacy and tolerability of osilodrostat in paediatric patients with CD.

Methods: Patients (6-<18 years old) with confirmed CD started osilodrostat 1 mg once/twice (<60/>60 kg) daily. Dose was titrated according to weight and response. Visits were every 3 weeks (W) to assess pharmacokinetic, pharmacodynamic, efficacy and tolerability parameters. Primary endpoint: pharmacokinetic parameters of osilodrostat up to W12. Secondary endpoints: efficacy of osilodrostat assessed by proportion of patients with normal mean urinary free cortisol (mUFC) and change from baseline in mUFC at W6 and W12, and safety and tolerability of osilodrostat up to W12. Analyses were descriptive, with no formal statistical testing.

Results: Of the 13 enrolled patients with CD (median [min–max] age: 11 years [8-15]), three (23.1%) had previously undergone pituitary surgery and nine (69.2%) were ineligible for surgery. Median (min–max) osilodrostat exposure was 12 W (11.4-12.7). Median average and highest median (min–max) daily osilodrostat doses were 4.2 mg (1.5-6.8) and 8.0 mg (2.0-10.0), respectively. Median C_{max} of osilodrostat (6.36 ng/mL) was achieved at a median time of 1.03 hours after the first dose of osilodrostat 1 mg. Median elimination half-life was 3.03 hours ($n = 7$). Treatment-emergent adverse events (TEAEs) occurred in 11 patients (84.6%). Five patients (38.5%) experienced TEAEs suspected as related to osilodrostat (all mild or moderate severity). No serious TEAEs or deaths were reported. No patients discontinued osilodrostat because of TEAEs. Two patients (15.4%) experienced an adverse event related to hypocortisolism (decreased UFC, $n = 1$) and adrenal-hormone-precursor accumulation (acne, $n = 1$). No patients experienced an adverse event related to pituitary-tumour enlargement, arrhythmogenic potential or QT prolongation. Median mUFC (nmol/24 h) values decreased from 408 at baseline to 341 at W6 and 99 at W12. The proportion of patients with mUFC not exceeding the upper limit of normal increased from 0.0% at baseline to 7.7% at W6 and 53.8% at W12. There were no clinically relevant changes from baseline in the signs and symptoms of hypercortisolism, systolic or diastolic blood pressure, pulse rate, or body mass index standard deviation score.

Conclusions: Osilodrostat demonstrated pharmacokinetic, safety and efficacy profiles consistent with adult data, supporting a positive benefit–risk profile in paediatric CD.

Abstract citation ID: lvag096.160

RC3.4 - ECE_1029 - Effect of CAM2029 on long-term biochemical and symptom control in patients with acromegaly according to prior injectable somatostatin receptor ligand

Maria Fleseriu[1], Irina Bancos[2], Timo Deutschbein[3], Diego Ferone[4], Mônica Gadelha[5], Aleksandra Gilis-Januszewska[6], Elena Isaeva[7], Pinar Kadioglu[8], Robert D Murray[9], Joanna L. Spencer-Segal[10], Jacob Råstam[11], Maria Harrie[11], Agneta Svedberg[11], Alberto M. Pedroncelli[11], Fredrik Tiberg[11] and Beverly M.K. Biller[12]
[1]Pituitary Center, Departments of Medicine and Neurological Surgery, Oregon Health and Science University, Portland, OR, United States; [2]Division of Endocrinology, Mayo Clinic, Rochester, MN, United States; [3]Medicover Oldenburg MVZ, Oldenburg, Germany; [4]Endocrinology Unit, Department of Internal Medicine, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [5]Neuroendocrinology Research Center/Endocrinology Division, Medical School and Hospital Universitario Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil; [6]Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland; [7]Interregional Clinical Diagnostic Center, Kazan, Russia; [8]Division of Endocrinology-Metabolism and Diabetes, Department of Internal Medicine, Istanbul University-Cerrahpaşa, Istanbul, Türkiye; [9]Department of Endocrinology, St James's University Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; [10]Department of Internal Medicine and Michigan Neuroscience Institute, University of Michigan, Ann Arbor, MI, United States; [11]Camurus AB, Lund, Sweden; [12]Neuroendocrine and Pituitary Tumor Clinical Center, Massachusetts General Hospital, Boston, MA, United States

Background: Many patients with acromegaly do not achieve biochemical control (insulin-like growth factor I [IGF-I] ≤ upper limit of normal [ULN]) or symptom remission when treated with standard-of-care (SoC) somatostatin receptor ligands (SRLs; eg octreotide long-acting repeatable [LAR], lanreotide Autogel [ATG]). CAM2029 is a long-acting octreotide subcutaneous depot approved for maintenance treatment in adults with acromegaly in Europe and the UK. CAM2029 has demonstrated improved biochemical control in patients with IGF-I ≤ 2 × ULN on baseline SoC. Here, we report the effect of CAM2029 on both biochemical control and acromegaly symptoms in this subset of patients based on the previously received SRL (either octreotide LAR or lanreotide ATG).

Methods: Patients directly enrolled on day 1 of ACROINNOVA 2 had IGF-I ≤ 2 × ULN on prior baseline SoC. CAM2029 20 mg was administered every 4 weeks (W) (±1 W) via a pre-filled pen for 52 W. The primary endpoint was long-term safety; secondary endpoints included biochemical control rate (IGF-I ≤ ULN per age and sex; W50/52 mean) and symptom control (Acromegaly Index of Severity [AIS]; range 0-18, lower scores indicate better symptoms) over time.

Results: A total of 81 patients were directly enrolled, of which 59 previously received octreotide LAR and 22 lanreotide ATG.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

CAM2029 was well tolerated, with a safety profile consistent with SoC. The observed proportion of patients with biochemical control increased from baseline (14.8%) to W50/52 (36.5%) following CAM2029 treatment (Table). Similar increases were observed from baseline to W50/52 in both the prior octreotide LAR (15.3% to 37.0%) and lanreotide ATG (13.6% to 35.0%) groups (Table). Acromegaly symptoms improved from baseline to W52 in all groups (Table).

	Any SRL	Octreotide LAR	Lanreotide ATG
Patients with mean IGF-I ≤ ULN, *n*/*N* (%)			
SoC baseline	12/81 (14.8)	9/59 (15.3)	3/22 (13.6)
W24	26/75 (34.7)	22/54 (40.7)	4/21 (19.0)
Mean W50/52	27/74 (36.5)	20/54 (37.0)	7/20 (35.0)
Mean AIS overall score (standard deviation)			
SoC baseline	(*n* = 81) 4.4 (3.6)	(*n* = 59) 4.4 (3.6)	(*n* = 22) 4.5 (3.6)
W24	(*n* = 76) 3.5 (2.7)	(*n* = 55) 3.5 (2.8)	(*n* = 21) 3.6 (2.7)
W52	(*n* = 73) 3.3 (2.9)	(*n* = 53) 3.4 (2.9)	(*n* = 20) 3.1 (2.9)

Conclusions: CAM2029 provides sustained improvements in biochemical and symptom control in patients with IGF-I ≤ 2 × ULN, regardless of previous SRL treatment. These results support CAM2029 as a long-term treatment option for acromegaly, including in patients without normalised IGF-I on octreotide LAR or lanreotide ATG.

Abstract citation ID: lvag096.161

RC3.5 - ECE_2991 - Cancer risk and GLP-1 receptor agonist use in patients with Cushing syndrome

Idit Dotan[1], Yaron Rudman[1], Ilan Shimon[1], Maria Fleseriu[2] and Amit Akirov[1]
[1]*Beilinson Hospital, Institute of Endocrinology, Petah Tikva, Israel;* [2]*Departments of Medicine and Neurological Surgery, Oregon Health & Science University, Portland, United States*

Introduction: Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are commonly used for the treatment of type 2 diabetes mellitus and obesity; however, their impact on cancer in patients with Cushing syndrome (CS) remains unknown. We have previously reported a higher incidence of malignancy in patients with CS compared with matched population controls. We aimed to assess the association between GLP-1RA treatment and malignancy risk in patients with CS.

Methods: We conducted a nationwide retrospective cohort study including patients with endogenous CS diagnosed between 2000 and 2023 using the Clalit Health Services database in Israel. Patients with adrenal carcinoma or ectopic CS were excluded. Exposure to GLP-1RAs was defined as ≥3 prescription dispensations following CS diagnosis, including patients who initiated treatment prior to diagnosis. Patients treated with GLP-1RAs were compared with those never exposed (≤2 prescriptions). Time-varying analyses were performed. The primary outcome was incident malignancy following CS diagnosis. A secondary outcome included malignancy occurring after at least 6 months of GLP-1RA treatment and up to 12 months after treatment discontinuation.

Results: The cohort included 609 patients with CS (mean age ± SD, 48.05 ± 7.17 years; 65.02% women), of whom 137 received GLP-1RAs and 472 were not treated. Median GLP-1RA treatment duration was 44.80 months (IQR, 25.26-76.71). Age, sex distribution, and prevalence of malignancy prior to CS diagnosis were similar between groups. Median BMI at CS diagnosis was higher among GLP-1RA–treated patients (34.57 vs 27.74 kg/m^2), as were rates of hypertension (66.42% vs 53.39%), diabetes mellitus (48.91% vs 15.47%), and ischemic heart disease (17.52% vs 9.75%). Two-year CS remission rates were comparable. Over up to 15 years of follow-up, malignancy following CS diagnosis occurred in 10.22% of GLP-1RA–treated patients and 16.53% of non-treated patients. In a time-varying Cox model, GLP-1RA treatment was not associated with increased malignancy risk (HR 0.79; 95% CI, 0.48-1.29). GLP-1RA–treated patients experienced a reduction in median BMI during follow-up, whereas BMI remained stable in non-treated patients. In an exploratory early analysis, all-cause mortality was lower among GLP-1RA–treated patients (16.06% vs 25.21%).

Conclusions: In this large nationwide CS cohort, GLP-1 RA treatment, used in approximately 20% of patients, was not associated with an increased risk of malignancy. These findings support the oncologic safety of GLP-1RAs in this high-risk population. Observed differences in mortality should be interpreted cautiously and warrant further investigation.

Abstract citation ID: lvag096.162

RC3.6 - ECE_2932 - Voice-based machine learning model in acromegaly: single-center cohort

Seyma Aksoy[1], Emre Saygili[2], Esra Hatipoglu[1] and Mutlu Niyazoğlu[1]
[1]*Basaksehir Cam and Sakura City Hospital, Department of Endocrinology, University of Health Sciences, Istanbul, Türkiye;* [2]*Department of Endocrinology, Canakkale Onsekiz Mart Universty, Canakkale, Türkiye*

Background: Acromegaly, a rare endocrine disorder driven by excessive growth hormone (GH) and insulin-like growth factor-1 (IGF-1) production, is often characterized by insidious onset and prolonged diagnostic delays. While vocal changes are recognized clinical features, the diagnostic utility of advanced deep learning architectures for non-invasive screening remains underexplored. Although a single study has utilized machine learning for acoustic assessments in this population (Vouzouneraki K. et al.), integration of the Wav2vec 2.0 model has not yet been evaluated. This study aimed to assess the efficacy of voice analysis using Wav2vec 2.0-based machine learning as a novel digital biomarker for identifying acromegaly.

Methods: This single-center case-control study included 70 patients with acromegaly and 68 age- and sex-matched controls with non-functional pituitary adenomas. Clinical status was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

defined by standard biochemical guidelines, assessing GH/IGF-1 levels, symptoms, comorbidities, and residual tumor presence. Voice samples were acquired using a standard mobile phone in a quiet clinical setting; participants recorded three repetitions of the Turkish words "zaman" and "simit". Acoustic signals were resampled to 16 kHz using Wav2vec 2.0 to extract high-dimensional embedding vectors (size 1024). Embedding vectors were combined with patient and control labels. These features were used to train and validate Random Forest (RF), Extreme Gradient Boosting (XGBoost), Logistic Regression (LR), and Support Vector Machines (SVM) algorithms via 80:20 test split and five-fold cross-validation.

Results: No significant demographic disparities existed between the acromegaly (mean age 45.5 years) and control (mean age 47.5 years) cohorts. In acromegaly group, the gender ratio was 57.1% female ($n = 40$) and 42.9% male ($n = 30$); in control group, it was 61.8% female ($n = 42$) and 38.2% male ($n = 26$). Within acromegaly group, 40% had active disease, 60% in remission. Median IGF-1 levels were 1.8 × upper limit of normal (ULN) (inter quantile range (IQR) 1.4-2.8) in active disease and 1.0 × ULN (IQR 1.0-1.0) in remission ($P < .01$). The patient group included both newly diagnosed and long-term following patients. Mean disease duration was 62 months (range:1 month-37 years). In the five-fold cross-validation, LR model demonstrated superior performance with an Area Under the Curve (AUC) of 0.86 (95% confidence interval (CI): 0.83-0.89), sensitivity of 0.83 (CI:0.78-0.88) and a specificity of 0.90 (CI: 0.86-0.94). Independent test set validation confirmed high accuracy in the LR model (AUC: 0.847; specificity:0.93; sensitivity:0.82).

Conclusions: Digital voice analysis leveraging the Wav2vec 2.0 model provides high diagnostic accuracy for acromegaly. Voice-based analysis serves as a promising, non-invasive digital biomarker for acromegaly.

Keywords acromegaly, digital biomarker, machine learning, Wav2vec 2.0, voice analysis

Abstract citation ID: lvag096.163

RC4.1 - ECE_2133 - Loss of Y chromosome in male infertility

Valentina Griseta[1,2], Giorgia Spaggiari[1,3], Samantha Sperduti[2], Antonio Raffaele Michele Granata[1,3], Livio Casarini[2], Manuela Simoni[1,2] and Daniele Santi[1,2,3]
[1]*Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy;* [2]*Modena, Italy;* [3]*Unit of Andrology and Sexual Medicine of the Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy*

Introduction: When alterations in semen parameters cannot be explained, the contribution of as-yet-unidentified genetic factors is advocated. The Y chromosome (chrY) includes many genes essential for spermatogenesis. It is susceptible to age-related mitotic errors that may lead to chrY loss in some of the germ cells, negatively impacting fertility. Loss of chrY has been associated with several pathological conditions, but its potential role in the pathogenesis of male infertility remains poorly investigated. This study aims to explore the association between chrY loss and male infertility.

Methods: Male partners of infertile couples attending our Unit were prospectively enrolled and divided into cases (semen parameters <5th WHO percentile) and controls (semen parameters >5th WHO percentile). In addition to semen analysis, all participants underwent blood testing for follicle-stimulating hormone (FSH), luteinizing hormone (LH), total testosterone, estradiol, prolactin and prostate-specific antigen (PSA) levels. To quantify the percentage of chrY loss, genomic DNA was extracted from peripheral blood, and X and Y chromosome copy numbers were assessed using droplet digital-PCR. Target genes on chromosome X (*AMELX* and androgen receptor gene, *AR*) and Y (*AMELY* and *USP9Y*) were selected. The analysis was performed in technical duplicate by counting the copies of *AMELY* and *AMELX*, *USP9Y* and *AR* genes by TaqMan assays, and calculating the percentage loss of chrY using the equation: (copies of Y/copies of X) × 100.

Results: This 'interim analysis' included 114 patients: 73 cases (64.0%) and 41 controls (36.0%). Age (38.0 ± 5.7 vs 35.3 ± 5.0 years) and FSH levels (7.8 ± 5.7 vs 4.9 ± 2.5 IU/mL) were significantly higher in cases than in controls ($P = .014$ and $P = .004$, respectively, Mann–Whitney's *U*-test). No differences were observed for BMI ($P = .921$), LH ($P = .252$), and estradiol levels ($P = .730$). The *AMELY/AMELX* ratio was 0.983 ± 0.034 in cases and 0.999 ± 0.001 in controls ($P = .003$, Welch's t-test). Comparable results were obtained considering the *USP9Y/AR* ratio.

Discussion: Patients with altered semen parameters had higher FSH levels, consistent with impaired spermatogenetic function. At the same time, they had greater loss of chrY compared with controls. Although these patients were also significantly older than controls, the average age of both groups remains deeply below 50, the age threshold after which the loss of chrY has been widely demonstrated in the literature. For this reason, our finding may represent a factor directly associated with poorer semen quality.

Conclusions: These results suggest that chrY loss assessment may represent a new potential etiology of male infertility, possibly independent of ageing.

Abstract citation ID: lvag096.164

RC4.2 - ECE_2674 - Efficacy of gonadotropin therapy to induce spermatogenesis and fertility in men with pathologic gonadotropin deficiency

Joshua Gialouris[1,2], Ann Conway[1,2], Amanda Idan[2], Sasha Savkovic[2], Raquel Hermosilla[2], Christopher Muir[2], Feyrous Bacha[2], Ting Zhang[1,2], Wanxin Hou[1,2], Veena Jayadev[2] and David Handelsman[1,2]
[1]*Andrology, ANZAC Research Institute, Sydney, Australia;* [2]*Andrology, Concord Repatriation General Hospital, Concord West, Australia*

Gonadotropin treatment to induce spermatogenesis for gonadotropin-deficient men is the only medically treatable cause of male infertility. However, time-dependent analyses of fertility outcomes in large cohorts are lacking. We evaluated the time to, and determinants of, fertility outcomes in men with pathologic gonadotropin-deficiency undergoing gonadotropin treatment. Consecutive infertile men ($n = 99$) with congenital or acquired pathologic gonadotropin deficiency were treated with urinary or recombinant hCG and FSH according to

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

a standardized protocol between 1983 and 2024. Kaplan-Meier and multivariate Cox regression analyses examined time to prespecified sperm density thresholds and pregnancy. Men aged 35 ± 1 years with female partners 30 ± 1 years underwent 160 treatment cycles. The proportion (%) and median time (months) to achieve sperm thresholds of >0, >2, >5, >10 and >20 million sperm/mL was 78% (5 months), 56% (12 months), 49% (14 months), 37% (21 months) and 24% (not determined) respectively. The major determinant of successful pregnancy was the presence of adverse fertility factors in the female partner (HR 0.20, 95% CI 0.10-0.40; $P < .001$), with time to pregnancy also significantly increased by the presence of adverse female factors (15 vs 43 months; $P < .0001$). The median sperm concentration associated with partner pregnancy was 2.8 (0.2, 52.6) M/mL without and 35.4 (15.1, 52.6) M/mL with adverse female factors. Most men with pathologic gonadotropin deficiency treated with hCG/FSH achieve sperm output and fertility within a year, with greatest impact on fertility outcomes being detrimental female fertility factors.

Abstract citation ID: lvag096.165

RC4.3 - ECE_1016 - Manipulation of peripheral androgen signaling in the treatment of PCOS-associated metabolic dysfunction

Caitlin MacRae[1,2], Elodie Kip[1], Benjamin Garfinkel[3] and Rebecca Campbell[1,2]
[1]Centre for Neuroendocrinology, University of Otago, Dunedin, New Zealand; [2]Maurice Wilkins Centre, Auckland, New Zealand; [3]Alnylam Pharmaceuticals, Cambridge, United States

Hyperandrogenism is the most common diagnostic criterion of polycystic ovary syndrome (PCOS), and androgen signalling through the androgen receptor (AR) is implicated in promoting reproductive and metabolic dysfunction. However, the specific physiological targets of female androgen excess in driving PCOS-associated pathology remain poorly understood. Studies in animal models of PCOS suggest liver and adipose tissue may be critical sites of androgen-induced metabolic dysfunction in mouse models of PCOS. We therefore aimed to investigate the therapeutic potential of tissue-specific AR silencing RNA (siRNA) for alleviating PCOS-like metabolic dysfunction. Two preclinical mouse models of PCOS, exposing female mice to androgens (or vehicle controls) either during the prenatal period (gestation day 16-18; prenatal androgenisation, PNA) or chronically from postnatal day 21 (peripubertal androgenisation, PPA), were treated with PBS or with proprietary, tissue-specific AR siRNA to induce AR-knockdown (ARKD). Delivery of AR siRNA, initiated at 3 weeks of age, was directed to either the liver (liver-ARKD), adipose tissue (adipose-ARKD), or both (combination-ARKD). Male and female PNA mice demonstrated mild metabolic impairments (significantly increased weight gain, impaired glucose homeostasis) compared to controls, while PPA females were significantly heavier and showed robust impairments in glucose and insulin homeostasis compared to control females. However, ARKD was unable to alleviate these effects regardless of target tissue, despite inducing a 5-fold reduction in AR gene expression as measured by qPCR. While tissue-level analysis is ongoing to investigate AR protein knockdown, lipid accumulation and metabolic gene expression, evidence to date does not support liver or adipose tissue-specific silencing of AR as a therapeutic treatment for PCOS-associated metabolic dysfunction. These data suggest that other tissues such as the brain may be responsible for androgen-induced metabolic disturbances in PCOS. Alternatively, hyperandrogenism during key developmental windows may program future androgen-independent alterations in metabolic tissue function. Further understanding of how androgens drive reproductive and metabolic programming in females will be critical for the future development of targeted treatments for PCOS.

Abstract citation ID: lvag096.166

RC4.4 - ECE_3142 - Androgen receptor PROTAC ARV-110 ameliorates cardiometabolic complications in a mouse model of polycystic ovary syndrome

Damian Romero[1,2], Jelina Basnet[1], Samar Rezq[1], Alexandra Huffman[1] and Licy Yanes Cardozo[1]
[1]Jackson, United States; [2]Pharmacology and Toxicology, University of Mississippi Medical Center, Jackson, United States

Background: Polycystic ovary syndrome (PCOS) is characterized by hyperandrogenism and metabolic dysfunction. Androgens act primarily through the androgen receptor (AR); however, AR antagonists are limited by hepatotoxicity. ARV-110 is a novel AR proteolysis-targeting chimera (PROTAC) that induces AR degradation. We hypothesized that ARV-110 would dose-dependently improve androgen-mediated metabolic dysfunction in a hyperandrogenemic mouse model of PCOS, with tissue-specific molecular effects.

Methods: Three-week-old female C57BL/6N mice were rendered hyperandrogenemic by chronic dihydrotestosterone (DHT, 8 mg) exposure for 12 weeks and treated with vehicle (VEH), low-dose ARV-110 (ARV-L, 1 mg/kg/day), or high-dose ARV-110 (ARV-H, 10 mg/kg/day) for the last 8 weeks. Body weight, body composition, adipose tissue depot mass, glucose homeostasis, renal and hepatic injury markers, and liver and kidney proteomics were assessed.

Results: DHT-VEH mice exhibited significant increases in body weight, total fat mass, and lean mass compared with controls. Both ARV-L and ARV-H attenuated DHT-induced body weight gain and fat mass expansion without reducing lean mass. DHT increased visceral (retroperitoneal and mesenteric) and subcutaneous adipose tissue depot weights, all of which were dose-dependently reduced by ARV-110.

DHT impaired glucose homeostasis, evidenced by increased fasting glucose, elevated HOMA-IR, and worsened glucose tolerance during oral glucose challenge. ARV-110 improved glucose tolerance at both doses, with ARV-H additionally attenuating fasting insulin resistance. DHT-induced hyperleptinemia was dose-dependently reversed by ARV-110, while adiponectin levels remained suppressed.

DHT increased kidney weight and markers of renal injury, which were partially or fully improved by ARV-L. In contrast, ARV-H increased renal injury markers in control mice. Hepatic analysis showed that ARV-L had minimal effects on liver weight and circulating ALT, AST, and LDH, whereas ARV-H caused marked

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hepatomegaly, increased liver enzymes, and worsened steatosis, indicating hepatotoxicity.

Proteomic analysis revealed that in the liver, ARV-110 treatment was the primary driver of gene expression changes, with similar effects in control and DHT-treated mice, while DHT contributed modest, secondary effects. In the kidney, DHT strongly altered gene expression, and ARV-110 produced a dose-dependent modulation in DHT-treated mice without fully restoring control profiles. Pathway analysis showed that many DHT-activated translational and proteostatic pathways were reversed by ARV-110, particularly at the high dose.

Conclusion and Significance: ARV-110 improves hyperandrogenemia-driven obesity, adipose expansion, and glucose intolerance in a mouse model of PCOS. Low-dose ARV-110 provides metabolic and renal benefits with minimal toxicity, whereas high-dose ARV-110 induces hepatic and renal injury. These findings support AR PROTACs as promising, dose-sensitive therapeutic candidates for PCOS-related metabolic disease.

Abstract citation ID: lvag096.167

RC4.5 - ECE_2775 - The anti-Müllerian hormone suppresses uterine leiomyoma growth via a miR-181a-regulated molecular switch

Oana Lupu[1,2], Gabriela Milewska[1], Donata Ponikwicka-Tyszko[2,3], Piotr Bernaczyk[1], Aleksandra Lupinska[1], Ewelina Palak[1], Weronika Szucio[1], Michal Szamatowicz[1], Kamila Pulawska[2], Monika Lesniewska[1], Xiangdong Li[1,4], Ilpo Huhtaniemi[2,5], Slawomir Wolczynski[1] and Nafis Rahman[1,2]

[1]Department of Reproduction and Gynecological Endocrinology, Medical University of Białystok, Białystok, Poland; [2]Integrative Physiology and Pharmacology, University of Turku, Institute of Biomedicine, Turku, Finland; [3]Clinical Research Centre, Medical University of Białystok, Białystok, Poland; [4], State Key Laboratory for Agrobiotechnology, China Agricultural University, BeijingBeijing, China; [5]Institute of Reproductive and Developmental Biology, Department of Metabolism, Digestion and Reproduction - Faculty of Medicine, Imperial College London, London, United Kingdom

Uterine leiomyomas (ULs) are common, benign neoplasms, in women of reproductive age. ULs may cause severe anemia, after heavy menstrual bleeding, pelvic pain, infertility and significant morbidity, often necessitating invasive, surgical intervention. Despite their prevalence, the pathogenesis of ULs remains not fully elucidated, with roles for both hormonal and epigenetic factors, which modulate gene expression, through variations of micro-ribonucleic acids (miRNAs). Anti-Müllerian hormone (AMH) has been shown to be a potential suppressor of ULs, but its interactions with regulatory miRNAs, like miR-181a, is still unexplored in this context.

In this study, we investigated the interplay between the AMH and miR-181a, in UL pathophysiology. The expression profiles of AMH, AMHRII, and miR-181a were characterized in UL tissue versus normal myometrium. The functional relationship and downstream molecular mechanisms were examined in UL cells, focusing on SMAD and PI3K/AKT/mTOR signaling pathways, along with cellular outcomes, like proliferation and senescence.

We found that both AMH and its receptor, AMHRII, were overexpressed in ULs compared to normal myometrium, as was miR-181a. Functionally, AMH upregulated miR-181a expression in UL cells. This interaction induced a tumor-suppressive state, by activating the SMAD1/4 pathway, as well as the phosphorylation and nuclear translocation of SMAD1. Concurrently, AMH inhibited the pro-proliferative PI3K/AKT/mTOR axis, through PTEN upregulation and triggering cellular senescence. Notably, the absence of miR-181a reversed this effect of AMH, causing it to promote proliferation via the PI3K/AKT/mTOR pathway, by increasing the expression of pro-proliferative proteins, such as XIAP.

Our results revealed that AMH and miR-181a maintain a homeostatic, growth-suppressive axis in ULs. Disruption of this balance, particularly miR-181a deficiency, can convert the role of AMH, from inhibitor to promoter of proliferation. A critical protective mechanism is shown in ULs, where AMH and miR-181a cooperate to inhibit growth. This positioned AMHRII signaling and the AMH/miR-181a axis as crucial therapeutic targets for non-surgically treating UL and other benign, Müllerian-related conditions.

Abstract citation ID: lvag096.168

RC4.6 - ECE_3769 - Optimizing the GnRH stimulation test in central precocious puberty: a multicenter accuracy study

Ana Leite[1,2], Luís Azevedo[3], Brígida Robalo[4], Sofia Ferreira[5], Francisco Caetano[6], Suzana Figueiredo[7], Elisa Galo[8], Ana Monteiro[9], Joana Freitas[10], Teresa Monjardino[11] and Catarina Limbert[6,12]

[1]Pediatrics and Pediatric Endocrinology, Clínica CUF São João da Madeira, São João da Madeira, Portugal; [2]Unidade Local de Saúde Gaia e Espinho, Pediatrics, Vila Nova de Gaia, Portugal; [3]Faculty of Medicine, RISE-Health, Department of Community Medicine, Information and Health Decision Sciences - MEDCIDS, University of Porto, Porto, Portugal; [4]Unidade Local de Saúde de Santa Maria, Lisboa, Portugal; [5]Unidade Local de Saúde de São João, Porto, Portugal; [6]Unidade Local de Saúde de São José, Pediatric Endocrinology, Pediatrics, Lisboa, Portugal; [7]Unidade Local de Saúde de Alto Minho, Viana do Castelo, Portugal; [8]Hospital da Luz, Pediatrics, Lisboa, Portugal; [9]Unidade Local de Saúde Amadora/Sintra, Amadora, Portugal; [10]Unidade Local de Saúde de Santo António, Porto, Portugal; [11]iBiMED - Institute of Biomedicine, Aveiro, Portugal; [12]NOVA Medical School, Comprehensive Health Research Centre (CHRC), NOVA University of Lisbon, Lisboa, Portugal

Background: The gonadotropin-releasing hormone (GnRH) stimulation test remains the gold standard for diagnosing central precocious puberty (CPP), however, it is invasive and time and resource consuming. Traditional sampling schedules were defined using outdated assay technologies, and their current diagnostic relevance warrants reassessment.

Purpose: To evaluate the diagnostic performance of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) at specific sampling time points during the GnRH stimulation test, aiming to determine whether the protocol can be simplified without compromising diagnostic accuracy.

Materials and Methods: This multicenter, cross-sectional study included children aged ≥3 years with suspected CPP who underwent a standard GnRH stimulation test between 2015 and 2024. Serum LH and FSH were measured by electrochemiluminescence immunoassay at baseline and at 30, 60, 90, and 120 minutes following intravenous gonadorelin administration. CPP was defined as a peak LH ≥ 5 IU/L. Diagnostic performance

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

metrics were calculated for each time point, and agreement between the 60 and 120-minute protocols was assessed using the kappa coefficient (κ)

Results: Of the 209 included children (mean age 7.2 ± 1.3 years; 4.8% male), 146 (69.9%) were diagnosed with CPP. In the CPP group, mean LH peaked at 30 minutes (19.2 ± 15.3 IU/L); however, reliance on this time point alone would have missed 2 CPP cases. While LH measured at 60, 90, and 120 minutes achieved 100% sensitivity, specificity, and accuracy, the 30-minute time point demonstrated lower performance, with a sensitivity of 98.8%, a negative predictive value of 95.2%, and an accuracy of 99.1% (κ = 0.97). No additional diagnostic benefit was observed beyond 60 minutes.

Conclusions: LH measurement at 60 minutes after GnRH stimulation provides maximal diagnostic accuracy for CPP. Given the almost perfect agreement with the standard 120-minute test, a shortened 60-minute protocol can safely replace longer schedules, reducing invasiveness for the patient and resource utilization without compromising diagnostic reliability.

Abstract citation ID: lvag096.169

RC5.1 - ECE_1698 - Adherence to ESE and SfE guidance in the management of severe hyponatraemia: a multicentre audit of real-world practice

Amanda Ling Jie Yee[1,2], Samama Rafi[3], Aspasia Manta[1,2], Alexander Chandran[4], Sam Solanki[4,5], Poppy Wardley[5], Azheem Ijaz[4], Aravind Manoj[4], Zain Mahmood[4], Ahmed Iqbal[4,5], Muhammad Fahad Arshad[4,5] and Punith Kempegowda[1,2]

[1]Department of Applied Health Sciences, University of Birmingham, Birmingham, United Kingdom; [2]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [3]Birmingham, United Kingdom; [4]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom; [5]University of Sheffield, Sheffield, United Kingdom

Background: Severe hyponatraemia is a high-risk endocrine emergency. The European Society of Endocrinology (ESE) and the Society for Endocrinology (SfE) guidelines recommend symptom-based use of hypertonic saline (HTS), monitored care, and prevention of overly rapid sodium correction. However, real-world adherence is uncertain.

Objectives: To evaluate adherence to ESE and SfE guidelines in severe hyponatraemia management and identify key patient safety gaps and real-world practice patterns.

Methods: We conducted a retrospective, multicentre audit of adult inpatient admissions between 1 January and 31 December 2024 with a serum sodium concentration ≤125 mmol/L. Adherence to key standards from ESE and SfE guidelines was assessed, including documentation of symptom severity, appropriate use of HTS for moderate or severe symptoms, monitoring following HTS administration, correction rates within recommended limits, location of care during HTS administration, completeness of diagnostic evaluation, and involvement of specialist endocrinology services.

Results: A total of 1121 admissions were analysed. Median age was 72.0 years (IQR 62.0-82.0), and 52.0% ($n = 583$) were female. Symptom-based assessment was documented in 87.8% ($n = 984$) of admissions; 13.9% ($n = 137$) had severe and 19.9% ($n = 196$) moderate symptoms. Based on ESE/SfE criteria, 29.7% ($n = 333$) of patients met indications for HTS, yet only 26 (7.8%) received HTS. In contrast, 7 patients with mild symptoms received HTS despite not meeting guideline criteria.

Among 33 HTS prescriptions, 54.5% ($n = 18$) were administered in monitored environments (emergency department or intensive care), and 54.5% ($n = 18$) followed bolus-based regimens. Serum sodium was rechecked within one hour of the first bolus in 66.7% ($n = 22$) of cases.

Sodium correction data at 24 hours were available in 58.9% ($n = 661$) of admissions, and overcorrection (>10 mmol/L/24 h) occurred in 4.7% ($n = 53$). Diagnostic evaluation was incomplete, with urine sodium and osmolality measured in 50.0% and 50.9% of admissions, respectively. Specialist endocrinology input was documented in 27.0% of cases. Osmotic demyelination syndrome was confirmed in one case (0.1%) and suspected in three (0.3%).

Conclusions: Management of severe hyponatraemia was suboptimal, characterised by underutilisation of HTS in eligible patients, inconsistent monitoring, and incomplete diagnostic evaluation. These findings highlight significant patient safety gaps and underscore the need for system-level interventions, including education, standardised pathways, and improved access to specialist endocrine input.

Abstract citation ID: lvag096.170

RC5.2 - ECE_2298 - Empagliflozin for paraneoplastic SIAD-related hyponatraemia: real-world multi-centre evidence

Mohammed Ahmed[1], Mark Pearce[1], Maria Michaelidou[1], Shaishav Dhage[1], Jamie Weaver[1], Tim Cooksley[1], Jan Hoong Ho[1], Laura Cove-Smith[2,3] and Safwaan Adam[1]

[1]The Christie NHS Foundation Trust, Endocrinology, Manchester, United Kingdom; [2]Manchester, United Kingdom; [3]Manchester University NHS Foundation Trust, Manchester, United Kingdom

Background: Hyponatraemia secondary to paraneoplastic syndrome of inappropriate antidiuresis (SIAD) is common and often refractory to conventional therapies such as fluid restriction. Treatment with tolvaptan is associated with significant risk of over-correction.[1] Empagliflozin has demonstrated an aquaretic sodium-raising effect in randomised trials, but real-world durability and clinically useful predictors of early response remain uncertain.[2]

Methods: We analysed 42 adults with confirmed SIAD treated with empagliflozin. Demographics, baseline biochemistry, and serial sodium measurements were extracted from clinical records. The primary aim was the assessment of early sodium correction (day 4 and week 1) and long-term sustained response. Predictors of the magnitude of sodium rise were assessed using Spearman correlation (ρ). Overall hyponatraemia outcome was categorised based on the latest available sodium measurement. Continuous variables are presented as median (IQR).

Results: The results are summarised in the table. No sodium overcorrection was observed (>12 mmol/l rise in 48 hours). One patient developed ketonuria without acidosis and other developed genital thrush. The degree of absolute sodium rise at one month was strongly associated with baseline severity of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hyponatraemia, with lower baseline sodium predicting a greater absolute rise ($\rho = -0.53$, $p = 0.005$).

Table. Baseline characteristics and clinical outcomes ($N = 42$).

Variable	Value
Median age (IQR), years	71 (64-74)
Female, *n* (%)	21 (50%)
BMI, kg/m^2 (IQR)	24.3 (21.6-27.9)
Baseline Na, mmol/L (IQR)	122 (118-124)
Empagliflozin dose: 10 mg/25 mg	19 (45%)/23 (55%)
Median sodium (mmol/l) rise (IQR) at:	
48 hours	4 (2-5)
Day 4	7.5 (5-12)
1 week	8.5 (3.8-12.3)
Day-4 responders (sodium rise ≥5), *n* (%)	19/24 (79%)
Week-1 responders (sodium rise ≥5), *n* (%)	26/36 (72%)
Normal sodium at 1 month (≥133 mmol/L), *n* (%)	15/26 (58%)
Sustained sodium ≥125 mmol/L, *n*/*N* (%)	
1 month	24/26 (92%)
3 months	18/19 (95%)
6 months	12/13 (92%)
12 months	5/5 (100%)
Median follow-up, days (IQR)	77 (17-194)
Overall hyponatraemia outcome, *n* (%):	
Normalised	25 (60%)
Improved	11 (26%)
Relapsed	4 (10%)
Stabilised	2 (5%)

Conclusions: Empagliflozin was effective in achieving and sustaining sodium correction in SIAD, with 86% of the cohort showing normalised or improved outcomes. These real-world data support the use of SGLT2-inhibitors as a potent and well-tolerated treatment option for SIAD.

References

1. Verbalis JG, Greenberg A, Burst V, et al. Diagnosing and treating the syndrome of inappropriate antidiuretic hormone secretion. *J Clin Endocrinol Metab*. 2021;106(11):e4766-e4784.
2. Refardt J, Imber C, Nobbenhuis R, et al. Treatment effect of the SGLT2 inhibitor empagliflozin on chronic syndrome of inappropriate antidiuresis: results of a randomized, double-blind, placebo-controlled, crossover trial. *J Am Soc Nephrol*. 2023;34:322-332.

Abstract citation ID: lvag096.171

RC5.3 - ECE_2604 - IGF1-SDS as a marker for progressive central precocious puberty: a multicenter prospective diagnostic accuracy study

Ana Leite[1,2,3], Luís Azevedo[4], Maria Rangel[2], Mariana Oliveira[2], Elisa Galo[5], Filipa Espada[6], Joana Freitas[7], Ana Monteiro[8], Brigida Robalo[9], Sofia Ferreira[10] and Catarina Limbert[11,12]

[1]Clínica CUF São João da Madeira, Pediatrics and Pediatric Endocrinology, São João da Madeira, Portugal; [2]Unidade Local de Saúde Gaia e Espinho, Pediatrics, Vila Nova de Gaia, Portugal; [3]Unidade Local de Saúde Vila Nova de Gaia, Pediatrics, Vila Nova de Gaia, Portugal; [4]Faculty of Medicine, RISE-Health, Department of Community Medicine, Information and Health Decision Sciences - MEDCIDS, University of Porto, Porto, Portugal; [5]Hospital da Luz, Pediatrics, Lisboa, Portugal; [6]LISBOA, Portugal; [7]Unidade Local de Saúde de Santo António, Porto, Portugal; [8]Unidade Local de Saúde Amadora/Sintra, Amadora, Portugal; [9]Unidade Local de Saúde de Santa Maria, Lisboa, Portugal; [10]Unidade Local de Saúde de São João, Porto, Portugal; [11]NOVA Medical School, Comprehensive Health Research Centre (CHRC), NOVA University of Lisbon, Lisboa, Portugal; [12]Unidade Local de Saúde de São José, Pediatric Endocrinology, Pediatrics, Lisboa, Portugal

Context: Early recognition of progressive central precocious puberty (CPP) from benign variants of puberty can be challenging. Insulin-like growth factor 1 (IGF-1) reflects both growth acceleration and early gonadal maturation and is typically elevated in progressive CPP cases.

Purpose: To validate the diagnostic performance of IGF1-SDS in the evaluation of precocious puberty and to assess an IGF1-SDS cutoff of 1.44.

Methods: Prospective multicenter study conducted from September 2024 to September 2025. Among 431 participants referred for early signs of puberty, 385 were eligible and enrolled in the study protocol, with clinical, laboratory and radiologic evaluation. Serum IGF-1 was assessed using IMMULITE assay and IGF1-SDS were calculated.

Results: 305 (79%) participants had progressive CPP, 92% were girls and 48% were diagnosed on tanner stage II. IGF1-SDS values were significantly higher in progressive CPP cases (mean 2.35 ± 0.95 versus 0.94 ± 0.69; $P < .001$) and its area under the curve (AUC) was 0.866 (95% confidence intervals (IC) 0.826-0.907). Using a predefined IGF1-SDS cutoff of 1.44, sensitivity was 82.3% (95% CI 78.0-86.6), specificity of 81.3% (95% CI 72.7-89.8), overall accuracy 82.1% (95% CI 78.2-85.9), positive predictive value 94.4% (95% CI 91.6-97.1), positive likelihood ratio 4.39 (95% CI 3.90-4.94), negative likelihood ratio 0.22 (95% CI 0.20-0.24) and diagnostic odds ratio of 19.7 (10.3-37.7).

Conclusions: IGF-1 SDS assessment in children presenting with early pubertal signs provides meaningful risk stratification between progressive and non-progressive or incomplete forms of puberty. An IGF-1 SDS value above 1.44 is associated with a significantly increased post-test probability of progressive central precocious puberty, supporting its use as a rule-in threshold. However, values ≤1.44 do not allow reliable exclusion of the disease.

Abstract citation ID: lvag096.172

RC5.4 - ECE_3805 - Clinical, biochemical, radiological, and pathological features of micromegaly in a multicenter cohort

Kübra Sayım Aydoğan[1,2], Simge Saydam[1], Sema Ciftci[1], Mine Adaş[3], Hatice Deniz Yücel[3], Esra Hatipoglu[4], Eda Karakullukçuoğlu[4], Aylin Coşkun[4], Feyza Yener Ozturk[5], İrem Abdulhayoğlu Erim[5], Kadriye Aydin[6] and Senem Boz Aksoy[6]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Istanbul, Istanbul, Türkiye; [2]Endocrinology, Istanbul, Türkiye; [3]Faculty of Health Sciences, Okmeydanı Prof. Dr. Cemil Taşçıoğlu City Hospital, Endocrinology, İstanbul, Türkiye; [4]Faculty of Health Sciences, Başakşehir Çam ve Sakura City Hospital, Endocrinology, İstanbul, Türkiye; [5]İstanbul, Türkiye; [6]Kartal Dr. Lütfi Kırdar City Hospital, Endocrinology, Faculty of Health Sciences, İstanbul, Türkiye

Aim: Micromegaly refers to a subgroup of patients who exhibit clinical features suggestive of acromegaly, have mildly elevated IGF-1 levels, normal basal GH concentrations, and GH suppression during an oral glucose tolerance test (OGTT). In this study, we aimed to present the clinical, biochemical, imaging characteristics, and pathological findings of micromegaly cases.

Methods: A total of 46 patients followed at five tertiary endocrinology centers were included in the study. Eligibility criteria comprised IGF-1 levels between 1.0 and 1.3 times the upper limit of normal (ULN), basal GH $\leq$ 2 ng/mL, and availability of pituitary MRI imaging. Demographic characteristics, comorbidities, clinical features including acral and facial changes, headache, sweating, and snoring, as well as laboratory, radiological, and pathological data were retrospectively reviewed.

Results: 27 (58.6%) were female and 19 (41.4%) were male in this study. The mean age at diagnosis was 46 years (range 19-70). Diabetes mellitus was present in 9 patients (19%) and hypertension in 19 (41%). Acral features were observed in 31 patients (67%). Enlargement of the hands and feet was reported in 14 patients (30%), headache in 15 (32%), snoring in 13 (28%), and excessive sweating in 18 (39%). Mean IGF-1 levels were 1.18-fold above the upper limit of normal. The mean basal GH concentration was 0.89 ng/mL, and the mean nadir GH level during OGTT was 0.53 ng/mL. In all patients who underwent OGTT, nadir GH values after OGTT were suppressed to below 1 ng/mL. Pituitary MRI revealed microadenomas in 22 patients (47%) and macroadenomas in 7 (15%). No pituitary lesion was detected in 14 patients (30%), while 3 patients exhibited an empty sella. All patients with macroadenomas underwent surgery. Among those with microadenomas, 9 underwent surgery, 2 received medical therapy, and 11 were managed with follow-up. Of the 16 operated patients (34%), immunohistochemistry demonstrated isolated GH positivity in 3, combined GH, PRL, and PIT-1 positivity in 3, plurihormonal staining patterns in 3, and isolated PIT-1 positivity in 1. No adenomatous tissue was identified in 2 patients, while pathology results remain pending in 4. In patients managed with follow-up, no acromegaly-specific treatment has yet been initiated; comorbidities were treated, and patients are being monitored clinically, biochemically, and radiologically for a mean duration of 3.6 years.

Conclusions: Pituitary lesions and variable hormone co-expression patterns accompanying GH positivity in micromegaly indicate that these patients should be monitored using a clinical approach similar to that applied in acromegaly.

Abstract citation ID: lvag096.173

RC5.5 - ECE_1468 - Three-week actigraphy to characterise sleep behaviour and circadian rest-activity patterns in suspected and confirmed Cushing's syndrome: a prospective cohort study

Annika Steinkogler[1], Stephanie Zopp[1], Adriana Albani[1], Marily Theodoropoulou[1], Isabel Stüfchen[1], Júnia Ribeiro De Oliveira Longo Schweizer[1], Friederike Völter[1,2], Katrin Ritzel[1], Kathrin Moser[1], Katharina Schilbach[1,3], Martin Bidlingmaier[1], Martin Reincke[1] and Elisabeth Nowak[1]

[1]Department of Medicine IV, LMU University Hospital, LMU Munich, Munich, Germany; [2]Department of Nuclear Medicine, LMU University Hospital, LMU Munich, Munich, Germany; [3]Deggendorf Institute of Technology, Deggendorf, Germany

Background: Sleep disturbances and fatigue are common early features of CS, often persist after remission, and substantially impair quality of life. Despite their high prevalence, the objective characteristics and determinants of sleep disturbances in CS remain poorly characterised.

Aim: Our aim was to assess the diagnostic utility of actigraphy in suspected endogenous cortisol excess, to chracterise sleep patterns in patients with CS in long-term remission with persistent versus recovered adrenal insufficiency, and to examine associations between late-night salivary cortisol (LNSC) and actigraphy-derived sleep parameters.

Methods: In this prospective single-centre cohort study conducted at LMU Hospital Munich, two cohorts were enrolled: patients undergoing diagnostic evaluation for suspected CS (cohort 1) and patients with CS in remission (cohort 2), stratified by adrenal recovery status. All participants completed continuous 21-day wrist actigraphy (ActTrust 2, Condor Instruments), provided daily LNSC samples, and answered the Munich ChronoType Questionnaire.

Results: Among individuals evaluated for suspected CS, 16 were diagnosed with active disease and 13 had CS excluded. Actigraphy revealed similarly reduced sleep quality in both groups with low sleep efficiency, increased nocturnal wakefulness, and fragmented but overall largely preserved circadian rest-activity patterns. No actigraphy parameters differentiated active CS from excluded CS (all $P > .1$), except for an earlier chronotype in active CS ($P = .022$). In the remission cohort (total $n = 23$), sleep quality and circadian rest-activity patterns were similarly impaired in those with persistent ($n = 13$) and recovered ($n = 10$) adrenal insufficiency, with no significant group differences in sleep efficiency, nocturnal wakefulness, chronotype, or social jetlag (all $P > .1$). Circadian metrics were largely comparable, with only non-significant trends toward earlier acrophase and onset of the least active nocturnal period in patients with persistent adrenal insufficiency ($P = .079$ and $P = .095$, respectively). LNSC measurements showed pronounced intra- and interindividual variability across all groups, with consistent evaluations in active CS, partial evaluations in individuals with excluded CS, and frequent evaluations in patients with persistent adrenal insufficiency receiving hydrocortisone replacement, likely reflecting replacement pharmacokinetics. Correlations between LNSC and actigraphy-derived sleep parameters were weak ($r < 0.3$) and inconsistent across groups.

Conclusions: Extended actigraphy demonstrated clinically relevant sleep impairment across all patients assessed for CS but did not provide diagnostic discrimination for active disease. During remission, sleep quality remained impaired irrespective of adrenal recovery status. Given the marked variability of LNSC and its limited relationship with objective sleep measures, improved biomarkers and monitoring strategies are needed to enhance the detection and follow-up of CS.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.174

RC5.6 - ECE_2859 - Mitochondrial metabolic dependencies shape anterior pituitary homeostasis and disease

James Kaufman-Cook[1], Yasmine Kemkem[1], Miriam Vazquez Segoviano[1], Olivia Sherwin[1], Bence Kover[1], Paul Carroll[2] and Cynthia Andoniadou[1]

[1]*King's College London, Centre for Craniofacial and Regenerative Biology, London, United Kingdom;* [2]*Guy's and St. Thomas' NHS Foundation Trust, Department of Endocrinology, London, United Kingdom*

Cell metabolism is fundamental to anterior pituitary (AP) function, enabling endocrine cells to meet the energetic and biosynthetic demands of hormone production and secretion. While pituitary cell types are presumed to rely on distinct metabolic pathways to support hormone synthesis and cell fate decisions, these dependencies remain poorly defined. Notably, mutations in mitochondrial metabolic enzymes, including succinate dehydrogenase (SDH) and isocitrate dehydrogenase (IDH), are associated with endocrine tumours, including the pituitary, implicating metabolic dysregulation in pituitary disease. However, whether altered cellular metabolism is sufficient to drive pituitary pathology *in vivo* is unknown. Understanding the metabolic dependencies that govern AP homeostasis has translational relevance for regenerative strategies and targeted metabolic therapies.

Using mouse models, we disrupted key oxidative metabolic enzymes, including Succinate Dehydrogenase B (SDHB) in the TCA cycle and electron transport chain (ETC), and NDUFS4 in Complex I of the ETC, to define the role of oxidative metabolism in pituitary homeostasis and disease.

We used complementary *Cre* drivers to mutate *Sdhb* either during embryonic pituitary development (*Hesx1*$^{Cre/+}$;*Sdhb*$^{fl/fl}$) or postnatally in the SOX2^{+} stem cell compartment (*Sox2*$^{CreERT2/+}$;*Sdhb*$^{fl/fl}$). In both models, *Sdhb* loss activated pseudohypoxic signalling in the AP, with upregulation of *Hif1a* and downstream targets, and induced metabolic reprogramming in pituitary stem cells consistent with a Warburg-like shift. Despite these tumour-associated metabolic changes, SDHB deficiency alone was insufficient to drive pituitary tumour formation. Instead, SDHB loss resulted in marked pituitary hypoplasia with preserved lineage commitment and differentiation.

Consistent with this, *Ndufs4*$^{-/-}$ mice exhibited pituitary hypoplasia with reduced AP proliferation, increased lactate dehydrogenase expression, and expansion of the SOX2^{+} stem cell compartment, without loss of endocrine cell identity. Notably, *Ndufs4* deficiency also led to the formation of ectopic, fully specified pituitary tissue connecting the anterior and intermediate lobes, characterised by a patterned SOX2^{+} stem cell epithelium.

Together, these findings reveal that intact oxidative metabolism is a critical constraint on AP growth and tissue architecture but is dispensable for lineage specification and endocrine identity. This unexpected dissociation between growth and differentiation highlights a remarkable capacity for metabolic adaptation in the AP and provides new insight into how mitochondrial dysfunction contributes to pituitary hypoplasia, ectopia, and tumour susceptibility, with implications for regenerative and metabolic therapeutic strategies.

Abstract citation ID: lvag096.175

RC6.1 - ECE_3949 - Combining bulk, single nuclei and single cell RNA sequencing of phaeochromocytomas and paragangliomas to gain insights into metastatic potential

Mark Quinn[1], Dimitria Brempou[1], Harit Kohli[1], Bertille Montibus[1], Louise Izatt[2], Paul Carroll[2], Cynthia Andoniadou[1] and Rebecca Oakey[1]

[1]*King's College London, London, United Kingdom;* [2]*Guy's and St Thomas' N H S Foundation Trust, London, United Kingdom*

Background: Phaeochromocytomas and paragangliomas (PPGLs) often display a unique pattern of metastatic spread whereby, following initial tumour resection, there is a prolonged period of remission before recurrence arises with metastatic spread. Treatment options for metastatic PPGLs are limited and outcomes are poor. Current tools used to predict metastatic risk underperform. A biomarker is urgently needed to identify patients at high risk of metastasis. This is especially relevant given the genetic drivers involved in PPGLs and the ever-increasing pool of patients identified as carries of these variants through cascade screening. RNA-sequencing has shown significant utility in increasing our understanding of PPGLs. Bulk RNA sequencing (RNA-seq) has been used to describe PPGLs in clusters and single nuclei RNA sequencing (SnRNA-seq) has helped to refine this classification even further. With this work we will combine bulk, single nuclei and single cell RNA sequencing (ScRNA-seq) to identify transcriptomic markers of metastatic disease in PPGLs.

Methods: We have collated bulk RNA-seq datasets from publicly available sources ($n = 326$) with data from our own, local tumour collections ($n = 27$) to compare the transcriptome of metastatic to non-metastatic PPGLs focusing on *SDHx* mutations. We have performed a differentially expressed gene (DEG) analysis of metastatic and non-metastatic PPGLs to identify genes that may have a role in metastatic disease. We have also performed Sn and ScRNA-seq on 8 samples including one that had metastasized at the time of resection and another that metastasized following a period of remission.

Results: Our bulk RNA-seq analyses identified the following overexpressed genes in metastatic PPGLs: *FN1, VEGFA, CDK1, PTTG1, ABCA12* and *MMP9*. Both *ABCA12* and *MMP9* were consistently overexpressed when our analyses isolated *SDHx* samples. ScRNA-seq provided a detailed picture of the tumour microenvironment (TME) of PPGLs when compared to SnRNA-seq. The cellular populations seen in PPGLs across the spectrum of genotypes were comparable. There were differences in the expression of *PTTG1*, *MMP9* and *ABCA12* in the chromaffin cells and TME of pre-metastatic and metastatic PPGLs that warrant further investigation.

Discussion: We have demonstrated that bulk RNA-seq can be used to identify genes that are overexpressed in metastatic PPGLs. Sn and ScRNA-seq allow us to explore the expression profile of tumour cells and the TME. *PTTG1* and *MMP9* have a defined role in the development of metastasis in a number of cancers. By combining these state-of-the-art techniques we show that their overexpression in the TME of PPGLs may have a role in metastatic spread.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.176

RC6.2 - ECE_3507 - Genotype–phenotype correlations in pheochromocytomas and paragangliomas: results from a large multicenter Italian cohort

Bianca Golisano[1], Martina Fano[1], Andrea Contarino[2,3], Matteo Procopio[4], Antonio Prinzi[5,6], Gianfranco Di Iasi[7], Franz Sesti[8], Monica Verrico[9], Elisa Giannetta[10], Pasqualino Malandrino[6], Roberta Modica[7], Serena Palmieri[2], Mirko Parasiliti Caprino[4] and Antongiulio Faggiano[1]

[1]Endocrinology Unit, Department of Clinical and Molecular Medicine, Sant'Andrea Hospital, ENETS Center of Excellence, Sapienza University of Rome, Rome, Italy; [2]Unit of Endocrinology, Fondazione IRCCS Ca' Granda-Ospedale Maggiore Policlinico, Milan, Italy; [3]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [4]Endocrinology, Diabetes and Metabolism; Department of Medical Sciences, University of Turin, Turin, Italy; [5]Department of Precision Medicine in Medical, Surgical and Critical Care (Me.Pre.C.C.), University of Palermo, Palermo, Italy; [6]Endocrinology Unit, Department of Clinical and Experimental Medicine, Garibaldi-Nesima Medical Center, University of Catania, Catania, Italy; [7]Endocrinology, Diabetology and Andrology Unit, Department of Clinical Medicine and Surgery, University of Naples "Federico II", Naples, Italy; [8]Department of Wellbeing, Health and Environmental Sustainability - BeSSA, Sapienza University of Rome, Rieti, Italy; [9]Oncology, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy; [10]Endocrinology, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy

Pheochromocytomas and paragangliomas, collectively known as PPGLs, are a group of neuroendocrine neoplasms originating from the adrenal medulla or from the sympathetic or parasympathetic extra-adrenal paraganglia. These tumors are characterized by the highest reported rate of heritability. We conducted a multicenter retrospective study to investigate the association between genetic alterations and PPGLs' clinical characteristics.

Data were collected across six Italian centers, involving a total of 346 patients: 227 (65.6%) pheochromocytomas and 119 (34.4%) paragangliomas. The cohort consisted of 56.4% females and 43.6% males, with a mean age at diagnosis of 46.6 ± 16.8 years and a mean survival from diagnosis of 10.4 ± 8.3 years. The overall mortality rate was 9%, but only 6 patients (1.7%) died because of tumor progression.

Incidental detection of PPGL was the most frequent diagnostic modality (47.2%, $n = 161$), followed by diagnosis guided by clinical symptoms (42.2%), mainly palpitations and hyperhidrosis. Genetic screening was the least common, accounting for 10.6% of cases ($n = 36$). As expected, tumor size correlated significantly with the mode of diagnosis ($P < .0001$): symptomatic patients presented with larger lesions (55.0 ± 31.2 mm), while tumors identified through genetic screening were the smallest (37.6 ± 23.7 mm).

Germline mutations were found in 44.9% of cases, more frequently in extra-adrenal than in adrenal PPGLs (64.0% vs 41.4%). Furthermore, gene mutation varied by site ($P < .0001$): NF1 and VHL predominated in adrenal locations, SDHB was the most frequent in extra-adrenal abdominal, while SDHD in the head-and-neck and PPGLs. Genetic analysis revealed a strong link between germline mutations and markers of tumor aggressiveness. Indeed, 20/141 (14.2%) of genetic PPGLs had metastatic spread compared to 12/167 (7.2%) of sporadic cases. Specifically, SDHB-mutated PPGLs showed a highest frequency of metastases (10/18 cases, $P < .0001$), while SDHD-mutated tumors were significantly associated with multifocality (4/5 cases, $P < .001$). Recurrence rate was significantly higher in genetic than in sporadic tumors (20.3% vs 8.4%, $P = .004$).

This large multicenter Italian cohort confirms that PPGLs carry a high germline mutation burden comparable to contemporary European series. Genetic status strongly correlates with aggressive clinical behavior, particularly in SDHB-mutated tumors, which showed the highest metastatic risk, while SDHD mutations were associated with multifocality and increased recurrence. Importantly, genetically screened patients presented with significantly smaller tumors, underscoring the clinical value of early genetic testing. Overall, germline alterations emerge as the major determinants of phenotype and prognosis in PPGLs.

Abstract citation ID: lvag096.177

RC6.3 - ECE_1687 - Menopause and its associated hormonal shifts define distinct cytokine and immune cell profiles

Angela Rubio Tenor[1,2,3], Jesús Roca-García[1,2,3], Alicia Santamaría-Quiles[1,2,3] and Ines Pineda-Torra[1,2,3]

[1]Cabimer, Sevilla, Spain; [2]Andalusian Public Foundation for Progress and Health ("Fundación Progreso y Salud"-"FPS"), Seville, Spain; [3]Universidad de Sevilla, Seville, Spain

Cardiovascular disease (CVD) is the leading cause of mortality for women worldwide. Atherosclerosis is the main pathology underlying ischemic CVD events, resulting from abnormal blood lipid concentrations and exacerbated inflammation. The menopausal transition represents a profound endocrine, metabolic and immune change in women's cardiovascular risk trajectory. Hormonal changes after menopause include elevated gonadotropins (FSH, LH) and decreased levels of oestrogens, progesterone and testosterone. Loss of estrogen compromises endothelial function and the atheroprotective properties of high-density lipoprotein (HDL), accelerating immune cell activation, foam cell formation, and early plaque development. The overall aim of this study was to understand how menopause and associated hormonal changes affect CV risk in women to improve prevention strategies and personalized health. Specifically, we aimed to understand the molecular and immune alterations associated with menopause.

Women with no history of CVD aged 21-35 and 57-63 years ($n = 127$) were recruited, menopausal status was recorded as well as clinical data to stablish their CV risk. Women with autoimmune diseases, pregnant or recently vaccinated were excluded. Hormone and cytokine serum profile and PBMC immunophenotyping by Cytometry by time of flight (CyTOF) was performed. Post-menopausal women were further stratified by their inflammatory status using the GlycA "inflammaging" biomarker.

CyTOF experiments revealed changes in postmenopausal women with pro-inflammatory trends in $CD4^+$ T cell subpopulations, including an increase in Th17 cells and a concomitant increase in Th2 and Tregs. Moreover, postmenopausal women exhibited a significant increase of CCL11 (eotaxin) compared to pre-menopausal women. Stratification of postmenopausal women by inflammation using GlycA revealed a pro-inflammatory profile in the high inflammation group with higher levels of CCL5, implicated in monocyte-driven atherosclerosis, and other

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

cytokines such as TNF-α, a central driver of chronic inflammation linked to CVD. Additionally, these postmenopausal women with elevated inflammation showed significantly increased oestradiol concentrations and a trend towards increased total testosterone alongside reduced levels of LH and FSH. Across the cohort, estrone showed the highest number of significant positive correlations with cytokines. When restricting the analysis to only postmenopausal women, total testosterone and estrone were positively correlated with a core set of pro-inflammatory cytokines (CCL4, CCL5, IL-9, and TNF-α).

In conclusion, our findings show that postmenopausal status is associated with a pro-inflammatory T-cell landscape and elevated CCL11. Notably, we demonstrate that high-inflammation postmenopausal women exhibit a distinct hormonal and cytokine profile, implicating an altered hormonal environment as a driver of the chronic low-grade inflammation that accelerates atherosclerotic pathology.

Abstract citation ID: lvag096.178

RC6.4 - ECE_2095 - Multicentre radiomic prediction of genetic signature in adrenocortical carcinoma

Lorenzo Tucci[1,2,3], Anne Jouinot[4,5], Abubaker Mohamed[6], Maxime Barat[7], Antonio De Leo[1,8], Kassiani Skordilis[6], Lisa James[6], Cristina Mosconi[1,9], Balraj Dhesi[10], Dario De Biase[11], Guillaume Assié[4,5], Guido Di Dalmazi[1,2] and Cristina L Ronchi[3,12]

[1]Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy; [2]Sant'Orsola Malpighi Polyclinic, Division of Endocrinology and Diabetes Prevention and Care, Bologna, Italy; [3]Department of Metabolism and System Science, Birmingham, University of Birmingham, United Kingdom; [4]CNRS, Inserm, Institut Cochin, Université Paris Cité, Paris, France; [5]Hôpital Cochin, Department of Endocrinology and National Reference Center for Rare Adrenal Disorders, AP-HP, Paris, France; [6]Queen Elizabeth Hospital Birmingham, Department of Histopathology, Birmingham, United Kingdom; [7]Hôpital Cochin, Department of Radiology A, AP-HP, Paris, France; [8]Sant'Orsola Malpighi Polyclinic, Solid Tumor Molecular Pathology Laboratory, Bologna, Italy; [9]Sant'Orsola Malpighi Polyclinic, Radiology Unit, Bologna, Italy; [10]Queen Elizabeth Hospital Birmingham, Department of Radiology, Birmingham, United Kingdom; [11]Department of Pharmacy and Biotechnology, University of Bologna, Bologna, Italy; [12]Queen Elizabeth Hospital Birmingham, Department of Endocrinology, Birmingham, United Kingdom

Background: Radiogenomics, early recognition of genomic profile exploiting radiomics, is an emerging approach for non-invasive tumor characterization, never performed in adrenocortical carcinoma (ACC). However, its clinical translation is limited by poor generalisability and small single-center cohorts. Early non-invasive genomic profiling could enhance risk stratification of ACC patients.

Methods: From 123 patients, we selected 81 patients (28 males) with histologically confirmed ACC from three tertiary referral centers (Bologna $n=5$; Birmingham, $n=31$; Paris, $n=45$) with availability of S-GRAS parameters plus sex, pre-operative contrast-enhanced venous-phase CT scan and targeted next-generation sequencing on formalin-fixed paraffin-embedded tumor tissue for *NF1* and genes of β-catenin (*CTNNB1, ZNRF3, APC*), tumor suppressor (*TP53, RB1, CDK4*) and chromatin remodeling (*TERT, MEN1*) pathways. IBSI-compliant radiomic features were independently extracted using harmonized parameters. Only reproducible, multicenter-shared features were retained, followed by correlation-based reduction to eight informative variables. Predictive models were developed to identify overall mutational status and gene-cluster alterations (β-catenin, tumor suppressor, chromatin remodeling) using: radiomics-only, clinical-only (S-GRAS parameters and sex), and combined models (best four radiomic and best four clinical features). Overall mutational status was predicted using deep learning with 10-fold cross-validation (60% training, 20% testing, 20% holdout), while cluster-specific predictions used logistic regression.

Results: Overall, a wild-type genetic profile was observed in 41 ACCs (51.0%). Alterations of tumor suppressor genes were most frequent ($n=20$ (24.7%); *TP53* = 15; *RB1* = 4; *CDK4* = 1), followed by those of β-catenin signalling ($n=17$ (21.0%); *CTNNB1* = 9; *ZNRF3* = 8; *APC* = 0), chromatin remodeling genes ($n=12$ (14.8%); *MEN1* = 8; *TERT* = 5) and *NF1* ($n=9$ (11.1%)). The eight most informative variables were Ki67 (weighted importance = 0.18), maximum intensity (0.17), ENSAT stage (0.14), intensity variance (0.14), median intensity (0.12), GLCM joint maximum (0.11), resection status (0.07) and age (0.07). Combined clinical–radiomic models outperformed single-modality approaches for overall mutational status prediction, achieving higher F1-score (0.8) compared with radiomics-only (0.73) or clinical-only models (0.75). Cluster-specific alteration prediction was feasible across all genomic groups, with the highest performance for β-catenin pathway variants hold by combined model (0.57), for tumor suppressor mutations hold by clinical-only model (0.54) and for chromatin remodeling alterations hold by radiomics-only model (0.56).

Conclusions: This multicenter radiogenomic study demonstrates that integrating radiomic features with clinical variables enables non-invasive prediction of mutational status in ACC. The use of harmonized feature extraction and cross-center validation supports the generalisability of these models. Combined clinical–radiomic approaches appear most robust and may represent a valuable tool for early recognition of ACC genetic variants.

Abstract citation ID: lvag096.179

RC6.5 - ECE_1812 - 18F-CETO in adrenocortical carcinoma: first clinical-translational study of an adrenocortical-targeted PET tracer

Adam Edholm[1], Liang Zhang[1], James MacFarlane[2], Tobias Åkerström[3], Russell Senanayake[2], Staffan Welin[1], Agnes Hegedus[4], Cheow Heok[5], Aloj Luigi[5], Per Hellman[3], Hanna-Linn Wargelius[6], John Tadross[7], Gunnar Antoni[8], Franklin Aigbirhio[9], Britt Skogseid[3], Mark Gurnell[2], Samuel Backman[3], Anders Sundin[8], Ruth Casey[2] and Joakim Crona[1]

[1]Medical Sciences, Uppsala Universitet, Uppsala, Sweden; [2]Endocrinology, Cambridge University Hospitals Nhs Foundation Trust, Cambridge, United Kingdom; [3]Surgical Sciences, Uppsala Universitet, Uppsala, Sweden; [4]Immunology, Genetics and Pathology, Uppsala Universitet, Uppsala, Sweden; [5]Nuclear Medicine, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [6]Medical Sciences, Uppsala Universitet, Uppsala, Sweden; [7]Histopathology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [8]Nuclear

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Medicine, Uppsala Universitet, Uppsala, Sweden; [9]Wolfson Brain Imaging Centre, Cambridge University, Cambridge, United Kingdom

Background: Adrenocortical-specific PET tracers, such as 11C-metomidate (11C-MTO), show high diagnostic accuracy in adrenocortical carcinoma (ACC), but unfavorable radiochemical properties had limited its clinical implementation. Para-chloro-2-[18F]fluoroethyletomidate (18F-CETO), a new PET tracer with improved radiochemical properties, may enable broader use.

Aims: To assess the diagnostic performance of 18F-CETO-PET/CT in ACC as compared with 18F-FDG-PET/CT, and explore how their combined use correlates with ACC phenotype.

Methods: In this bicentric study, ACC patients underwent 18F-CETO-PET/CT and 18F-FDG- PET/CT. A validation cohort included patients undergoing PET/CT with either 18F-CETO or 11C-MTO. Lesions were classified as having low or high PET-uptake. Tumors underwent RNA-sequencing or immunohistochemistry to characterize adrenocortical-specific features.

Results: Twenty patients underwent combined CETO-FDG-PET/CT and 235 ACC lesions were detected; 21 18F-CETO-high/18F-FDG-low, 162 18F-CETO-high/18F-FDG-high and 52 18F-CETO-low/18F-FDG-high. For the initial tumor staging of 13 patients, compared with 18F- FDG, 18F-CETO detected more lesions in 5/13 and an equivalent number in 8/13. Contrary, at restaging 5/7 patients had fewer lesions on 18F-CETO than on 18F-FDG ($P = .002$). A similar pattern was observed in the validation cohort, that also identified 11% (8/70) patients with heterogenous 18F-CETO/11C-MTO uptake, associated with poor survival (median 9 months).

Conversely, patients with homogenously 18F-CETO-low ACC uptake showed favorable survival (median 56 months). 11C-MTO/18F-CETO-PET tracer uptake showed positive correlation to CYP11B1 mRNA expression as well as adrenocortical differentiation.

Discussion: 18F-CETO-PET/CT shows promise for phenotyping as well as staging therapy- naïve ACC, but its role in other diagnostic applications, especially for restaging, remains to be defined.

Abstract citation ID: lvag096.180

RC6.6 - ECE_2726 - Survival prediction in adrenocortical carcinoma using time-to-event machine learning with updated follow-up data: comparison of ensemble methods, deep learning, and cox regression

Emre SAYGILI[1], Otilia Kimpel[2], Marta Laganà[3], Soraya Puglisi[4], Darko Kastelan[5], Jessica Remfry[6], Rossella Libe[7] and Cristina L Ronchi[6]

[1]Faculty of Medicine, Division of Endocrinology and Metabolism, Department of Internal Medicine, Canakkale Onsekiz Mart University, Çanakkale, Türkiye; [2]Division of Endocrinology and Diabetes, Department of Medicine, University Hospital, University of Würzburg, Würzburg 97080, Germany; [3]Medical Oncology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, ASST Spedali Civili, Brescia 25123, Italy; [4]Department of Clinical and Biological Sciences, Internal Medicine, San Luigi Hospital, University of Turin, Turin, Italy; [5]Department of Endocrinology, University Hospital Centre Zagreb, Zagreb, Croatia; [6]Department of Metabolism and Systems Science, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom; [7]Department of Endocrinology and National Reference Center for Rare Adrenal Disorders, AP-HP, Hôpital Cochin, Paris, France

Background: Adrenocortical carcinoma (ACC) is a rare aggressive malignancy with difficult-to-predict clinical outcomes. We previously demonstrated that the S-GRAS score—based on clinical-histopathological characteristics—is the most relevant prognostic tool for ACC, and subsequently developed the first ML-based survival prediction web tool using classification algorithms with binary outcome analysis.[1,2] However, classification approaches do not account for censored survival data, potentially leading to limited generalizability. This study aimed to advance prognostic modeling by applying survival-specific ML algorithms with extended follow-up data.

Methods: A total of 1062 ACC patients from our previously published cohorts were analyzed using follow-up data extended through 2025 (median 81.0 months by reverse Kaplan-Meier method).The dataset was stratified into training (70%, $n = 743$) and test (30%, $n = 319$) sets. Cox Proportional Hazards (Cox PH) regression was compared with three ML approaches: Random Survival Forest (RSF), XGBoost, and DeepSurv. All models were optimized using 5-fold cross-validation with 95% confidence intervals. Performance was assessed using Concordance Index (C-index) and time-dependent AUC for discrimination, Integrated Brier Score (IBS) for calibration, and Decision Curve Analysis (DCA) for clinical utility.

Results: All models demonstrated high discriminative performance in training: Cox PH C-index 0.773 (95% CI: 0.72-0.83), RSF 0.761 (0.70-0.82), XGBoost 0.765 (0.72-0.82), and DeepSurv 0.765 (0.72-0.81). In the test set, performance remained consistent: Cox PH 0.746, RSF 0.739, XGBoost 0.742, and DeepSurv 0.740. Time-dependent AUC exceeded 0.82 at 1-, 3-, and 5-year timepoints. Compared to our previous classification approach (training AUC 0.85, validation AUC 0.79), current models showed improved consistency between datasets. Cox PH (IBS: 0.134) and RSF (0.135) demonstrated superior calibration compared to DeepSurv (0.152) and XGBoost (0.217). DCA confirmed clinically meaningful net benefit for Cox PH and RSF across the 20-50% risk threshold range.

Conclusions: With extended follow-up and survival-specific methodology, all models achieved high discriminative ability (C-index >0.73) with more consistent performance between training and test sets compared to our previous classification-based approach, indicating improved generalizability. Cox regression and RSF demonstrated superior calibration and clinical utility, representing optimal approaches for individualized prognostic assessment in ACC. These survival models will be integrated into our web-based prediction tool to enable continuous survival probability estimation (https://acc-survival.streamlit.app).

References

1. Elhassan YS, Altieri B, Berhane S, et al. S-GRAS score for prognostic classification of adrenocortical carcinoma: an international, multicenter ENSAT study. *Eur J Endocrinol*. 2021;186(1):25-36.
2. Saygili ES, Elhassan YS, Prete A, Lippert J, Altieri B, Ronchi CL. Machine learning-based survival prediction tool for

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

adrenocortical carcinoma. *J Clin Endocrinol Metab*. 2025;110(10):e3185-e3192.

Abstract citation ID: lvag096.181

RC7.1 - ECE_3645 - Serum steroid metabolomics is inferior to urine steroid metabolomics in the detection of adrenocortical carcinoma

James M. Hawley[1,2], Angela Taylor[3], Roland Veen[4], Lida Abdi[1], Alessandro Prete[3], Vasileios Chortis[3], Vera Dosedelova[1], Carl Jenkinson[1], Michael Dennedy[5], Magalie Haissaguerre[6], Dimitra Vassiliadi[7], Urszula Ambroziak[8], Martin Fassnacht[9], Darko Kastelan[10], Irina Bancos[11], Alice J. Sitch[12], Michael Biehl[4] and Wiebke Arlt[1]

[1]Medical Research Council Laboratory of Medical Sciences, London, United Kingdom; [2]Clinical Biochemistry, Manchester University NHS Foundation Trust, Manchester, United Kingdom; [3]Department of Metabolism and Systems Science, University of Birmingham, Birmingham, United Kingdom; [4]Computer Science and Artificial Intelligence, University of Groningen, Bernoulli Institute of Mathematics, Groningen, The Netherlands; [5]The Lambe Institute for Translational Research, University of Galway, Galway, Ireland; [6]Hopital Haut Leveque, Endocrinology and Endocrine Oncology, Bordeaux, France; [7]Evangelismos Hospital, Department of Diabetes, Endocrinology and Metabolism, Athens, Greece; [8]Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland; [9]Department of Endocrinology and Disabetes, University Hospital Wurzburg, Wurzburg, Germany; [10]Department of Endocrinology, University Hospital Centre Zagreb, Zagreb, Croatia; [11]Division of Endocrinology, Metabolism and Nutrition, Mayo Clinic, Rochester, United States; [12]Department of Applied Health Sciences, University of Birmingham, Birmingham, United Kingdom

Background: Differentiating malignant adrenocortical carcinoma (ACC) from benign adrenocortical adenoma (ACA) remains challenging. Diagnosis often relies on multimodal imaging; however, this lacks specificity. Urine steroid metabolomics (USM), a combination of multi-steroid profiling by LC-MS/MS and machine learning, has been shown to significantly improve diagnostic accuracy over imaging only. LC-MS/MS analysis is more widely available for serum steroids than urinary steroid metabolites. However, to date, the comparative utility of serum steroid metabolomics (SSM) has not been investigated.

Objectives: The primary aim was to compare the utility of SSM and USM for detecting ACC. As a secondary objective, we investigated the diagnostic accuracy of reduced steroid panels in both matrices.

Design: We included paired 24-h urine and morning serum samples from 471 patients (87 ACC, 384 ACA) from the prospective EURINE-ACT study ($n = 2017$). All samples were analysed by LC-MS/MS, measuring 14 serum steroids (androgens, glucocorticoids, core precursors) and 14 related urinary steroid metabolites. ACA and ACC were randomly selected into training and test sets. We trained serum- and urine-specific machine learning algorithms using the results from 157 patients (40 ACC, 117 ACA). USM and SSM algorithms were generated for both the 14-steroid and 8-steroid panels. Locked algorithms were then applied to the serum and urine steroid results in the test cohort ($n = 314$; 47 ACC, 267 ACA). Diagnostic performance was assessed using Receiver Operating Characteristic curve (AUROC) analysis and chi squared tests.

Results: Applying the locked USM algorithm based on the 14-steroid panel to the 24-h urine steroid profiling results of the test cohort produced an AUROC of 0.90 (95% CI 0.85-0.96). By contrast, the SSM algorithm applied to the serum steroid profiling results of the test cohort produced an AUROC of 0.77 (95% CI 0.68-0.85). Chi squared analysis revealed a significant difference between USM and SSM ($P = .005$). Application of the algorithm based on the 8-steroid panel to the 24-h urine data generated an AUROC of 0.91 (0.86-0.96); the equivalent 8-steroid serum algorithm produced an AUROC of 0.80 (0.72-0.89) ($P = .03$). USM results (8 vs 14 steroids) were not statistically different ($P = .68$).

Conclusions: SSM is diagnostically inferior to USM. The performance of an 8-steroid profile is similar to the larger, 14-steroid profile. This unequivocally answers which biological matrix is superior for use in the steroid metabolomics approach to ACC detection. Identification of a reduced profile with similar diagnostic performance will facilitate the translation of this powerful technique into routine clinical use.

Abstract citation ID: lvag096.182

RC7.2 - ECE_1530 - Targeting FAK signaling overcomes drug resistance in gastrointestinal neuroendocrine tumor cell lines

Francesco Gambera, Anna Chinnì, Alice Castenetto, Clarissa Gissi, Angeliki Ditsiou and Teresa Gagliano

Udine, Italy

Gastrointestinal neuroendocrine tumors (GI-NETs) are a rare and heterogeneous group of neoplasms originating from neuroendocrine cells dispersed throughout the gastrointestinal epithelium. Although many GI-NETs exhibit indolent clinical behavior, a significant subset develops aggressive and invasive features and becomes largely refractory to standard therapies. In the metastatic setting, treatment options are mainly limited to chemotherapy, targeted agents, and peptide receptor radionuclide therapy; however, durable clinical responses remain uncommon due to the frequent development of intrinsic or acquired resistance. Therefore, the identification of novel molecular targets able to overcome resistance mechanisms represents an urgent unmet clinical need.

Recent evidence from our laboratory suggests that focal adhesion kinase (FAK), a non-receptor tyrosine kinase that integrates signals from the extracellular matrix and growth factor receptors, plays a central role in regulating GI-NET cell proliferation and survival. Beyond its enzymatic activity, FAK also exerts kinase-independent scaffold functions that coordinate multiple oncogenic signaling pathways. The aim of this study was to investigate whether comprehensive inhibition of FAK, targeting both its kinase and scaffold functions, can modulate GI-NET sensitivity to anticancer therapies and counteract tumor-promoting microenvironmental effects.

We employed two GI-NET cell lines (GOT1 and COLO320DM) and normal human fibroblasts as experimental models to recapitulate key aspects of tumor–stroma interactions. To achieve complete functional inhibition of FAK, we used a proteolysis-targeting chimera-based FAK degrader (PROTAC-FAK), which induces selective ubiquitination and proteasomal degradation of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

the FAK protein. Antiproliferative responses were evaluated in both two-dimensional monolayers and three-dimensional spheroid cultures, alone or in combination with etoposide and rapamycin.

Our results demonstrate that PROTAC-FAK markedly enhances the antiproliferative effects of both etoposide and rapamycin in GI-NET cells across culture systems. In addition, FAK degradation significantly impairs clonogenic growth, indicating a long-lasting suppression of tumor-initiating capacity. Importantly, PROTAC-FAK effectively counteracts the pro-proliferative influence exerted by fibroblasts, highlighting its ability to disrupt microenvironment-driven resistance mechanisms.

In conclusion, our findings indicate that dual targeting of FAK kinase and scaffold functions through PROTAC-mediated degradation potentiates therapeutic efficacy, reduces drug resistance, and mitigates tumor-promoting signals derived from the tumor microenvironment. These results support FAK as a promising combinatorial target for the treatment of GI-NETs and provide a strong rationale for further preclinical and translational studies to validate this strategy.

Abstract citation ID: lvag096.183

RC7.3 - ECE_2613 - Association between metabolic profile and tumour phenotype in lung neuroendocrine neoplasms

Violetta Rosiek, Ksenia Janas, Olga Grzelak and Beata Kos-Kudła

Endocrinology, Department of Endocrinology and Neuroendocrine Tumors, Department of Pathophysiology and Endocrinology, Medical University of Silesia, Katowice, Poland

Introduction: Data on the relationship between routinely available metabolic parameters and tumour phenotype in lung neuroendocrine neoplasms (LNENs) are limited. It remains unclear whether simple metabolic measures differ across histological subtypes, proliferative grade and disease stage in LNENs.

Aim: To evaluate associations between metabolic profile and tumour phenotype in patients with LNENs.

Methods: We analysed 158 patients with LNENs. Metabolic parameters included body mass index (BMI), fasting glucose, total cholesterol and triglycerides. Tumour phenotype was characterised by histopathological subtype (typical carcinoid [TC], atypical carcinoid [AC], large-cell neuroendocrine carcinoma [LCNEC]), Ki-67 groups (G1/G2/G3) and TNM stage (I-IV). Group comparisons were performed using Kruskal–Wallis and χ^2 tests, as appropriate. Multinomial logistic regression was used for histological subtype and ordinal logistic regression for Ki-67 groups and stage. All models included BMI, glucose, lipid parameters, age and sex.

Results: BMI differed significantly across histological subtypes, Ki-67 groups and disease stages (all $P < .01$), with progressively lower BMI observed in more aggressive tumour categories. Fasting glucose showed a weak association with disease stage but did not differ across histological subtypes or Ki-67 groups. Total cholesterol and triglycerides did not differ across tumour phenotype categories. In multivariable models, lower BMI remained independently associated with more aggressive tumour phenotype across all endpoints. In the Ki-67 model, lower BMI was associated with higher proliferative grade (OR per 1 kg/m^2 0.91, 95% CI 0.85-0.97, $P = .0039$). In the histological model, BMI independently differentiated LCNEC and AC from TC ($P < .01$). In the stage model, fasting glucose showed only a weak and borderline independent association with more advanced stage (OR per 1 mg/dL 1.014, 95% CI 1.000-1.027, $P = .042$), while lipid parameters were not independently associated with tumour phenotype in any model.

Conclusions: Among routinely available metabolic parameters, BMI consistently differs across histological subtype, proliferative grade and disease stage in LNENs, whereas glucose shows only a weak association with stage and lipid parameters provide no additional discriminatory information. These findings suggest that lower BMI reflects tumour phenotype and disease aggressiveness rather than representing a causal factor. Due to the retrospective design, the potential contribution of cancer-related weight loss, treatment effects and comorbidities cannot be disentangled.

Abstract citation ID: lvag096.184

RC7.5 - ECE_2228 - Antitumoral effects of splice-switching oligonucleotides targeting insulin receptor alternative splicing in adrenocortical carcinoma cells

Sonia Di Bari[1], Luca Bosoni[1], Rosa Catalano[1], Emanuela Esposito[1], Emma Nozza[1], Genesio Di Muro[1], Sandra Sigala[2], Laura Sophie Landwehr[3], Guido Di Dalmazi[4,5], Serena Palmieri[6], Emanuele Ferrante[6], Giovanna Mantovani[1,6] and Erika Peverelli[1,6]

[1]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [2]Section of Pharmacology, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy; [3]Department of Internal Medicine I, Division of Endocrinology and Diabetes, University Hospital Würzburg, Würzburg, Germany; [4]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [5]Department of Medical and Surgical Sciences, Alma Mater University of Bologna, Bologna, Italy; [6]SC Endocrinology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

The majority of adrenocortical carcinomas (ACC) overexpress insulin-like growth factor 2 (IGF2), which is a driving force for the neoplastic progression via the autocrine activation of its receptors insulin-like growth factor 1 receptor (IGF1R) and insulin receptor (IR). Although previous efforts focusing on IGF1R targeting have shown limited efficacy, recent evidence highlights IR as a promising therapeutic target. Alternative splicing of exon 11 of IR generates two isoforms: IR-A, mediating mitogenic effects, and IR-B, involved in metabolic regulation. Higher IR-A than IR-B expression has been observed in ACC samples and in ACC cell lines H295R and JIL-2266 (derived from primary tumors) and TVBF-7 (derived from an ACC metastasis).

The aim of this study is to manipulate IR splicing to imbalance the ratio between the two IR isoforms favoring the metabolic one (IR-B) at expense of the mitogenic one (IR-A) and to evaluate the downstream effects of the IR splice-switching in ACC cell lines and primary ACC cultured cells. To this aim we transfected cells with splice-switching oligonucleotides (SSOs) that target the CUGBP1 binding site, thereby preventing this splicing factor from promoting IR-A formation. We then measured IR-A and IR-B expression, cell proliferation, apoptosis and migration.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Our results showed that SSO transfection decreased IR-A and increased IR-B levels in all cell lines and in two ACC primary cultures.

Furthermore, consistent with the altered IR-A/IR-B ratio, cell proliferation decreased in H295R (-27.6 (IQR:13.3)%, $P < .05$), JIL-2266 (−62.5 (30.5)%, $P < .05$) and TVBF-7 (−43.3 (13.1)%, $P < .05$) as well as in primary cultured cells (−35.2% and −42.3%, $P < .01$). Apoptosis also increased (+24.3 (13.3)%, +136.2 (74)%, +100.5 (91.3)%, all $P < .05$ in cell lines; and +41.3%, +56.4% $P < .01$, in primary cultures, respectively). A decrease in cell migration was also observed in all cell lines (−53.5 (22.4)%, −37.7 (22.6)%, −64.8 (21.3)%, all $P < .05$).

In conclusion, our results demonstrated that the SSO targeting IR exerted antitumoral effects in ACC cells, supporting a therapeutic potential of modulating IR alternative splicing as a promising strategy for the development of innovative, precision-based therapies in ACC.

Abstract citation ID: lvag096.185

RC7.6 - ECE_3817 - Ten years of clinical experience with lenvatinib therapy for advanced thyroid cancer in a tertiary care center

Elisa Minaldi, Carla Gambale, Loredana Lorusso, Laura Valerio, Carlotta Giani, Virginia Cappagli, Alessandro Prete, Laura Agate, Valeria Bottici, Sandra Brogioni, Eleonora Molinaro, Antonio Matrone and Rossella Elisei
Pisa, Italy

Introduction: Lenvatinib is approved in Italy for the treatment of progressive iodine-refractory thyroid cancer. The objective of the study was to evaluate the clinical presentation at diagnosis and response to therapy in patients treated with lenvatinib and followed at our center.

Patients and Methods: We analyzed data from 207 patients treated and followed at the Endocrinology Unit of the University Hospital of Pisa between 2014 and 2025.

Results: Among 207 patients, 53.6% were males and 46.4% females. The median age at diagnosis was 59 years (IQR 50-66). Histotypes were distributed as follows: 51.7% ($n = 107$) were papillary carcinomas, 23.2% ($n = 48$) poorly differentiated, 17.9% ($n = 37$) follicular, and 7.2% ($n = 15$) oncocytic. At diagnosis, 27.5% ($n = 57$) T3a, 17.9% ($n = 37$) were T2, 15% ($n = 31$) T3b, and 13.5% ($n = 28$) T4a, according to TNM VIII edition. 55% ($n = 114$) had lymphnode metastases (87.7% N1b; 12.3% N1a) and 44.8% ($n = 86$) had distant metastases. Staging at diagnosis was: Stage I in 23.5% ($n = 42$), II in 35.2% ($n = 63$), III in 7.3% ($n = 13$), IVA in 1.7% ($n = 3$), IVB in 32.4% ($n = 58$).

After a median follow-up of 7.4 years (IQR 2.7-12.6), 60.9% had died and 39.1% were still alive. The median age at initiation of lenvatinib was 65 years (IQR 59-74), and therapy was initiated a median of 4.5 years (IQR 1.2-10.4) after diagnosis. 57.8% of patients started on 24 mg/day, 22.2% on 14 mg/day, 9.3% on 10 mg/day, and lower percentages on other doses. Overall survival (OS) after initiation of therapy was 27 months (95% CI 19.2-34.8). Older age (>61 vs ≤60 years) and higher ECOG (≥2 vs 0-1) were the only factors significantly associated with shorter OS. The Disease-specific survival (DSS) was 52.6 months (95% CI 35.9-69.4). Higher ECOG (≥2 vs 0-1) was the only factor significantly associated with shorter DSS. The median progression-free survival (PFS) after lenvatinib was 21 months (95% CI 11.7-30.3). Histology was the only factor significantly associated with PFS: poorly differentiated and oncocytic histotypes showed shorter PFS (8 and 21 months), whereas follicular and papillary histotypes were associated with longer PFS (40 and 30 months). Of 181 assessable patients, the best clinical response was 56.9% stable disease, 29.3% partial response, and 13.8% progressive disease.

Conclusions: After more than ten years of experience, the analysis confirms the good efficacy of lenvatinib in iodine-refractory advanced thyroid cancer, especially in the short term. The main challenge remains maintaining the response over time, balancing therapeutic efficacy and tolerability.

Abstract citation ID: lvag096.186

RC8.1 - ECE_3487 - High salt intake does not guarantee adequate iodine status: evidence from the lithuanian NATRIJOD study

Lina Zabuliene[1], Urte Zakauskiene[1,2], Ernesta Macloniene[1,2], Nomeda Bratcikoviene[3,4], Valdas Banys[5], Ausra Linkeviciute Dumce[2], Dovile Karosiene[2], Mykolas Urbonas[6], Algirdas Utkus[2,4] and Marius Miglinas[1,2]
[1]Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius, Lithuania; [2]Vilnius University Hospital "Santaros klinikos", Vilnius, Lithuania; [3]Faculty of Fundamental Sciences, Vilnius Gediminas Technical University, Vilnius, Lithuania; [4]Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania; [5]Centro Outpatient Clinic, Vilnius, Lithuania; [6]Antakalnio Outpatient Clinic, Vilnius, Lithuania

Background: Despite established policies for salt iodization, iodine deficiency remains a public health issue in Europe. High salt consumption persists, yet it is unclear whether excessive salt intake ensures adequate iodine intake in everyday diets. Changes in dietary patterns, inconsistent use of iodized salt, and reduced consumption of iodine-rich foods may undermine the effectiveness of iodine fortification efforts. This study investigated the association between salt intake and iodine status in a nationally representative sample of adults.

Methods: The NATRIJOD study is a cross-sectional, population-based study conducted in Lithuania. The study assessed sodium, potassium, and iodine intake using 24-hour urine collections, the gold standard for evaluating population-level dietary intake. Urinary iodine concentration (UIC) was measured to classify iodine status according to WHO criteria. Salt intake was estimated from 24-hour urinary sodium excretion. Information on iodized salt use, dietary patterns, and iodine-containing supplements was collected via questionnaires. Multivariable logistic regression was used to identify factors independently associated with iodine sufficiency. A two-sided P-value <.05 was considered statistically significant.

Results: A total of 662 adults (52.0% men) with a mean age of 47.3 ± 12.0 years were included. The median UIC was 96.6 µg/L (IQR 54.4-159.5), indicating borderline iodine sufficiency at the population level. Overall, 51.7% of participants had iodine insufficiency, including 10.6% with severe deficiency.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Median salt intake was 9.08 g/24 h (IQR 6.46-12.19); 40.8% of participants consumed ≥10 g/24 h of salt. UIC increased across salt intake categories, yet iodine insufficiency remained common even among high salt consumers. Participants consuming ≥10 g/24 h of salt had a higher median UIC than those consuming 5-9.99 g/24 h (112.7 vs 91.4 µg/L, $P = .005$) and a lower prevalence of iodine insufficiency (44.1% vs 55.7%, $P = .005$).

In multivariable analysis, salt intake category was independently associated with iodine status ($P = .005$). Compared with participants consuming <5 g/24 h of salt, those consuming ≥10 g/24 h had higher odds of iodine sufficiency (OR 2.03, 95% CI 1.20-3.43; $P = .008$). Dietary factors, including bread, milk, and cheese consumption, were not independently associated with iodine sufficiency.

Conclusions: More than half of adults in Lithuania had iodine insufficiency despite high salt intake. These findings show that excessive salt consumption does not ensure adequate iodine status, highlighting the need for improved practices in using iodized salt and incorporating dietary iodine sources. To ensure sufficient iodine levels without increasing salt consumption, it is essential to strengthen iodization strategies and continue monitoring the population's iodine status.

Abstract citation ID: lvag096.187

RC8.2 - ECE_2631 - DEHP disrupts adrenal steroidogenesis via rapid membrane depolarization and subsequent calcium influx mediated by L-type voltage-dependent calcium channels

Erik Petersenn[1], Stefan Bernard[1,2], Sonja Kunz[1], Martin Bidlingmaier[1], Marily Theodoropoulou[1], Tracy Ann Williams[1], Martin Reincke[1] and Isabel Stüfchen[1]
[1]*Department of Medicine IV, Endocrinology, Diabetology and Metabolism, LMU University Hospital, Munich, Germany;* [2]*Medicine IV, Endocrinology, Diabetology & Metabolism, LMU University Hospital, Munich, Germany*

Background: Di(2-ethylhexyl) phthalate (DEHP) is among the most widely used plasticizers and ubiquitously present in everyday products. In humans, it is metabolized to mono(2-ethylhexyl) phthalate (MEHP). Due to their interference with multiple hormonal pathways phthalates are classified as endocrine disrupting chemicals. Recent *in vitro* studies suggest that DEHP impairs adrenal steroidogenesis; however, the underlying mechanisms and the differential effects of metabolites remain poorly understood.

Objective: This study aimed to investigate the effects of DEHP and its primary metabolite MEHP on steroidogenic enzyme expression and steroid secretion in adrenocortical HAC15 cells under basal conditions and upon co-stimulations with angiotensin II (AngII) or forskolin.

Methods: Cultured HAC15 cells were treated with DEHP (0.1-10 µM) for 24 and 72 hours under basal conditions, and co-stimulation with angiotensin II (AngII) (10 nM) or forskolin (10 µM). Cell viability was assessed to exclude cytotoxic effects. Gene expression of key steroidogenic enzymes and transcription factors was quantified using qPCR, and steroid hormone concentrations in cell supernatants were measured by LC-MS/MS. Co-stimulation with nifedipine (1 µM) served to investigate involvement of voltage-dependent L-type calcium channels (L-VGCCs). Voltage-sensitive fluorescent dye $DiBAC_4$ was used to detect changes in membrane potentials.

Corresponding experiments were conducted with MEHP (10 µM, 50 µM) under basal conditions. Multiple testing was corrected using the Benjamini–Hochberg method.

Results: No significant changes in cell viability were observed under any treatment condition. Exposure to DEHP for 72 h resulted in a dose-dependent upregulation of *CYP11B1*, *CYP11B2*, accompanied by a downregulation of *HSD11B2* (all $P < .001$). Steroid profiling showed concordant increases in secretion of most mineralocorticoids and glucocorticoids synthesized by the respective enzymes (eg, a five-fold increase of aldosterone, $P < .01$). Co-stimulation with forskolin for 24 h potentiated DEHP-induced enzyme expression and steroid secretion, indicating a strong additive effect (all $P < .05$). In contrast, AngII co-stimulation resulted only in a modest enhancement of DEHP effects, suggesting convergence on a shared signaling pathway, which was further supported by gene expression pattern of the key transcriptional factor *NR4A2*.

Notably, DEHP-induced effects were reversed upon co-stimulation with nifedipine ($P < .05$), indicating involvement of L-VGCCs. Consistently, DiBAC membrane potential analysis revealed depolarization within 1-5 minutes upon DEHP exposure ($P < .05$). MEHP mirrored DEHP effects at higher concentrations (50 µM).

Conclusions: The data suggest that DEHP, and similarly MEHP in higher concentration, increases steroidogenic enzyme expression and hormone secretion via membrane depolarization and L-VGCCs calcium influx, partially sharing a signaling pathway with AngII.

Abstract citation ID: lvag096.188

RC8.3 - ECE_1394 - Urinary non-persistent pollutants and thyroid cancer: a case–control study highlighting associations with phthalate metabolites and bisphenol F

Marina Lugaresi[1], Patrice Dufour[2,3], Valentina Cirello[4,5], Claudia Moneta[1], Erika Carbone[4], Laura Fugazzola[1,6], Corinne Charlier[2,3] and Catherine Pirard[2,3]
[1]*Department of Health Sciences, University of Milan, Milan, Italy;* [2]*Center for Interdisciplinary Research on Medicines (C.I.R.M.), University of Liege, Liege, Belgium;* [3]*Department of Clinical, Forensic and Environmental Toxicology, University Hospital of Liege, Liege, Belgium;* [4]*Department of Endocrine and Metabolic Diseases, Istituto Auxologico Italiano IRCCS, Milano, Italy;* [5]*Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy;* [6]*Department of Endocrinology, ASST Santi Paolo e Carlo, Milano, Italy*

Introduction: Human activities lead to the release of several chemicals into the environment with a significant impact on human health. Some of these substances are classified as endocrine disruptors due to their ability to interfere with endocrine systems, in addition to their carcinogenic potential. Considering that the incidence of thyroid cancer (TC) has been steadily increasing over last decades, a potential role of these compounds can be hypothesized. The aim of the present study was to evaluate the association between urinary concentrations of non-persistent pollutants and TC, as well as with its clinical characteristics.

Materials and Methods: wThis was a cross-sectional case-control study. Urine samples of 109 patients with TC and 100 control

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

subjects were collected at the Istituto Auxologico Italiano Hospital of Milan (Italy). Samples were analyzed for 7 bisphenols, triclosan, 4 parabens, 8 phthalate metabolites and benzophenone-3 (BP3) using gas or liquid chromatography coupled to a mass spectrometer, depending on the specific analyte.

Results: The mean age of the study population was 50 years, and females accounted for 75% of participants. Among cases, 84% had papillary thyroid cancer. Among the pollutants investigated, bisphenol A and S, methylparaben, BP3 and 4 phthalate metabolites (MEP, MnBP, 5-OH-MEHP and 5-oxo-MEHP) were detected in more than 70% of the samples. Among phthalate metabolites, urinary levels of MEP (OR = 1.16, 95% CI: 1.01-1.34), 5-OH-MEHP (OR = 1.34, 95% CI: 1.07-1.72) and 5-oxo-MEHP (OR = 1.36, 95% CI: 1.10-1.70), as well as the presence of MBzP (OR = 3.24, 95% CI: 1.74-6.19) were positively associated with TC. Moreover, the presence of bisphenol F was positively associated with TC (OR = 3.44, 95% CI: 1.81-6.55).

Conclusions: This is the first European study to evaluate the association between urinary levels of non-persistent pollutants and thyroid cancer, identifying several positive associations. Our findings are consistent with data reported in some Chinese cohorts. However, due to the cross-sectional design of the study and the short half-life of the investigated compounds, the direction of the causality could not be inferred.

Abstract citation ID: lvag096.189

RC8.4 - ECE_3813 - Exposure to per- and polyfluoroalkyl substances and Its association with blood pressure: insights from patients with endocrine and essential hypertension

Isabel Stüfchen[1], Bettina Aschenbrenner[2], Lea Grümme[2], Erik Petersenn[1], Moritz Baumgärtner[1], Tracy Ann Williams[1], Friederike Völter[1], Júnia Ribeiro De Oliveira Longo Schweizer[1], Elisabeth Nowak[1,3], Wolfgang Völkel[2], Caroline Herr[2], Stefanie Heinze[2] and Martin Reincke[1]
[1]Munich, Germany; [2]Bavarian Health and Food Safety Authority, Institute for Occupational Health and Product Safety Environmental Health, Munich, Germany; [3]Department of Medicine IV, LMU University Hospital, LMU Munich, Munich, Germany

Background: Per- and polyfluoroalkyl substances (PFAS) have been associated with an increased risk of arterial hypertension. However, their role in endocrine forms of hypertension remains insufficiently characterized.

Objective: To analyze serum PFAS concentrations, temporal trends, and their association with blood pressure (BP) in patients with primary aldosteronism (PA) and Cushing syndrome (CS), and respective controls.

Methods: This retrospective study included patients with CS ($n = 90$) and controls with excluded CS ($n = 94$) from the German Cushing Registry (CS cohort), and patients with PA ($n = 389$) and controls with excluded PA ($n = 165$) from the German Conn Registry (PA cohort) at the LMU University Hospital Munich. Serum samples collected at the timepoint of diagnosis between 2012 and 2024 were analyzed for nine different PFAS using liquid chromatography–tandem mass spectrometry (LC-MS/MS). In both cohorts, each including patients and respective controls, multiple linear regression models were used to assess the overall association between log-transformed PFAS concentrations and systolic and diastolic BP across different hormonal states. Models were further adjusted for disease status and corticosteroid concentrations as well as for age, sex, BMI, antihypertensive medication, year of sampling and smoking status.

Results: Most detected PFAS were perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorohexane sulfonate (PFHxS) in both cohorts. Concentrations of those four were strongly intercorrelated and consistently higher in males compared to females (all $P < .05$). Summed PFAS ($\sum$PFAS) were correlated with higher age and earlier year of blood sampling in both cohorts (all $P < .05$). In crude models, higher $\sum$PFAS concentrations were associated with higher systolic BP in both cohorts (CS: $\beta = 4.26$, $P = .03$; PA: $\beta = 3.59$, $P = .01$). However, these associations were no longer statistically significant upon adjustment for age. In fully adjusted analyses, neither total PFAS nor individual compounds were independently associated with systolic or diastolic blood pressure.

Conclusions: The findings of this study suggest that within two independent, predominantly hypertensive populations, PFAS exposure correlates with age and sampling year, but does not contribute additional explanatory value for blood pressure beyond clinical and endocrine determinants.

Abstract citation ID: lvag096.190

RC8.5 - ECE_2702 - A mobile application as a tool for reducing exposure to endocrine disrupting chemicals (EDCs)

Marcin Lewicki[1] and Mateusz Górecki[2]
[1]Endocrine Protect sp. z o.o., Lublin, Poland; [2]Endocrine Protect, Lublin, Poland

Endocrine-disrupting chemicals (EDCs) are substances capable of interfering with the hormonal system and inducing adverse health effects. EDCs constitute a significant and growing challenge. Nevertheless, awareness of EDCs among patients remain insufficient. To assess the level of knowledge in this area we have conducted an original survey among patients of outpatient clinic. The survey study was carried out among 51 respondents. More than half of the participants reported a diagnosed endocrine disorder, most commonly thyroid diseases, and nearly all (96.1%) actively sought information related to endocrine health, primarily via the Internet and consultations with medical specialists. The results indicated heterogeneous levels of knowledge regarding EDCs. Approximately half of the respondents declared familiarity with the term EDC and its effects, while the remaining participants reported limited or uncertain knowledge. The survey revealed a significant gap between the growing interest in EDC-related issues and the actual level of patient knowledge. In response to the aforementioned problem, we developed a mobile application designed to enable the identification of EDCs in industrial products—particularly food and cosmetic products—using a smartphone. The application allows for rapid and user-friendly analysis of product composition with respect to the presence of harmful EDCs by scanning the product's EAN barcode or by using optical character recognition (OCR) to analyze ingredient lists directly. Additionally, it offers access to interactive, expert-prepared educational materials designed to support informed health-related choices. By combining digital technology with evidence-based content, the application seeks to enhance

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

awareness of EDC exposure and support individual efforts to reduce associated potential health risks.

Abstract citation ID: lvag096.191

RC8.6 - ECE_1563 - Study of the interaction of bisphenol A with the expression of P16, interleukin-6, apelin and PPAR gamma genes in patients with type 2 diadetes mellitus

Marwa Salah
Faculty of medicine, Internal Medicine, Endocrine, Alexandria University, Alexandria, Egypt

Background: Endocrine-disrupting chemicals have currently drawn attention for causing metabolic aberrations to obesity, insulin resistance, type 2 diabetes mellitus, and other metabolic diseases. So, the present study aimed to study the level of serum bisphenol-A, expressions of P16, interleukin-6, apelin, and peroxisome proliferator-activated receptor gamma messenger ribonucleic acids and determine the association of these markers with glycemic control in patients with type 2 diabetes mellitus.

Methods: A case-control study included 80 patients with type 2 diabetes in addition to 80 healthy controls. Serum bisphenol-A was measured by the enzyme-linked immunosorbent assay technique. In addition to measuring relative quantification of P16, interleukin-6, apelin, and peroxisome proliferator-activated receptor gamma messenger ribonucleic acids by real-time quantitative polymerase chain reaction.

Results: Serum bisphenol-A concentration among patients with diabetes was statistically significantly higher compared to controls (mean 94.10 ± 55.46, 57.03 ± 24.98, respectively, $P < .001$) and had a significant positive correlation with glycemic parameters. There was a significant increase in the relative expression of p16 (mean 10.06 ± 25.79, 1.40 ± 0.98, $P < .001$) and interleukin-6 in diabetic patients compared to healthy subjects (mean 6.68 ± 9.48, 1.45 ± 1.18, $P < .001$). On the other hand, there was a significant decrease in relative expression of apelin and peroxisome proliferator-activated receptor gamma in diabetic patients compared to controls ($P < .001$), and BPA was positively correlated to p16 ($r = 0.252$, $P = .001$) and negatively correlated with apelin ($r = -0.180$, $P = .022$).

Conclusions: Our results suggested that elevated serum bisphenol-A (BPA) levels in T2DM patients correlate significantly with poor glycemic control, pro-inflammatory markers (IL-6), increased cellular senescence (p16), and downregulated metabolic parameters (apelin and PPAR-γ). These findings establish BPA as a modifiable environmental risk factor for the development of diabetes as well as a biomarker of metabolic dysfunction.

Keywords bisphenol-A, p16, apelin, interleukin-6, PPAR-γ, type 2 diabetes mellitus

Abstract citation ID: lvag096.192

RC9.1 - ECE_1491 - Association of non-contrast CT adrenal features with histopathology and genotype in unilateral primary aldosteronism

Lukas Gold[1], Nabeel Mansour[1], Markus Kroiss[2], Moritz Schrenk[2], Felix Herr[1], Isabel Stüfchen[2], Jens Ricke[1], Wolfgang Kunz[1], Christine Schmid-Tannwald[1], Petra Zimmermann[3], Tracy Williams[2], Nicole Reisch[2], Martin Reincke[2] and Matthias Oettle[2]
[1]*Department of Radiology, LMU University Hospital, LMU Munich, Munich, Germany;* [2]*Department of Medicine IV, LMU University Hospital, LMU Munich, Munich, Germany;* [3]*Department of General, Visceral and Transplantation Surgery, LMU University Hospital, LMU Munich, Munich, Germany*

Purpose: Accurate characterization of adrenal adenomas is essential for the management of unilateral primary aldosteronism (uPA). Although non-contrast computed tomography (CT) is widely used in clinical practice, its ability to reflect histopathologic and genetic features of aldosterone-producing adenomas has not been fully elucidated.

Methods: This retrospective study includes 99 patients with uPA and available genotypic data from the German Conn Center of the Ludwig-Maximillian-University Hospital Munich. Preoperative non-contrast CT scans were reviewed by a board-certified radiologist to assess adenoma number, maximal diameter, and attenuation in Hounsfield units (HU). Postoperative histopathologic findings and genotypes were correlated with CT-derived features using Pearson correlation and independent t test. A *P*-value <.05 was considered statistically significant.

Results: The median interval between non-contrast CT imaging and surgery was 92 days (interquartile range, 106 days). Adenoma size measured on non-contrast CT correlated strongly with the size of the surgical specimen ($n = 67$; 1.77 ± 0.59 cm vs 1.66 ± 0.75 cm; Pearson $r = 0.83$, $P < .001$). However, adenomas smaller than 1.0 cm on histopathology ($n = 35$) were frequently not detected as focal lesions on non-contrast CT ($n = 25$, 71%). Patients were stratified into two groups based on genotype: KCNJ5-mutated ($n = 36$) and non-KCNJ5 adenomas ($n = 63$). The non-KCNJ5 group included ATP1A1 ($n = 17$), CACNA1D ($n = 12$), ATP2B3 ($n = 8$), CTNNB1/GNAQ ($n = 1$), SLC30A1 ($n = 1$), as well as KCNJ5 wild-type tumors ($n = 24$). Due to limited sample sizes of individual genotypes, analyses were restricted to this binary classification. In cases with a radiologically identifiable adenoma ($n = 69$), KCNJ5-mutated tumors did not differ in size on non-contrast CT compared with non-KCNJ5 adenomas (1.89 ± 0.55 cm vs 1.64 ± 0.61 cm; $P = .078$), but demonstrated significantly lower attenuation values (2.71 ± 10.2 HU vs 13.3 ± 17.6 HU; $P = .003$). Absence of a detectable adenoma on preoperative non-contrast CT at the surgical site was observed in 30 cases and was substantially more frequent in non-KCNJ5 ($n = 25$) than in KCNJ5-mutated adenomas ($n = 5$).

Conclusions: Non-contrast CT imaging serves as a useful, non-invasive tool to infer underlying histopathologic and genetic features in patients with uPA. Future studies integrating advanced imaging methods and larger genetic datasets may further enhance the precision of adenoma characterization.

Abstract citation ID: lvag096.193

RC9.2 - ECE_3101 - Survival in ectopic Cushing syndrome in Sweden—a nation-wide study

Marta Piasecka[1,2], Jacob Järås[3], Daniel Bengtsson[4,5], Eleni Papakokkinou[2] and Oskar Ragnarsson[1,2,6]
[1]*Department of Endocrinology, Sahlgrenska Universitetssjukhuset, Göteborg, Sweden;* [2]*Department of Internal Medicine and Clinical Nutrition, Sahlgrenska Universitetssjukhuset, Institute of Medicine, Göteborg, Sweden;* [3]*JRS Statistics AB, Stockholm, Sweden;* [4]*Department of Health, Medicine and Caring Sciences, Linköping*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

University, Linköping, Sweden; [5]Department of Internal Medicine, Kalmar County Hospital, Kalmar, Sweden; [6]Wallenberg Center for Molecular and Translational Medicine, University of Gothenburg, Göteborg, Sweden

Context: Ectopic Cushing syndrome (ECS) is a rare disorder with a poor prognosis.

Objective: To investigate survival in a large ECS cohort, stratified by aetiology.

Methods: This was a nationwide cohort study based on data on all patients who had received the diagnostic code for ECS in the Swedish National Patient Register between 1997 and 2024.

Results: In total, 224 patients (53% women) diagnosed with ECS were identified. The mean age at diagnosis (± standard deviation) was 59 ± 18 years. The 1-year and 5-year survival probabilities for the entire cohort were 58% and 40%, respectively. When stratified by calendar period, the estimated 1-year survival was 57% in 1997-2006, 66% in 2007-2016, and 48% in 2017-2024. The corresponding 5-year survival estimates were 39%, 46%, and 30%, respectively.

Of 224 patients, 88 (39%) had occult ECS, 73 (33%) had pulmonary ECS, 34 (15%) had metastatic disease with unknown primary tumour, 19 (9%) pancreatic ECS, 7 (3%) thymic ECS and 3 (1%) thyroid. The 1-year and 5-year survival probabilities were 89% and 75% for patients with occult ECS, 32% and 18% for patients with ECS of pulmonary origin, 29% and 33% for tumour of unknown origin, 100% and 43% for thymic ECS, 53% and 18% for pancreatic ECS and each at 33% for thyroid.

Conclusions: In this nationwide cohort, ECS was associated with poor overall survival, with fewer than 40% of patients alive at five years. Survival differed markedly by aetiology, with better outcomes in occult, thymic and thyroid ECS and poor prognosis in pulmonary, pancreatic, and cancer of unknown primary. No clear improvement in survival over time was observed, underscoring the need for earlier diagnosis and improved management strategies in high-risk subgroups.

Abstract citation ID: lvag096.194

RC9.3 - ECE_1649 - Cortisol and steroids circadian variations are higher in Cushing syndrome patients treated with metyrapone than osilodrostat and follow daily drug levels fluctuations

Louis Thomeret[1], Fidéline Bonnet-Serrano[1,2], Juliette Blondel[3], Patricia Vaduva[1], Lucas Bouys[4], Florian Violon[1,5], Bruno Ragazzon[1], Annabel Berthon[1], Karine Perlemoine[1], Jean Guibourdenche[2,6], Léopoldine Bricaire[4], Laurence Guignat[4], Rossella Libe[1,4], Lionel Groussin[1,4], Guillaume Assié[1,4], Anne Jouinot[1,4], Alicja Puszkiel[3,6], Benoît Blanchet[3,6] and Jérôme Bertherat[1,4]
[1]CNRS, Inserm, Institut Cochin, Team " Genomics and Signaling of Endocrine Tumors", Université Paris Cité, Paris, France; [2]Hôpital Cochin, Hormonology Department, AP-HP, Paris, France; [3]Hôpital Cochin, Drug Biology and Toxicology department, AP-HP, Paris, France; [4]Hôpital Cochin, Endocrinology department, AP-HP, Paris, France; [5]Hôpital Cochin, Pathology department, AP-HP, Paris, France; [6]Université Paris-Cité, Paris, France

Introduction: Osilodrostat and Metyrapone are two 11beta-hydroxylase inhibitors used in the pharmacological treatment of Cushing syndrome (CS). However, they differ in half-lives (4 h vs 1.8 h, respectively), in half maximal inhibitory concentrations IC_{50}, and impact differently global steroidogenic profile according to previous studies. The aim of our work was to investigate diurnal fluctuations of plasma steroids concentrations, cortisol but also precursors and androgens (classical and 11-oxygenated), in patients treated by either Metyrapone or Osilodrostat for CS.

Methods: Diurnal profiles (6 samples a day) of 12 plasma steroids and drug concentrations were determined using UPLC-tandem mass spectrometry (UPLC-MS/MS) in patients treated for CS with Metyrapone ($n = 17$; median dose 1250 mg/day; various dosing regimens; median treatment duration 112 days) or Osilodrostat ($n = 28$; 10 mg/day; equivalent dose twice daily; 107 days), as well as in 13 untreated patients with CS and 16 healthy controls. Concentrations fluctuations over 24 hours were expressed by MAX-MIN range (MMR, nmol/L) and Coefficient of Variation (CV, %), reported as median [10th-90th percentiles].

Results: In treated patients, 24-hour plasma concentrations of Osilodrostat were more stable than those of Metyrapone (CV = 57.0% [36.1-101] vs 102.6% [65.2-172.2], $P < .0001$), including when compared to the subgroup of 10 Metyrapone cycles with the most regular drug intake (≥3 doses per day, ±1-dose variation; CV = 87.1% [61.0-164.0], $P = .0006$).

Diurnal plasma cortisol levels were more stable in the Osilodrostat group compared to the Metyrapone group (MMR = 126.1 [5.8-240.3] vs 230.9 [87.3-519.1] nmol/L, $P = .0003$) and to the regular-intake Metyrapone subgroup (229.4 [130.1-540.1] nmol/L, $P = .0008$). Cortisol concentrations were higher at 8:00 and lower at 20:00 and 24:00 with the use of Metyrapone compared to Osilodrostat, including in the subgroup of patients with normalized urinary free cortisol ($n_{Osilodrostat} = 25$, $n_{Metyrapone} = 8$).

Glucocorticoid precursors, mainly 11-deoxycortisol, showed higher plasma values and greater fluctuations with Metyrapone than with Osilodrostat (MMR = 62.9 [25.2-323.4] vs 16.2 [0.9-86.3] nmol/L, $P < .0001$).

Classical androgen levels were constantly higher with Metyrapone, whereas 11-oxygenated androgens were markedly decreased in both groups.

Discussion: Our study shows that Osilodrostat is associated with greater stability of plasma cortisol levels whereas Metyrapone is associated with a more physiological rhythm, a higher value in the morning and a lower value at midnight, including in the controlled patients. The findings also suggest lower increases in glucocorticoid precursors and classical androgens with Osilodrostat compared to Metyrapone. Differences in pharmacokinetic profiles could likely explain these findings, including greater plasma drug fluctuations with Metyrapone despite regular dosing.

Abstract citation ID: lvag096.195

RC9.4 - ECE_1118 - Clinical and pharmacological determinants of serum dexamethasone concentrations during the dexamethasone suppression test

Irene Tizianel[1,2], Elena Pagin[1,2], Pierluigi Mazzeo[1,2], Giulia Bovo[1,2], Giacomo Voltan[1,2], Mattia Barbot[1,2] and Filippo Ceccato[1,2]
[1]Endocrine Disease Unit, University Hospital of Padova, Padova, Italy; [2]Department of Medicine DIMED, University of Padova, Padova, Italy

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: The dexamethasone suppression test (DST) is recommended by the European Society of Endocrinology for the evaluation of endogenous hypercortisolism, including Cushing's syndrome (CS) and autonomous cortisol secretion (MACS) in adrenal incidentalomas. A 1 mg DST is considered normal when post-test serum cortisol is suppressed below 50 nmol/L (<1.8 μg/dL). Simultaneous measurement of serum dexamethasone allows for accurate identification of suboptimal drug exposure (<4.5 nmol/L), which may compromise test reliability. Interindividual variability in dexamethasone pharmacokinetics, influenced by patient clinical conditions and concomitant medications, represents a major challenge in clinical interpretation.

Objective: To investigate the clinical and pharmacological determinants of serum dexamethasone concentrations during the DST.

Materials and Methods: We conducted a retrospective observational study including 546 patients who underwent 1 mg DST overnight, with concurrent serum dexamethasone measurement. Serum dexamethasone concentrations were quantified using validated LC-MS/MS assays. The study population included 54 patients with CS (25 active CS and 29 with previously treated disease), 287 patients with adrenal incidentaloma (160 non-functioning adrenal incidentalomas and 127 MACS) and 205 suspected CS. Patients with known conditions potentially affecting dexamethasone metabolism, including hepatic insufficiency, were excluded. Data were analyzed to assess the relationships between serum dexamethasone levels and clinical and pharmacological variables.

Results: Patients aged ≥65 years exhibited higher dexamethasone concentrations compared with younger individuals (13.6 vs 10.4 nmol/L, $P < .001$), as did patients with BMI ≥ 25 kg/m^2 (12.2 vs 9.6 nmol/L, $P = .004$). Dexamethasone concentrations were progressively higher with decreasing renal function, when patients were categorized into four estimated glomerular filtration rate (eGFR) classes ($P < .01$); on the contrary cortisol levels after 1 mg DST overnight were progressively lower with eGFR reduction. In age-stratified linear regression analyses (cut-off 65 years), serum dexamethasone levels showed a significant positive association with creatinine concentrations ($P = .002$). Concomitant use of proton pump inhibitors, statins or calcium channel blockers was independently associated with increased serum dexamethasone levels (all drugs $P < .001$). Suboptimal dexamethasone exposure (<4.5 nmol/L) was observed in 17 patients (3.1%), of whom 11 (64.7%) showed lack of cortisol suppression following DST.

Conclusions: Serum dexamethasone levels are significantly affected by patient clinical characteristics and concomitant medications. Recognition of these factors is crucial for optimizing the reliability of hypercortisolism screening, minimizing diagnostic errors and supporting personalized evaluation. Clinicians should consider age, BMI, renal function and potential drug interactions when interpreting DST results to ensure accurate diagnosis and avoid misclassification.

Abstract citation ID: lvag096.196

RC9.5 - ECE_2071 - Replacing early morning cortisol reduces fatigue: post-hoc analysis of AddiQol in CHAMPAIN, a double-blind study comparing Chronocort and Plenadren

Irina Chifu[1], Alessandro Prete[2], Verena Theiler-Schwetz[3], Wiebke Arlt[4], Birgit Harbeck[5], Catherine Napier[6], John Newell-Price[7], Aled Rees[8], Nicole Reisch[9], Günter Stalla[10], Helen Coope[11], John Porter[11], Jo Quirke[11], Peter Treasure[11], Irmina Wlodarczyk[11], Hanna Bendfeldt[11] and Richard Ross[7]

[1]Würzburg University Hospital Straubmühlweg Heliport, Würzburg, Germany; [2]University of Birmingham, Birmingham, United Kingdom; [3]University of Graz, Graz, Austria; [4]Medical Research Council Laboratory of Medical Sciences, London, United Kingdom; [5]Amedes MVZ Hamburg, Hamburg, Germany; [6]Newcastle University, Newcastle upon Tyne, United Kingdom; [7]University of Sheffield, Sheffield, United Kingdom; [8]University of Cardiff, Cardiff, United Kingdom; [9]Ludwig-Maximilians-Universitat Munchen, Munchen, Germany; [10]Medicover, Munchen, Germany; [11]Immedica UK Ltd, London, United Kingdom

Background: Cortisol has a circadian rhythm with an early morning rise; loss of this rhythm is associated with poor health. In the CHAMPAIN study we demonstrated that twice daily Chronocort (Efmody, Immedica Netherlands B.V.), which replaces the early morning rise in cortisol, improved QoL compared to Plenadren (Takeda Ltd. UK), which only replaces daytime cortisol levels. This post-hoc analysis looked at the subdomains of the disease specific questionnaire, AddiQoL (Addison's disease Quality of Life questionnaire) and SF-36 V2, compared to other questionnaires.

Methods: CHAMPAIN was a double-blind cross-over study in 58 patients with primary adrenal insufficiency (AI) comparing Chronocort, 15 mg at night and 10 mg in the morning, with once daily Plenadren 25 mg. The primary endpoint was waking cortisol and secondary endpoints were measures of fatigue and QoL. Patients signed informed consent and the trial was registered (NCT NCT05222152; Eudract 2021-000144-21). AddiQoL has four subdomains: fatigue, emotions, symptoms, and miscellaneous and was completed every 4 weeks within 2 hours of waking. A sensitivity analysis was done on period 1 of the cross-over which was randomised parallel-arm and blinded. P was one-sided, significance at $P < .025$.

Results: In the cross-over analysis treatment effect was in favour of Chronocort for AddiQoL: Total Score (+3.214, $P = .024$), and subdomain Fatigue (+1.234, $P = .014$), but not different for Emotions (+0.861, $P = .032$), Symptoms (+0.500, $P = .157$) and miscellaneous (+0.676, $P = .033$). In the sensitivity analysis Total Score was positive (+6.3, $P = .0175$). The SF-36 V2 physical component score which includes fatigue was in favour of Chronocort (+3.2, $P = .01$) but the Mental Component Score was not different (−0.6 $P = .7$). In the sensitivity analysis the following SF-36 subdomains significantly favoured Chronocort: Physical Functioning (+5.42 $P = .004$), Role Limitations due to Physical Health (+7.59 $P = .001$), Bodily Pain (+4.99 $P = .022$), General Health Perceptions (+5.70 $P = .004$), and Vitality (+7.16 $P = .002$). The PROMIS 7b, a specific fatigue questionnaire, was in favour of Chronocort (−2.6, $P =$

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

.024). The most common adverse event was fatigue, reported by twice as many during Plenadren treatment (44.6%) compared to Chronocort (20.7%).

Conclusions: Replacing the early morning cortisol improved health related QoL in AI based on the disease specific questionnaire AddiQoL. This was primarily due to reduced fatigue which was also seen in the SF-36 physical component score and fatigue specific questionnaire PROMIS 7b and there were fewer reports of fatigue on Chronocort compared to Plenadren.

Abstract citation ID: lvag096.197

RC9.6 - ECE_3139 - Real-world effectiveness of modified-release hydrocortisone (Efmody®) in adults with classic 21-hydroxylase deficiency congenital adrenal hyperplasia: a 12-month longitudinal cohort study

Chiara Sola[1], Maria Chiara Di Carlo[1], Beatrice Bergoglio[1], Giovanna Motta[2], Mirko Parasiliti Caprino[3] and Roberta Giordano[2,4]

[1]University of Turin, Turin, Italy; [2]Division of Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [3]Volvera, Italy; [4]Department of Biological and Clinical Sciences, University of Turin, Turin, Italy

Background: Congenital adrenal hyperplasia (CAH) comprises a group of autosomal recessive disorders, with ~95% of cases caused by mutations in CYP21A2, the gene encoding adrenal steroid 21-hydroxylase (P450c21). Enzymatic deficiency leads to impaired cortisol biosynthesis, variable aldosterone deficiency and chronic ACTH-driven accumulation of cortisol precursors (17-hydroxyprogesterone [17-OHP] and progesterone), which are shunted toward androgen synthesis. Standard-of-care glucocorticoid (GC) formulations fall short of replicating the circadian rhythm of cortisol and controlling efficient ACTH-driven adrenal androgen production; moreover, supraphysiologic GC exposure is associated with metabolic and cardiovascular comorbidities and fertility impairment. Multiple alternative treatment approaches are being developed with the aim of tailoring therapy for improved patient outcomes. Efmody®, a modified-release hydrocortisone (MR-HC), is designed to better mimic the physiological circadian rhythm of cortisol, optimizing androgen control and minimizing metabolic burden.

Objective: To evaluate the real-world effectiveness of MR-HC in adults with classic CAH on disease control, metabolic and anthropometric outcomes and fertility parameters.

Methods: In this single-center observational cohort study, 15 adults with classic CAH were assessed at baseline (on conventional immediate-release hydrocortisone, HC) and at 3 (T1), 6 (T2), and 12 (T3) months after switching to an equivalent dose of MR-HC for hormonal, metabolic, anthropometric and fertility outcomes. Longitudinal changes in parameters were analyzed using linear mixed-effects models, including a random intercept for patient and fixed effects for time, total glucocorticoid dose, age, and sex; sex × time interactions were evaluated when clinically relevant.

Results: MR-HC was associated with a sustained reduction in 17-OHP at all follow-up time points (T1: $P = .033$; T2: $P = .059$; T3: $P = .029$). Androstenedione levels also declined (T1: $P = .023$; T3: $P = .070$), with sex-interaction analyses showing a significant reduction in females at T1 ($P = .007$) and T3 ($P = .031$). No significant changes were observed in testosterone levels. Anthropometric and most metabolic parameters remained stable; fasting glucose increased modestly at 12 months without a concomitant rise in HbA1c, and HDL cholesterol showed a nonsignificant upward trend (~+6 mg/dL). Regarding fertility, total sperm count improved in half of male patients, while no pregnancies were reported during follow-up. No adrenal crises or drug-related adverse events were observed.

Conclusions: These results support MR-HC as a physiologically aligned glucocorticoid replacement therapy in adults with CAH. Treatment with MR-HC was associated with improved biochemical androgen control, independent of dose, age or sex, without significant changes in metabolic or anthropometric parameters.

Abstract citation ID: lvag096.198

RC10.1 - ECE_2107 - How much is enough? Surgical extent of initial parathyroidectomy and long-term outcomes in MEN1-related primary hyperparathyroidism

Kosmas Daskalakis[1,2], Kostantinos Ntalaperas[1,2], Nektaria Papadopoulou[3], Marina Tsoli[3], Anna Angelousi[4], Evanthia Kassi[5] and Gregory Kaltsas[3]

[1]"Korgialenio-Benakio," Red Cross General Hospital, Athens 11526, Greece; [2]Second Department of Surgery, Athens, Greece; [3]Endocrine Oncology Unit, 1st Department of Propaedeutic Internal Medicine, Laiko Hospital, National and Kapodistrian University of Athens, Athens 11527, Greece; [4]First Department of Internal Medicine, Unit of Endocrinology, Laikon General Hospital, Athens 11527, Greece; [5]Department of Biological Chemistry, School of Medicine, National and Kapodistrian University of Athens,, Athens 11527, Greece

Context: Multiple Endocrine Neoplasia type 1 (MEN1)–associated primary hyperparathyroidism (PHPT) is typically multiglandular, which contributes to both persistent and recurrent disease following surgery. The optimal extent of initial parathyroidectomy in MEN1 remains debated.

Objective: To evaluate long-term outcomes of subtotal parathyroidectomy (SPTX) versus less-than-subtotal parathyroidectomy (LSPTX) in MEN1-related PHPT, specifically regarding persistence, recurrence, permanent hypoparathyroidism, and need for reoperation.

Methods: A retrospective cohort study was conducted including 65 MEN1 patients who underwent initial parathyroidectomy and were followed at a single tertiary referral center. Patients were stratified according to surgical extent (SPTX vs LSPTX), and rates of persistent and recurrent HPT and reoperation were analyzed. Kaplan-Meier survival curves were constructed for recurrence-free survival, and multivariable Cox regression was applied to identify independent predictors of adverse outcomes.

Results: The median follow-up was 133.1 months (range 2.4-442.2 months). Disease recurrence was observed in 72.2% of LSPTX ($n = 18$) versus 35.6% of SPTX ($n = 42$) and total parathyroidectomy with autotransplantation (TPTX-AT; $n = 3$; Chi-square test $P = .008$). Hypoparathyroidism 6 months postoperatively was recorded in 50% after SPTX and TPTX-AT (12/24) and 25% after LSPTX (2/8; Chi-square test $P = .217$). Time to reoperation was significantly shorter in the LSPTX group (median 65.9 months vs 192.7 months, log-rank $P < .001$). Cox-regression multivariable analysis identified LSPTX as

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

an independent predictor for shorter time to recurrence (HR = 6.1, 95% CI 1.64-22.86, $P = .007$).

Conclusions: In MEN1-relatedPHPT, limited parathyroidectomy (LSPTX) is associated with significantly higher recurrence rates, earlier reoperation, and independently predicts shorter recurrence-free survival. Although the risk of permanent hypoparathyroidism appeared lower after LSPTX, this difference did not reach statistical significance. These findings support subtotal parathyroidectomy as the preferred initial surgical strategy in MEN1, balancing long-term disease control with preservation of parathyroid function.

Keywords **Keyword** primary hyperparathyroidism, multiple endocrine neoplasia type 1, parathyroidectomy, surgical hypoparathyroidism, hyperparathyroidism recurrence

Abstract citation ID: lvag096.199

RC10.2 - ECE_2540 - Phenotypic spectrum of familial hypocalciuric hypercalcemia

Amina Attia[1], Nicolas Obtel[1], Albain Chansavang[2], Anne-Laure Lakhel[1], Franceska Kovaci[3], Frederic Vaysse[4], Frederique Savagner[5], Thomas Edouard[6], Agnès Linglart[7], Eric Pasmant[8], Fadil Hannan[9], Rajesh Thakker[10,11,12], Catherine Chaussain[1] and Jean-Philippe Bertocchio[13]

[1]UFR Odontologie, Inserm UMR1333 Santé Orale, Médecine buccodentaire, Hôpitaux Universitaires Bretonneau, APHP (CRMR calcium-phosphate, filière OSCAR et ERN Bond), Université Paris Cité, Paris, France; [2]Département de Médecine Génomique des Tumeurs et Cancers, Université Paris Cité, APHP, Paris, France; [3]UFR Odontologie, Inserm UMR1333 Santé Orale, Université Paris Cité, Paris, France; [4]Service d'Odontologie, CHU de Toulouse, CRMR ORares, Toulouse, France; [5]Inserm UMR1297, Université Paul Sabatier, Toulouse, France; [6]Service de Pédiatrie - Endocrinologie, maladies osseuses, génétique, CRMR calcium-phosphate réseau OSCAR, ERN, RESTORE, Inserm U1301, Toulouse, France; [7]Service d'endocrinologie et diabète de l'enfant, Inserm U1185 Physiologie et physiopathologie endocrinienne, Université Paris-Saclay, Hôpital Bicêtre AP-HP, Kremlin-Bicêtre, France; [8]Endocrine, Bone Diseases and Genetics Unit, Reference Centre for Rare Diseases of Calcium and Phosphate Metabolism, OSCAR Network, ERN BOND, Children's Hospital, Toulouse University Hospital, RESTORE, INSERM U1301, Toulouse, France; [9]Nuffield Department of Women's & Reproductive Health, University of Oxford, Oxford, United Kingdom; [10]Academic Endocrine Unit, Radcliffe Department of Medicine, University of Oxford, Oxford, UK; [11]National Institute for Health Research Oxford Biomedical Research Centre, Oxford, UK; [12]Centre for Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine, Queen Mary University of London, London, Oxford, United Kingdom; [13]Pathologies thyroïdiennes et tumorales endocrines, CCMR calcium-phosphate (réseau OSCAR) Hôpital Pitié-Salpêtrière, APHP, Université Paris Cité, Inserm UMR1333 Santé Orale, Paris, France

Background: Familial Hypocalciuric Hypercalcemia (FHH) is a rare autosomal dominant genetic disorder characterized by PTH-dependent hypercalcemia. It is caused by inactivating mutations of *CASR, GNA11,* or *AP2S1* (FHH type 1, 2, or 3 respectively). FHH represents the main differential diagnosis for primary hyperparathyroidism (PHPT) and is traditionally distinguished from PHPT by lower urinary calcium excretion and by less skeletal and renal complications. A better understanding of the tissue-specific effects may improve its differential diagnosis from PHPT and enhance patients care.

Objective: To characterize clinical and biological phenotypes of patients with FHH in order to optimize follow-up, establish genotype-phenotype correlations and propose new diagnostic criteria.

Patients and Methods: A prospective cohort of patients with FHH and of their disease-free relatives was established.

Results: At the time of the submission, a cohort of 27 patients with confirmed or suspected FHH from 13 families has been established (mean age: 44.4 ± 22.0 years). Five, three, and two families were diagnosed with FHH types 1, 2, and 3, respectively, while whole-genome sequencing is ongoing for three families with negative initial genetic testing. Patients with FHH have higher serum calcium concentrations than their disease-free relatives (2.68 ± 0.26 mM vs 2.37 ± 0.11 mM, $P = .0008$), while PTH levels were similar (0.72 vs 0.62 times the upper limit of normal range, $P = .3282$). Fractional excretion of calcium, which is classically used to differentiate FHH from PHPT, exceeded 1% in 45% of the patients with FHH, while the pro-FHH score, designed to distinguish FHH from PHPT was in favor of FHH for every FHH patients. Bone mineral density, bone remodeling markers, and presence of nephrolithiasis did not differ significantly between patients with FHH and their disease-free relatives. Patients with FHH exhibited enamel defects consistent with hypomineralized Amelogenesis Imperfecta, which appeared consistent across the 3 genetic subtypes and were absent in disease-free relatives. Our group identified enamel defects in murine models with loss-of-function of *Gna11*, mimicking FHH type 2. Indeed, heterozygous *Gna11* loss-of-function mice show lower enamel volume and density, raising questions about the underlying mechanisms of these defects.

Discussion and Conclusions: We describe a dental phenotype associated with FHH that appears consistent across the 3 genetic subtypes. Our cohort will be extended to confirm these findings. Further studies using mouse models will be pursued to better understand the mechanisms of enamel defects in patients with FHH. Study of rheumatological consequences of FHH must be further described. Improved diagnostic criteria to differentiate FHH from PHPT are needed.

Abstract citation ID: lvag096.200

RC10.3 - ECE_2577 - Real-world data for effectiveness and safety of palopegteriparatide in patients with chronic hypoparathyroidism. The PaTH REAL study

Maria Yavropoulou[1], Symeon Tournis[2], Maria-Eleni Chondrogianni[1], Dimos Florakis[1], Alexandra Chrisoulidou[3], Foteini Adamidou[4], Zoe Efstathiadou[4], Irini Giagourta[5], Alexandra Giannou[6], Theodora Stratigou[7], Athina Markou[5], Vasiliki Vasileiou[6], Georgia Ntali[7], Chrysanthi Balodimou[3], Nikolaos Kalogeris[8], Maria Evangelia Koloutsou[1], Polyzois Makras[9], Andromahi Vryonidou[8] and Eva Kassi[1]

[1]Endocrinology Unit, First Department of Propaedeutic and Internal Medicine, Centre of Expertise for Rare Endocrine Diseases (C.E.R.E.D), European Reference Network on Rare Endocrine Conditions (Endo-ERN), National and Kapodistrian University of Athens, Athens, Greece; [2]Laboratory for Research of the Musculoskeletal System 'Th. Garofalidis', Medical School, KAT General Hospital, Kifissia, National

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and Kapodistrian University of Athens, Athens, Greece; [3]Department of Endocrinology, Theagenio Hospital, Thessaloniki, Greece; [4]Department of Endocrinology, Diabetes and Metabolism, "Ippokratio" General Hospital of Thessaloniki, Thessaloniki, Greece; [5]Endocrinology Department and Diabetes Center, General Hospital of Athens, G.Gennimatas, Athens, Greece; [6]Department of Endocrinology and Diabetological Center Alexandra General Hospital of Athens, Athens, Greece; [7]Department of Endocrinology, Diabetes and Metabolism, "D. Ikkos", European Reference Network on Rare Endocrine Conditions, Endo-ERN, Evangelismos Hospital, Athens, Greece; [8]Department of Endocrinology & Metabolism – Diabetes Center, Korgialenio-Benakio General Hospital, Hellenic Red Cross, Athens, Greece; [9]Department of Endocrinology and Diabetes, 251 Hellenic Air Force & VA General Hospital, Athens, Greece

Context: Chronic hypoparathyroidism (HypoPT) is a rare endocrine disorder characterized by hypocalcemia and hyperphosphatemia, requiring lifelong treatment with activated vitamin-D and oral calcium supplements. Palopegteriparatide, a novel long-acting prodrug of PTH (1-34), has demonstrated efficacy in randomized controlled trials, but real-world data on its long-term effectiveness and safety remain limited.

Objective: To evaluate the efficacy and safety of long-term palopegteriparatide therapy in a real-world cohort of patients with HypoPT.

Design and Setting: Multicenter prospective cohort study conducted in tertiary referral hospitals. The study is registered at ClinicalTrials.gov under the identifier NCT07299838.

Patients and Intervention: Ninety-two adults with HypoPT (79 females, 13 males), previously treated with recombinant human PTH (1-84) or conventional therapy, initiated palopegteriparatide according to the National Hellenic Guidelines for the management of HypoPT.

Results: Patients were treated for a median duration of 6.5 months (range 2-14), with significant improvements in biochemical control of calcium-phosphate metabolism. Albumin-adjusted calcium increased from 8.14 ± 0.73 to 8.99 ± 0.94 mg/dL, and magnesium from 1.79 ± 0.17 to 1.96 ± 0.17 mg/dL (both $P < .001$). Phosphate decreased from 4.74 ± 0.97 to 4.02 ± 0.63 mg/dL, Ca × P product from 38.27 ± 6.92 to 36.04 ± 6.55 mg^2/dL^2, and 24-hour urinary calcium from 245.7 ± 125.5 to 164.5 ± 88.3 mg/24 h (all $P < .001$). Daily pill burden was markedly reduced; 58% of patients achieved independence from calcium supplements and alfacalcidol after a mean of 61 days. Adverse events were mostly mild and transient.

Conclusions: In a real-world setting, palopegteriparatide effectively normalizes calcium–phosphate homeostasis, reduces hypercalciuria, and substantially decreases reliance on conventional therapy, with a favorable safety profile.

Abstract citation ID: lvag096.201

RC10.4 - ECE_2919 - Eneboparatide: mechanism of action underlying the sustained regulation of calcium in chronic hypoparathyroidism

Xavier Gaume[1], Ying Kong[2], Guillaume Ravel[3], Corentin Berardet[4], Soraya Allas[5] and Myriam Aouadi[1]
[1]Alexion, AstraZeneca Rare Disease, Discovery Biology, Écully, France; [2]Alexion, AstraZeneca Rare Disease, Global Medical Affairs, Boston, MA, United States; [3]Alexion, AstraZeneca Rare Disease, Clinical Pharmacology and Safety Sciences, Écully, France; [4]Process Development and Clinical Supply, Alexion, AstraZeneca Rare Disease, Écully, France; [5]Alexion, AstraZeneca Rare Disease, Clinical Development, Écully, France

Premise: Chronic hypoparathyroidism (cHypoPT) leads to hypocalcemia due to insufficient parathyroid hormone (PTH). cHypoPT is often treated with therapeutic doses of calcium and active vitamin D, which may cause hypercalciuria. Eneboparatide (also called long-acting PTH, or LA-PTH or AZP-3601) is a peptide in development for HypoPT. In animal models and patients with cHypoPT, eneboparatide treatment led to sustained regulation of urinary and serum calcium (sCa) despite its short circulating half-life. Here, we investigated the mechanism whereby eneboparatide provides prolonged calcium regulation *in vivo*.

Methods: PTH 1 and 2 receptor (PTH1R and PTH2R) activation was evaluated using a cell-based cyclic adenosine monophosphate (cAMP) assay. Receptor binding affinity was assessed by radioligand competition assay. Kinetics of PTH1R activation were investigated by measuring cAMP production for 24 h after ligand washout in cells expressing PTH1R. Tissue distribution was examined by quantitative whole-body autoradiography in rats. Structure-function studies evaluated the effect of amino acid substitutions, additions, and truncations on the kinetics of PTH1R activation.

Results: Eneboparatide activated PTH1R and PTH2R, establishing it as a broad-spectrum PTH receptor agonist. Eneboparatide had high affinity for PTH1R R0 conformation, leading to extended cAMP signaling up to 24 h, contrary to the transient effect of PTH (1-34). Compared with PTH (1-34), eneboparatide showed prolonged and enhanced receptor occupancy in PTH1R-expressing tissues, particularly in the kidney, with structure-function studies identifying molecular features underlying sustained PTH1R activation.

Conclusions: These data revealed the unique properties of eneboparatide needed for sustained activation of PTH1R, resulting in extended regulation of sCa via retention, particularly in the kidney, despite rapid circulatory clearance.

Abstract citation ID: lvag096.202

RC10.6 - ECE_2734 - Muscle mass and strength are independent predictors of bone health in Klinefelter syndrome, the Klin-health study

Lucia Bedatsova[1], Eliane Maalouf[2], Mohamed Faouzi[2], Gonzalez Rodriguez Elena[3,4] and Georgios Papadakis[4,5,6]
[1]Lutry, Switzerland; [2]Biostatistics Consultation Unit, Center for Primary Care and Public Health, Division of Biostatistics, University of Lausanne, Lausanne, Switzerland; [3]Center of Bone Diseases, Lausanne University Hospital, Lausanne, Switzerland; [4]Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland; [5]Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; [6]University of Lausanne, Lausanne, Switzerland

Background: Klinefelter syndrome (KFS) is frequently associated with low bone mineral density (BMD), but bone defects are not fully explained by the underlying hypogonadism.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Aim: To characterize bone health in a large prospective cohort of men with KFS and examine associations of BMD with potential predictors such as testosterone replacement therapy (TRT) status, hormonal profile and body composition indexes.

Methods: We performed a cross-sectional analysis on the baseline data of an ongoing randomized trial (NCT05586802). Participants underwent a complete phenotypic evaluation, including a fasting blood sample and Dual X-ray absorptiometry. Primary outcomes included BMD at lumbar spine (LS), femoral neck (FN), and total hip (TH), and trabecular bone score (TBS). Data on age at initiation and overall TRT duration were collected. Sex hormone levels, body composition indexes and muscle strength (hand grip), metabolic markers and calcium physiology parameters were investigated.

Results: One-hundred five men with a mean age and BMI of 36.5 ± 13.2 years and 26.3 ± 6.8 kg/m^2 were analyzed. BMD T-scores indicated osteoporosis in 11.8% and osteopenia in 78.4% of participants. Only 9 (8.6%) patients had experienced low-energy fractures. Fifty-three men were on TRT, initiated at mean age of 27.3 ± 10.2 years for a duration of 10.0 ± 9.4 years. TRT-treated patients had significantly higher BMD-TH (+0.079 g/cm^2, $P = .006$) and BMD-FN (+0.070 g/cm^2, $P = .012$) levels after adjustment for age and BMI than those without TRT, while no difference was observed for BMD-LS. Longer TRT duration was however associated with higher BMD-LS (+0.008 g/cm^2 for each additional year, $P = .017$). Plasma FSH was the only sex hormone with significant inverse associations with all bone outcomes, although this was no longer significant after adjustment for BMI. Age- and BMI-adjusted appendicular lean mass index (ALMI) was positively associated with all BMD sites (TH: +0.061 g/cm^2, $P = .000$; FN: +0.065, $P = .000$; LS: +0.049, $P = .002$) and TBS (+0.037, $P = .000$). Muscle strength showed similar associations. Fat mass percentage (FM%) correlated positively with BMD-TH ($P = .04$), but this association inversed after adjustment for age and BMI (−0.008 g/cm^2 for each additional unit of FM%, 95% CI [−014, −0.02], $P = .01$). Serum PTH levels exhibited significant negative associations (also after adjustment) with BMD at both femoral sites (TH: −0.003 g/cm^2, $P = .002$; FN: −0.003 g/cm^2, $P = .000$).

Conclusions: Lean mass and muscle strength were the most consistent predictors of bone outcomes, with an association extending beyond BMI. Active TRT and optimal calcium-phosphate metabolism as expressed by lower serum PTH confer advantages only at femoral sites.

Abstract citation ID: lvag096.203

RC11.1 - ECE_1833 - Additive effects of semaglutide and peptide YY3-36 dual agonism on HFpEF: focus on mitochondrial function in obese rats

Niklas Geiger[1,2], Palina Zytner[1,2], Michael Kohlhaas[2], Alexander Nickel[2], Takahiro Higuchi[3], Paula Arias-Loza[3], Kristina Lorenz[4], Jana Gerner[2], Annika Engelhardt[2], Thorsten Bischler[5], Panagiota Arampatzi[5], Frank Stein[6], Simon Kloock[1], Tom Lunkwitz[1], Martin Fassnacht[1], Christioph Maack[2], Vasco Sequeira[2] and Ulrich Dischinger[1]
[1]*Division of Endocrinology and Diabetes, Department of Internal Medicine, University Hospital Würzburg, Würzburg, Germany;* [2]*Comprehensive Heart Failure Center (CHFC), Department of Translational Research, University Hospital Würzburg, Würzburg, Germany;* [3]*Department of Nuclear Medicine, Department of Nuclear Medicine, University Hospital Wüürzburg, Würzburg, Germany;* [4]*Institute of Pharmacology and Toxicology, University Hospital Wüürzburg, Würzburg, Germany;* [5]*Core Unit Systems Medicine, University of Würzburg, Würzburg, Germany;* [6]*European Molecular Biology Laboratory, Heidelberg, Germany*

Intro: Glucagon-like peptide (GLP) -1 receptor agonists like semaglutide have already emerged as promising therapeutics for heart failure with preserved ejection fraction (HFpEF), but their exact mechanisms of action are still unknown. In this study with diet-induced obese HFpEF rats with chronic NO-synthase inhibition, we investigated the individual and combined effects of semaglutide and the neuropeptide (NPY)-2 receptor agonist peptide YY_{3-36} (PYY) on cardiomyocyte metabolism.

Methods: Following an eight-week feeding period with a high-fat/fructose-diet (HFD) and L-NAME, male obese Wistar rats were randomized into the following treatment groups for another 8 weeks: Semaglutide (Sema, $n = 7$), PYY ($n = 4$), semaglutide in combination with PYY (Sema+PYY, $n = 7$) and saline treated control (HFpEF, $n = 10$). Sarcomere shortening was analysed via IonOptics microscopy and mitochondrial respiration was evaluated with an Orboros Respirometer. In addition, RNA-Sequencing was performed.

Results: Cardiomyocytes of the HFpEF group showed diastolic dysfunction in echocardiography and increased diastolic intracellular Ca^{2+}, consistent with an HFpEF phenotype. Sema and PYY mono and especially Sema+PYY significantly improved diastolic sarcomere shortening ($P < .001$). Sema+PYY rescued the E/A ratio in echocardiography compared to the individual application of Sema and PYY ($P < .05$). Mitochondrial respiration and ROS-emission was significantly increased in the Sema and PYY mono group with additive effects in the combination group compared to HFpEF ($P < .001$). In line, RNA sequencing showed upregulated oxidative phosphorylation pathways in the individual and combined Sema+PYY treated group ($P < .001$).

Discussion: This study highlights the additive effects of semaglutide+PYY mitigating cardiac mitochondrial dysfunction, sarcomere shortening and E/A ratio in HFpEF rats. These results provide novel insights into molecular mechanisms following the upcoming twincretin approach.

Abstract citation ID: lvag096.204

RC11.2 - ECE_3023 - A lifestyle program to improve infertility in women with overweight or obesity tends to be particularly effective in polycystic ovary syndrome: an RCT subgroup analysis

Christophe Richer dit Laflèche[1], Melissa Filippone[1], Matea Belan[1], Farrah Jean-Denis[2], Marie-France Langlois[1,2], Hélène Lavoie[3], Marie-Hélène Pesant[1,2], Belina Carranza-Mamane[1,2] and Jean-Patrice Baillargeon[1,2]
[1]*Sherbrooke, Canada;* [2]*Centre de Recherche du Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, Canada;* [3]*Université de Montréal, Montréal, Canada*

Polycystic ovary syndrome (PCOS) is the first cause of anovulatory infertility and is closely related to obesity, which is also associated with infertility even in ovulatory women.**Aim:** Evaluate the effects of Fit-For-Fertility lifestyle intervention in women

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

with overweight/obesity (OWOB) and infertility according to PCOS status and other subgroups.

Design: Women with OWOB and infertility who could naturally conceive followed a lifestyle intervention alone for 6 months, then combined to fertility care if necessary, vs uninterrupted fertility care (control group). 128 participants were enrolled (81 PCOS, 46 non-PCOS), and 108 were followed up $\geq 6 \pm 1$ months (68 PCOS, 40 non-PCOS). Subgroup analyses of a PCOS-stratified randomized controlled trial testing the Fit-For-Fertility intervention were conducted in addition to exploratory analyses for age, parity, BMI, self-reported activity level, and smoking status subgroups. Analyses were according to intention-to-treat (ITT) and modified per-protocol (mPP; participants who completed $\geq 6 \pm 1$ months of follow-up) principles. Fertility outcomes were the occurrence of live birth, and clinical and natural pregnancy within 18-months.

Results: Mean ± SD age and BMI were 29.1 ± 4.8 years and 39.4 ± 7.8 kg/m^2 in women with PCOS and was 30.5 ± 4.9 years and 40.3 ± 7.2 kg/m^2 in women without. In ITT analyses, the intervention significantly improved natural pregnancy rates in women with PCOS (21.4% vs 5.1%, OR = 5.05, $P = .048$). In mPP analyses, the intervention significantly or marginally significantly improved live birth (54.5% vs 31.4%, OR = 2.62, $P = .057$), clinical pregnancy (57.6% vs 34.3%, OR = 2.60, $P = .056$), and natural pregnancy (27.3% vs 5.7%, OR = 6.19, $P = .027$) rates in the PCOS subgroup, which tended to respond better than the non-PCOS subgroup. Indeed, no significant intervention effects were detected in the non-PCOS subgroup (all $P > .10$), but no group*PCOS status interventions were significant (all $P > .20$). Moreover, in mPP analyses, the intervention was significantly more effective to improve live birth rates in participants <30 years old (p for interaction = 0.012; OR = 5.54, $P = .007$) and those who smoked (p for interaction = 0.04; OR = 10.5, $P = .018$), but not according to parity (P for interaction = 0.19), class III obesity (P for interaction = 0.80; BMI ≥ 40 kg/m^2 cutoff), or activity level (P for interaction = 0.14; not active vs active or moderately active).

Conclusions: In women with OWOB and infertility, a lifestyle intervention improved natural and clinical pregnancy rates and tended to improve live birth rates in women with PCOS who persevered at least 6 months. Furthermore, the intervention was significantly more effective in improving fertility outcomes in women who completed ≥6 months and were aged <30 years or smoked.

Abstract citation ID: lvag096.205

RC11.3 - ECE_1896 - Higher maternal third trimester insulin resistance is linked to central fat deposition i 7-year-old girls. An Odense child cohort study

Matias Serup[1], Camilla Viola Palm[2], Anja Fenger Dreyer[3], Anders Grøntved[4], Jan Jørgensen[2], Henrik Christesen[5], Tina Kold Jensen[6], Dorte Glintborg[3] and Marianne Andersen[3]
[1]*University of Southern Denmark, Odense, Denmark;* [2]*Gynecology and Obstetrics, Odense University Hospital, Odense C, Denmark;* [3]*Endocrinology, Odense University Hospital, Odense C, Denmark;* [4]*Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark;* [5]*H.C. Andersen Children's Hospital, Odense University Hospital, Odense C, Denmark;* [6]*Clinical Pharmacology, Pharmacy and Environmental Medicine, University of Southern Denmark, Odense, Denmark*

Introduction: Maternal Insulin resistance is evident in third trimester and may have intergenerational effects on child fat deposition. More central fat in children has been associated with increased cardiovascular risk. Furthermore, there may be sexual dimorphism regarding susceptibility to pre-gestational metabolic environment.

Objectives: To examine associations between maternal third trimester insulin resistance, glucose status and child body composition, including gynoid and android fat deposition, in 7-year-old girls and boys.

Methods: 903 mother-child pairs (girls, $n = 449$) were included from the Odense Child Cohort. third trimester insulin resistance, homeostatic model assessment-insulin resistance (HOMA-IR), fasting plasma glucose (FPG), insulin, and HbA1c and first trimester HbA1c were measured. Child Dual X-ray Absorptiometry (DXA)-assessed body composition (total, android and gynoid fat mass) were estimated at 7 years. Participants and health professionals were blinded for maternal FPG, insulin and HbA1c results.

Results: In girls, a doubling in third trimester HOMA-IR was associated with a 7.1% ($P = .02$), 1.1% ($P = .008$) and 4% ($P = .008$) increase in android, gynoid and total fat mass percentages, respectively. One mmol/L higher maternal FPG was associated with 6.1% ($P = .02$) higher fat mass percentage in girls. Associations between third trimester HOMA-IR, FPG, insulin, HbA1c and child fat mass percentage were positive in girls (All $P \leq .02$) and boys ($P = .14$, .07, .19 and .15, respectively), but only significant in girls.

Conclusions: Insulin resistance in third trimester was linked to more central fat in 7-year-old girls, suggesting higher susceptibility to insulin resistance in girls compared to boys.

Abstract citation ID: lvag096.206

RC11.4 - ECE_3635 - Efficacy and clinical Impact of nitisinone in alkaptonuria: a follow-up study from the adult metabolic disorders unit at Virgen del Rocio university hospital

Luis Baena Ariza[1], Elena Dios[1], Bothayna Oulad Ahmed[2], Silvia Torres Degayon[1], Rosa Benitez Avila[1], Alfonso Soto[1] and Eva Venegas Moreno[3]
[1]*Clinical Management Unit of Endocrinology and Nutrition, Virgen del Rocio University Hospital, Sevilla, Spain;* [2]*Torrecardenas University Hospital, Almeria, Spain;* [3]*Endocrinologia y Nutrición, Instituto de biomedicina (IBIS), Campus Del Hospital Universitario Virgen del Rocio, Sevilla, Spain*

Study objective. Cross-sectional descriptive study on the characteristics of a cohort of patients with alkaptonuria under active follow-up at the HUVR, and the effects of nitisinone treatment on homogentisic acid and tyrosine levels.

Material and methods. Demographic (age, sex) and anthropometric (weight, body mass index [BMI]) data were collected. Specific alkaptonuria involvement (ochronosis, osteoarticular involvement, genitourinary lithiasis, valvular disease) and other comorbidities (hepatic, renal, muscular, metabolic) were recorded. Tyrosine and homogentisic acid levels were measured before, as well as 6 months and 1 year after treatment initiation.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Current treatments (diet, nutritional supplements, nitisinone dosage) were also documented.

Results. Data were collected from 8 patients with alkaptonuria from 6 different families: 3 females, mean age 57 ± 13 years. BMI was 27 ± 3.3 kg/m^2: 3 normal weight, 4 overweight, and 1 grade I obesity.

Ochronosis was present in all patients, affecting the auricular pavilion in all and the conjunctiva in 7/8.

Osteoarticular involvement was the most frequent: 7/8 had axial involvement (osteoarthritis and disc disease), 3/8 had peripheral osteoarthritis, 5/8 had osteoporosis, and the remaining 3 had osteopenia. Five patients had genitourinary lithiasis (only 1 prostatic). Cardiac involvement included two valvulopathies and one left ventricular hypertrophy. Auditory involvement was present in 3 patients: 2 with hearing loss and 1 with tinnitus. Renal involvement was found in 2 related patients.

Nitisinone was used in all patients at a dose of 2 mg/day (except one patient at 1 mg/day), reducing 24-hour urinary homogentisic acid by 82.2% at one year. The mean annual increase in tyrosine was 829%, consistent with the drug's mechanism of action, necessitating a low-tyrosine diet and the use of tyrosine-free nutritional supplements. Only 2 patients experienced ocular discomfort related to tyrosine levels.

Conclusions. In our cohort, patients with alkaptonuria presented significant and limiting osteoarticular involvement in daily life, as well as a history of genitourinary lithiasis.

Nitisinone treatment markedly reduced homogentisic acid levels and consequently increased tyrosine levels, requiring a strict low-tyrosine diet, tyrosine-free supplements, and close monitoring. Disease awareness is crucial for reducing morbidity and enabling early initiation of specific treatment to mitigate pathological alkapton deposition.

Abstract citation ID: lvag096.207

RC11.5 - ECE_1788 - An atypical PKC activator promotes intestinal glucose excretion and glycemic control in diabetes mellitus

Cheol Ryong Ku[1], Yoon-A Hwang[1] and Jae Won Hong[2]
[1]*Division of Endocrinology, Department of Internal Medicine, Institute of Endocrine Research, Yonsei University College of Medicine, Seoul, South Korea;* [2]*CHA Ilsan Medical Center, Division of Endocrinology, Department of Internal Medicine, CHA University, Goyang, South Korea*

Background: Intestinal glucose excretion, defined as the uptake of circulating glucose into intestinal epithelial cells followed by luminal secretion, has emerged as an important mechanism contributing to improved glycaemic control after bariatric surgery. Despite its metabolic relevance, the molecular pathways governing this process remain incompletely understood, and pharmacological approaches capable of reproducing this effect have not yet been established.

Methods: To identify molecular pathways associated with intestinal glucose excretion, transcriptomic signatures derived from multiple experimental models exhibiting differential intestinal glucose handling were analyzed using a Connectivity Map–based drug discovery platform. Candidate pathways were prioritized based on concordant transcriptional profiles and subsequently evaluated in intestinal epithelial cell models and mouse models of diabetes. Intestinal glucose uptake and luminal excretion were quantified using tracer-based assays, while systemic metabolic effects were assessed by fasting blood glucose measurements and glucose tolerance testing. Mechanistic studies focused on glucose transporter regulation and downstream signaling pathways.

Results: Transcriptome-driven screening consistently ranked protein kinase C signaling among the top mechanisms associated with glucose-excretory intestinal phenotypes. Pharmacological activation of atypical protein kinase C using prostratin, a non–tumour-promoting phorbol ester, significantly increased intracellular glucose uptake in intestinal epithelial cells by 1.7-fold compared with controls ($P = .009$). In diabetic mice, prostratin-induced activation of intestinal atypical protein kinase C increased luminal glucose excretion by 34%, accompanied by a 23% reduction in fasting blood glucose levels ($P = .031$) and a 27% decrease in glucose tolerance test area under the curve ($P = .004$). Mechanistic analyses demonstrated that atypical protein kinase C activation regulates glucose transporter 1 trafficking, promoting basolateral glucose uptake and coordinated apical glucose secretion in intestinal epithelial cells. These metabolic effects occurred without inducing intestinal epithelial proliferation, body weight loss, or hypoglycaemia, and were independent of changes in insulin secretion.

Conclusions: These findings demonstrate that atypical protein kinase C is a key molecular regulator of intestinal glucose excretion and systemic glucose homeostasis. Pharmacological activation of atypical protein kinase C induces a glucose-excretory intestinal phenotype and improves glycaemic control in diabetic mouse models, suggesting a potential therapeutic strategy to pharmacologically mimic the metabolic benefits of bariatric surgery.

Abstract citation ID: lvag096.208

RC11.6 - ECE_1419 - Lipidomic profiling identifies phosphatidylethanolamines as novel circulating markers of Fabry nephropathy

Dimitrios Chantzichristos[1,2], Mikael Oscarson[3], Andreas Kindmark[4], Malin Levin[1], Per-Olof Bergh[5], Jan Borén[1], Elias Björnson[1] and Maria Blomqvist[1]
[1]*Department of Internal Medicine and Clinical Nutrition, University of Gothenburg, Gothenburg, Sweden;* [2]*Department of Endocrinology, Diabetes and Metabolism, Sahlgrenska University Hospital, Gothenburg, Sweden;* [3]*Karolinska University Hospital, Stockholm, Sweden;* [4]*University of Uppsala, Uppsala, Sweden;* [5]*Chalmers University of Technology, Göteborg, Sweden*

Background: Fabry disease is a rare X-linked lysosomal storage disorder caused by pathogenic variants in the *GLA* gene, resulting in α-galactosidase A deficiency. It is a multisystem disease with substantial interindividual heterogeneity, particularly regarding renal involvement. Although plasma globotriaosylsphingosine (lyso-Gb3) is an established diagnostic biomarker, robust circulating markers reflecting the severity and progression of Fabry nephropathy are still lacking.

Methods: In a nationwide, prospective, cross-sectional, controlled study (ClinicalTrials.gov: NCT05046379), we included 54 adults with well-characterized Fabry disease and 54 control

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

subjects matched for age, sex, and estimated glomerular filtration rate (eGFR). Fasting morning blood samples were collected under standardized pre-analytical conditions. Targeted lipidomics quantified 179 lipid species across multiple lipid classes using four complementary mass spectrometry platforms. Between-group differences were assessed using multivariable logistic regression adjusted for age, sex, systolic blood pressure, and apolipoprotein B, with correction for multiple testing. Within the Fabry cohort, associations between lipid species and renal function were examined using multivariable linear regression. A multianalyte prediction model was developed using gradient boosting with 5-fold cross-validation.

Results: Compared with controls, Fabry disease was characterized by widespread lipidomic remodeling, including reduced concentrations of multiple sphingomyelin isoforms, lower levels of sphingosine-1-phosphate and sphinganine-1-phosphate, altered ceramide profiles, and increased ceramide ratios. A combined lipid model incorporating significantly differentiated lipid species and ceramide ratios achieved excellent discriminative performance (cross-validated ROC–AUC ≈ 0.994 in males and ≈0.997 in females). Importantly, analyses focusing on renal involvement identified phosphatidylethanolamines (PEs) as the lipid class most strongly associated with renal function in Fabry disease. Specifically, PE 38:6, PE 36:2, and the total sum of measured PEs were inversely associated with eGFR (adjusted $P = .016$, .031, and .031, respectively), whereas no such associations were observed in controls.

Conclusions: Our analyses reveal that Fabry disease is associated with previously unrecognized systemic lipidomic alterations extending beyond lyso-Gb3. Notably, specific circulating phosphatidylethanolamine signatures were independently associated with renal dysfunction in Fabry disease, consistent with lipidomic patterns reported in nephropathy across other diseases. These findings nominate phosphatidylethanolamines as novel candidate prognostic biomarkers of Fabry nephropathy and warrant validation in independent, preferably longitudinal, cohorts.

Abstract citation ID: lvag096.209

RC12.2 - LBA_ECE_1219 - Limited agreement between FibroScan and MR-based assessment of hepatic steatosis and fibrosis in acromegaly: a proof-of-concept study

Meliha Melin Uygur[1], Ayse Nur Gul[1], Damla Tufekci[1], Gulen Burakgazi[2] and Caglayan Keklikkiran[3]

[1]Department of Endocrinology and Metabolism, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye; [2]Department of Endocrinology, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye; [3]Department of Gastroenterology, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye, Rize, Türkiye

Background: Acromegaly is characterized by chronic excess of growth hormone (GH) and insulin-like growth factor-1 (IGF-1), resulting in insulin resistance and adverse cardiometabolic risk. Paradoxically, hepatic steatosis appears attenuated in acromegaly, likely due to GH-driven lipolysis and altered hepatic lipid handling. While FibroScan is widely used for noninvasive assessment of hepatic steatosis and fibrosis, its validity in acromegaly, an endocrine condition with distinct metabolic physiology, has not been systematically evaluated.

Objective: To conduct the first comparative evaluation of FibroScan and magnetic resonance (MR)–based liver assessment in patients with acromegaly and to examine the clinical utility of FibroScan in this setting.

Methods: In this cross-sectional proof-of-concept study, patients with acromegaly undergoing FibroScan and MR-based liver evaluation were included. FibroScan parameters comprised controlled attenuation parameter (CAP) for steatosis and liver stiffness measurement (LSM) for fibrosis. MR-based evaluation included quantitative liver fat assessment and MR elastography (MRE). Clinical and biochemical data, including body mass index (BMI), GH, and IGF-1, were collected. Associations between imaging modalities and clinical variables were assessed using Spearman correlation, and linear regression analyses were performed to explore predictors of MRE.

Results: A total of 8 patients were included depending on data availability (mean BMI 30.7 ± 4.3 kg/m^2). CAP values were within ranges suggestive of steatosis (248 ± 39 dB/m), whereas MR-based fat quantification consistently demonstrated low hepatic fat content ($4.25\% \pm 3.48\%$). Liver stiffness values were low by both FibroScan (3.77 ± 0.93 kPa) and MRE (2.38 ± 0.33 kPa), indicating absence of significant fibrosis.

No significant correlation was observed between CAP and MR-derived hepatic fat ($r = 0.203$, $P = .700$), indicating poor agreement for steatosis assessment. Similarly, FibroScan-derived liver stiffness showed weak and non-significant correlation with MRE ($r = 0.247$, $P = .637$), and regression analysis confirmed that FibroScan parameters were not significant predictors of MRE.

In contrast, CAP demonstrated a strong and statistically significant correlation with BMI ($r = 0.943$, $P = .005$), suggesting that CAP values may be driven by body composition rather than hepatic fat content in acromegaly.

Conclusions: In this first proof-of-concept study directly comparing FibroScan with MR-based liver assessment in acromegaly, FibroScan parameters showed limited agreement with MR findings. Notably, CAP appears to reflect BMI rather than hepatic steatosis, highlighting a potential limitation of FibroScan in this endocrine context. These findings provide novel insight into liver assessment in acromegaly and underscore the need for disease-specific validation of noninvasive diagnostic tools.

Figure 1

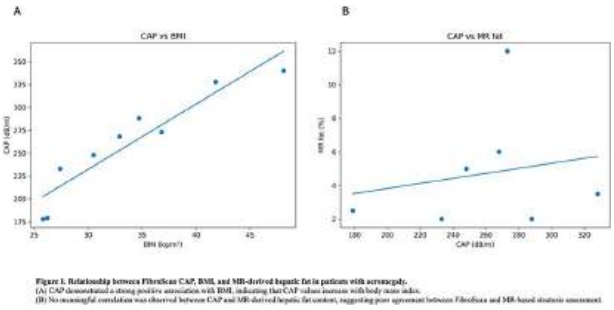


Figure 1. Relationship between FibroScan CAP, BMI, and MR-derived hepatic fat in patients with acromegaly.
(A) CAP demonstrated a strong positive association with BMI, indicating that CAP values increase with body mass index.
(B) No meaningful correlation was observed between CAP and MR-derived hepatic fat content, suggesting poor agreement between FibroScan and MR-based steatosis assessment.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.210

RC12.3 - LBA_ECE_1400 - Profiling of CYP17A1 mutations defines the molecular basis of partial enzyme deficiencies

Kaige Li, Jibira Yakubu and Amit Pandey
University of Bern, Bern, Switzerland

Context: 17α-hydroxylase/17,20-lyase deficiency (17-OHD) is a rare form of congenital adrenal hyperplasia characterized by hypertension, hypokalemia, and sexual infantilism. Its spectrum ranges from complete deficiency to partial forms with spontaneous puberty and fertility, yet the molecular basis of this heterogeneity remains unclear.
Objective: To elucidate the pathophysiology of 17-OHD by integrating phenotyping with functional and structural characterization of seven CYP17A1 variants: T131P, L209P, G303D, L361P, I296T, R340H, and R449H.

Methods: Clinical and hormonal data were obtained from seven probands, including one with the novel T131P mutation. Variants were generated by site-directed mutagenesis in pcDNA3.1 vectors and expressed in HEK-293T cells. Enzymatic activities of 17α-hydroxylase and 17,20-lyase were measured using 14C-progesterone and 3H-17OH-pregnenolone substrates and normalized to protein expression by Western blot. In silico structural modeling localized mutations to catalytic or regulatory domains.

Results: Western blot showed mutant proteins were expressed at levels comparable to wild-type, indicating preserved stability. L209P and G303D showed near-complete loss of hydroxylase activity (<9% of WT), consistent with severe phenotypes. The T131P variant retained ~7% activity, sufficient to permit spontaneous menarche. R449H retained lyase activity, consistent with a history of fertility. Structural modeling linked activity loss to disruptions in the F-helix (L209P), I-helix (G303D), or redox partner-binding surfaces (R449H), rather than gross protein misfolding.

Conclusions: These variants cause disease through specific catalytic or regulatory defects rather than protein instability. Residual activity showed a non-linear relationship with clinical severity, with <10% supporting secondary sexual development. Structural analysis may help predict clinical outcomes and fertility potential in 17-OHD.

Funding: This research was supported by Cancer Research Switzerland grant number KFS-5557-02-2022 to A.V.P. J.Y. is partially funded by a Swiss Government Excellence Scholarship (ESKAS) grant number 2022.0470

Abstract citation ID: lvag096.211

RC12.4 - LBA_ECE_1236 - Progress in the identification of the causal genetic alteration in carney complex patients with the 2026 tools

Patricia Vaduva[1], Albain Chansavang[2], Anne Anne Jouinot[1], Gerald Raverot[3], Marie-Christine Vantyghem[4], Espiard Stephanie[4], Anna Vaczlavik[5], Rachel Desailloud[6], Nicolas Chevalier[7] and Jérôme Bertherat[1,5]
[1]*Cochin, Genomics and Signaling of Endocrine Tumours, Paris, France;* [2]*Cochin, Genomic and Epigenetics of Rare Tumors Team, Paris, France;* [3]*Endocrinology, Hospices Civils de Lyon, Lyon, France;* [4]*Endocrinology and Metabolism, Lille University Hospital, Lille, France;* [5]*Hôpital Cochin, Paris, France;* [6]*Endocrinology, Amiens University Hospital, Amiens, France;* [7]*Endocrinology, Nice University Hospital, Nice, France*

Introduction: Carney Complex (CNC) is a rare genetic multiple neoplasia syndrome. While *PRKAR1A* pathogenic variants are the primary cause, *PRKACA* duplications have emerged as a causing genetic alteration. With the use in routine practice of next generation sequencing and whole genome sequencing the frequency of identification of genetic alterations might have change.

Methods: Retrospective analysis of 71 probands referred for genetic screening with a clinical suspicion of CNC between 2020 and 2025. Main clinical presentation were: Primary Pigmented Nodular Adrenocortical Disease (PPNAD) ($n = 32$), cardiac myxomas ($n = 24$), lentigines ($n = 18$), schwannomas ($n = 6$). *PRKAR1A* and *PRKACA* genes were screened for point variants and copy number variants (CNV), by targeted sequencing using NGS in all, and when non conclusive by WGS in a subset.

Results: The median age at genetic screening was 33 years (range: 2-70). A genetic alteration was found in 69% (22/32) of probands with PPNAD, up to 73% (8/11) in patient under 20 and 73% (8/11) if PPNAD was associated with other CNC features. *PRKAR1A* variants were found in 28 probands: half of them carried a splice-altering variant, the remaining being mostly truncating variant or CNVs. This group showed the most diverse phenotype, including PPNAD (61%), lentigines (39%), and myxomas (29%). *PRKACA* duplications were identified in 4 probands all presenting PPNAD and no other CNC features. No genetic alteration was found for probands presenting isolated schwannomas or isolated myxomas over 35 years old.

Discussion: Our results confirm that *PRKACA* duplications are almost exclusively associated with an adrenal-limited phenotype. The high rate of negative genetic results in patients with isolated myxomas or schwannomas suggests either genetic heterogeneity or the presence of variants in non-coding regions. A genetic alteration can now be identified in 3/4 of patients with PPNAD and/or multiple features of CNC, which is more frequently than previously reported.

Abstract citation ID: lvag096.212

RC12.5 - LBA_ECE_1293 - Assessment of germline variants by whole exome sequencing in patients with adrenocortical carcinoma

Erika Messina[1], Alessia Inglesi[2], Vittoria Basile[1], Soraya Puglisi[1], Deborah Cosentini[3], Marta Lagana[3], Marianna Torchio[1], Alfredo Berruti[3], Salvatore Grisanti[3], Maria Scatolini[2] and Massimo Terzolo[1]
[1]*Orbassano, Italy;* [2]*Molecular Oncology Laboratory, Fondazione Edo ed Elvo Tempia, Ponderano, Italy;* [3]*ASST Spedali Civili, Medical Oncology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, Brescia, Italy*

Background: Adrenocortical carcinoma (ACC) is a rare and aggressive endocrine malignancy with an incompletely defined genetic background. Although several predisposing genes have been identified, many cases remain genetically unexplained.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

This study aimed to identify novel germline variants (GVs) potentially involved in disease susceptibility in patients with sporadic ACC, by Whole Exome Sequencing (WES).

Methods: This retrospective analysis included patients with sporadic ACC stage I-IV. From our previously published cohort of 150 patients, we selected those who tested negative for alterations in the 17 genes most frequently implicated in adrenal tumor pathogenesis (AIP, APC, ARMC5, ARNT, BRCA1, BRCA2, CTNNB1, IGF2, MEN1, MSH2, MSH6, PDE8B, PDE11A, PRKACA, PRKACB, PRKAR1A, and TP53). Variant calling and interpretation were performed using SOPHIA Genetics pipeline. Filtering strategies prioritized genes associated with ACC predisposition and other hereditary cancer syndromes, mainly under a dominant inheritance model.

Results: Fifty-two patients were selected, with a predominance of females (75%, 39/52). Median age at diagnosis was 35 years (IQR 29-44). A personal history of malignancies other than ACC was reported in 29% of patients, while 31% had a positive family history for non-ACC malignancies. Most patients were diagnosed at stage II (63%). At a median follow-up of 45 months (IQR 22.5-77), 16 deaths were observed. Median overall survival was 176 months (95% IC 62-not reached). GVs of potential interest were identified in 6 patients (11.5%), involving the following genes: BARD1 ($n=1$), CHEK2 ($n=3$), MUTYH ($n=3$) and POLE ($n=1$). Most variants were classified as pathogenic/likely pathogenic, while one CHEK2 variant had conflicting pathogenicity interpretations according to available databases. Interestingly, patients carrying some of those alterations showed a family history of other neoplasia (breast, lung and colon rectal cancers), suggesting a potential hereditary predisposition. Somatic analyses on matched tumor samples are currently ongoing to investigate loss of heterozygosity (LOH) and second-hit mechanisms.

Conclusions: We identified GVs in a subset of patients with sporadic ACC who were selected for not being informative for the most common gene alterations. These findings support a potential role of additional genetic factors in predisposition to ACC. Their clinical significance remains to be fully defined.

Abstract citation ID: lvag096.213

RC12.6 - LBA_ECE_1193 - Mild autonomous cortisol secretion vs nonfunctional adrenal tumors and risk of psychiatric morbidity: a register-based cohort study

Hadis Mirzaei
Karolinska Institutet, Stockholm, Sweden

Background: Adrenal tumors are increasingly detected, and subtle cortisol excess may contribute to systemic disease morbidity. However, population-based data on psychiatric outcomes in relation to post–dexamethasone suppression test (DST) cortisol concentrations remain limited.

Objective: To examine the prevalence and incidence of psychiatric disorders in patients with adrenal tumors according to cortisol concentrations measured using the 1-mg dexamethasone suppression test (DST), comparing mild autonomous cortisol secretion (MACS) with nonfunctioning adrenal tumors (NFAT).

Methods: This regional population-based cohort study included patients with adrenal tumors and available DST results identified through Swedish national healthcare registries and three clinical laboratories in the Stockholm region. Overt functional adrenal tumors and primary adrenal malignancies were excluded. Patients were categorized according to post-DST cortisol concentrations (≤50 vs >50 nmol/L). Psychiatric outcomes were defined using ICD-10 diagnoses. Logistic regression and Cox proportional hazards models were used to assess prevalence and incidence outcomes, adjusted for age, sex, and socioeconomic variables.

Results: A total of 3195 patients with adrenal adenomas were included. The prevalence of psychiatric disorders at baseline was 47.3%. In crude analyses, MACS was not associated with baseline psychiatric disorders; however, after adjustment, MACS was associated with a higher prevalence (OR 1.14, 95% CI 0.95-1.37, aOR 1.35, 95% CI 1.11-1.64). During a median follow-up of 4.7 years (IQR 2.3-7.6), 334 individuals developed an incident psychiatric disorder. MACS was associated with an increased risk of incident psychiatric diagnoses (HR 1.66, 95% CI 1.34-2.06; adjusted HR 1.79, 95% CI 1.43-2.23). MACS was also associated with an increased risk of anxiety disorders (aHR 1.41, 95% CI 1.08-1.86), affective disorders (aHR 1.56, 95% CI 1.11-2.19), and substance use disorders (aHR 2.50, 95% CI 1.79-3.49). Stratified analyses suggested somewhat stronger associations among women and younger individuals, although formal interaction testing did not indicate a statistically significant effect modification.

Conclusions: Psychiatric disorders are common among patients with adrenal tumors. While post-DST cortisol concentrations were not clearly associated with baseline psychiatric prevalence, Patients with MACS showed an increased risk of incident psychiatric disorders. These findings suggest that even mild cortisol autonomy may contribute to psychiatric vulnerability over time.

Poster Presentations

Abstract citation ID: lvag096.214

P1 - ECE_2359 - Impact of P450 oxidoreductase mutation on drug metabolism: a case report

Ludmila Nicolazzi[1], Isabelle Gauchat-Bouchardy[2], Anne-Laure Rougemont[2], Nathalie Lin-Marq[2], Faiza Lamine[1], Haithem Chtioui[1] and Georgios Papadakis[1]
[1]Service of Endocrinology, Diabetology, and Metabolism, Lausanne University Hospital, Lausanne, Switzerland; [2]Service of Clinical Pathology, Geneva University Hospital, Geneva, Switzerland

Background: P450 oxidoreductase deficiency (PORD) is a rare form of congenital adrenal hyperplasia, characterized by variable degrees of primary adrenal insufficiency, ambiguous genitalia and skeletal malformations. It is caused by bi-allelic mutations in the *POR* gene, affecting the transfer of electrons to multiple cytochrome P450 (CYP) enzymes implicated in steroidogenesis but also in hepatic drug metabolism. Pharmacologic alterations have been reported in classic syndromic PORD. Data regarding pathways affected in milder PORD cases is currently scarce.

Method: We previously published the original case of a 36-year-old patient diagnosed with partial PORD due to a very mild phenotype (menstrual irregularity, infertility, ovarian macrocysts) (PMID 32242900). To evaluate the impact of POR mutations on drug metabolism beyond the classic PORD phenotype, we investigated CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4 metabolic pathways with CYPs genotyping in search of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

single nucleotide polymorphisms (SNP) to classify the predicted phenotype for each enzyme as poor (PM), normal (NM), rapid (RM) or ultrarapid metabolizer (UM); *in vivo* phenotyping using the Geneva CYP450 micrococktail (PMID 34512355) to measure metabolic ratios (MR) and characterize CYP-activities as slow, normal or rapid.

Results: Genotype revealed four SNPs in *CYP1A2* gene, one SNP in *CYP2C19* gene and three SNPs in *CYP2D6* gene, resulting in UM, RM and UM, respectively. NM was expected for the remaining CYPs in the absence of significant SNPs. Nevertheless, *in vivo* phenotyping revealed low MRs for CYP1A2 (0.19), CYP2C9 (0.02), CYP2C19 (0.14), CYP3A4 (0.06), consistent with slowed drug metabolism. CYP2B6 activity was mildly reduced (MR 0.31), while the observed phenotype was normal for CYP2D6 (MR 1.89). These alterations were expected to translate into decreased metabolism of several ongoing medications of the patient including estrogens, calcium channel blockers and proton pump inhibitors.

Discussion: A discordance between genotype and phenotype was observed for five out of the six CYP enzymes, reflecting a PORD-mediated decrease in their drug-metabolizing capacity. Our case highlights the impact of PORD on drug metabolism even in its milder, non-classic forms. Following these results, patient's affected medications were reduced to the lowest clinically effective dose. She was also instructed to be cautious when initiating new medications primarily metabolized by CYP1A2, CYP2C9, CYP2C19 or CYP3A4.

Conclusions: POR mutations can alter drug metabolism, but the resulting phenotype depends also on underlying CYP polymorphisms. In these patients, pharmacologic investigations with genotyping and phenotyping approaches can help to better appreciate metabolic alterations and guide personalized treatment adjustments.

Abstract citation ID: lvag096.215

P2 - ECE_3580 - Adrenal tumor shrinkage after osilodrostat therapy in patients with acth-independent cushing syndrome

Virginia Samaritani[1,2], Lorenzo Tucci[1,2], Francesca Donnarumma[1,2], Giada Ramundo[1,2], Giulia Zema[1,2], Valentina Vicennati[1,2], Caterina Balacchi[3], Uberto Pagotto[1,2], Cristina Mosconi[3] and Guido Di Dalmazi[1,2]
[1]*Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy;* [2]*Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy;* [3]*Radiology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*

Background and Aim: Adrenal tumor shrinkage after Osilodrostat therapy has been reported in ACTH-dependent hypercortisolism. However, data in ACTH-independent hypercortisolism are lacking. We describe two cases of adrenal nodule reduction following Osilodrostat therapy in patients with ACTH-independent hypercortisolism.

Case 1: A 57-year-old man was diagnosed with ACTH-independent Cushing syndrome associated with bilateral macronodular adrenal hyperplasia (urinary free cortisol [UFC]: 646 µg/day; serum cortisol after 1-mg overnight dexamethasone suppression test [1mg-ONDST]: 237 ng/mL; 23-salivary cortisol: 3.23 ng/ml). Computerized tomography (CT) showed a larger left adrenal gland (three nodules, maximum diameter 45 mm) compared with the right gland (three nodules, maximum diameter 34 mm). 18F-fluorodeoxyglucose positron emission tomography revealed higher uptake in the left adrenal gland compared to the right one (SUVmax 4.5 vs 3). The patient underwent left adrenalectomy, followed by adrenal insufficiency and recovery of adrenal function. Histology demonstrated macronodular adrenal hyperplasia (Weiss score 2). Germline DNA sequencing did not identify pathogenic *ARMC5* variants. Two years later, recurrence of ACTH-independent hypercortisolism was diagnosed (UFC: 140 µg/day; 1 mg-ONDST: 75 ng/mL). Metyrapone therapy was initiated. At treatment start, right adrenal nodules measured 26 × 20 mm, 34 × 26 mm, and 24 × 20 mm. After 43 months of therapy (weighted mean daily dose 750 mg), CT scan showed nodule growth over time (33 × 25 mm, 46 × 35 mm, and 30 × 20 mm, respectively). Metyrapone was discontinued and Osilodrostat initiated. After 7 months of Osilodrostat therapy (weighted mean daily dose 2.01 mg), CT demonstrated a reduction in the largest right adrenal nodules (38 × 28 mm vs 46 × 35 mm and 30 × 20 mm vs 33 × 25 mm).

Case 2: A 56-year-old woman was diagnosed with ACTH-independent Cushing syndrome (UFC: 441 µg/day; 1 mg-ONDST: 188 ng/mL; late-night salivary cortisol: 15.9 ng/mL). Abdominal CT revealed bilateral macronodular adrenal hyperplasia (left nodules: 32 mm, 13 mm, and 7 mm; right nodules: 20 mm and 7 mm). Osilodrostat therapy was initiated. After 16 months of treatment (weighted mean daily dose 5.10 mg), repeated CT showed a reduction in nodular size in both adrenal glands (left: 27 mm vs 32 mm and 5 mm vs 13 mm; right: 12 mm vs 20 mm and 6 mm vs 7 mm).

Conclusions: This is the first report of shrinkage of adrenal nodules in ACTH-independent Cushing syndrome. Recently, cases of adrenal shrinkage following Osilodrostat therapy have been emerging in patients with both ACTH-dependent and ACTH-independent Cushing syndrome. The underlying mechanism remains unknown. Targeted studies are needed to confirm this observation and to elucidate the potential pathophysiological mechanism.

Abstract citation ID: lvag096.216

P3 - ECE_1584 - A novel homozygous mutation of CYP17A1 gene in a 20-year old 46, XY phenotypical male with hypergonadotropic hypogonadism and gynecomastia

Karolina Kucharczyk[1], Anna Nogieć[1], Grzegorz Sokolowski[2], Anna Matrejek[1], Malgorzata Trofimiuk-Muldner[2] and Alicja Hubalewska-Dydejczyk[3]
[1]*University Hospital in Krakow, Krakow, Poland;* [2]*Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland;* [3]*Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland*

Introduction: Congenital adrenal hyperplasia (CAH) comprises autosomal recessive disorders of adrenal steroidogenesis. 17α-hydroxylase/17, 20-lyase deficiency (17-OHD) is a rare subtype (~1% of CAH) caused by pathogenic variants in *CYP17A1*. In 46, XY individuals, complete deficiency typically leads to female or ambiguous external genitalia at birth and later hypertension and/or hypokalaemia. However, partial enzyme deficiency

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

may preserve some androgen and glucocorticoid production, leading to atypical presentations and delayed diagnosis.

Case Report: A 20-year-old 46, XY phenotypic male was referred for progressive right-sided gynecomastia over five years and hypergonadotropic hypogonadism, initially suspected to represent Klinefelter syndrome. He reported impaired ejaculation with preserved erectile function and sparse facial hair. Past history included hypospadias repair in early childhood. Examination revealed normally virilized male genitalia without ambiguity, reduced penile length, and age-appropriate pubic and axillary hair.

Investigations: Biochemistry confirmed hypergonadotropic hypogonadism with low testosterone and elevated luteinizing hormone. Adrenal evaluation showed persistent ACTH elevation, markedly increased 17-hydroxyprogesterone, and low adrenal androgens, suggesting impaired steroidogenesis, while cortisol circadian rhythm was preserved. Renin was suppressed with normal aldosterone and normal blood pressure. Impaired glucose tolerance and osteopenia were also identified. Karyotype was 46, XY.

Dynamic testing demonstrated minimal testosterone response to hCG and an abnormal Synacthen steroid profile with pronounced 17-hydroxyprogesterone elevation, supporting a congenital steroidogenic defect. Imaging showed pituitary changes consistent with hyperplasia and a left adrenal lesion compatible with adenoma. Breast biopsy was benign.

Urinary steroid profiling revealed increased mineralocorticoid and progesterone metabolites with elevated 17-hydroxylated metabolites and normal cortisol metabolites, consistent with partial CYP17A1 deficiency, predominantly affecting 17, 20-lyase activity.

Genetics: Genetic testing identified a novel homozygous CYP17A1 missense variant (c.1234T>C, p.Phe412Leu; exon 7), classified as likely pathogenic and confirmed by Sanger sequencing. The variant has not been reported in major databases or the literature and is extremely rare in gnomAD (non-Finnish Europeans: 0.0000008993), with no previously described homozygous cases.

Conclusions: This case expands the genotypic and phenotypic spectrum of partial 17α-hydroxylase/17, 20-lyase deficiency. The patient presented with hypergonadotropic hypogonadism and progressive gynecomastia despite normal blood pressure, preserved circadian cortisol rhythm, and no genital ambiguity, with only subtle signs of undervirilization. These findings demonstrate that residual CYP17A1 activity can mask the classic phenotype. Therefore, 17-OHD should remain in the differential diagnosis of young men with unexplained hypogonadism, particularly when any features of disordered sex development are present.

Keywords CYP17A1, 17α-hydroxylase/17, 20-lyase deficiency (17-OHD), Congenital Adrenal Hyperplasia (CAH), Gynecomastia, Hypogonadism, c.1234T>C

Abstract citation ID: lvag096.217

P4 - ECE_2057 - Diagnostic jouney and delays in patients with pheochromocytoma and abdominal paraganglioma: from symptom onset to post-surgical outcomes

Emmanuelle Kamand[1], Elise Bouillet[2], Camille Marciniak[1], François Collet[1], Marine Mallea[1], Dupuis Hippolyte[1], Romain Vankemmel[1], Arnaud Jannin[1], Do Cao Christine[1], Guillaume Ledieu[1], Robert Caiazzo[1], Pattou François[1], Vantyghem Marie Christine[1], Cardot Catherine[1] and Stéphanie Espiard[1]

[1]CHU de Lille, Lille, France; [2]Centre Hospitalier de Tourcoing, Tourcoing, France

Background and Aim: Diagnostic delays in pheochromocytomas and paragangliomas (PPGL), their causes and consequences remain insufficiently documented, particularly from the patient perspective. While the classic Menard's triad is well-known, the full spectrum of patient-experienced symptoms remains poorly characterized. This study combines qualitative patient interviews with quantitative analysis to systematically characterize symptom burden, diagnostic delays, and post-operative outcomes.

Methods: A two-phase single-center prospective study was conducted. Qualitative interviews first identified patient experiences and symptom terminology. Based on these findings, a questionnaire capturing symptoms in patient-familiar language was developed and administered to patients operated for PPGL, assessing pre/postoperative symptoms, diagnostic pathways, and recovery patterns.

Results: Qualitative analysis revealed two symptom evolution patterns: slow progressive worsening over years and unpredictable paroxysmal crises. Patients frequently minimized their symptoms, attributing them to aging or stress, which promoted consultation delays. Many patients felt unheard by healthcare professionals unfamiliar with PPGL. In the quantitative study ($n = 83$, 70.3% response rate), chest tightness and palpitations were predominant symptoms (62.7%), while Menard's triad occurred in only 20.5%. Women reported significantly more symptoms than men (median 4.6 vs 2.9, $P = .006$). After surgery, 44% of patients reported improvement in symptoms that they had not initially attributed to their PPGL. Complete postoperative symptom resolution occurred in 60.8% overall, but was significantly higher when diagnostic delay was <5 years (81.3% vs 47.4%, $P = .006$). Weight gain was reported by 39.8% of the patients. Antihypertensive therapy was discontinued in 63.3% and antidiabetic medication in 77.4% postoperatively. The median diagnostic delay was 27 months [IQR 10-76], yet 28.8% and 22.9% reported symptom onset >10 years and 6-10 years before diagnosis, respectively. Discovery mode was incidental imaging (61.4%), symptomatic (31.3%), or genetic surveillance (7.2%). Importantly, the proportion of highly symptomatic patients was identical between incidentalomas and symptomatic presentations (35%), suggesting many incidentalomas represent unrecognized symptomatic cases. Consultation frequency correlated with symptom burden ($P < .001$). Paradoxically, diagnostic delay did not correlate with symptom count ($r = 0.19$, $P = .262$) but increased with consultation frequency ($P < .001$) and patient age ($P = .013$), suggesting repeated missed diagnoses in symptomatic patients rather than paucisymptomatic presentations.

Conclusions: Diagnostic delays in PPGL are common and impair postoperative recovery. Symptom onset often preceded diagnosis by years to decades. This study highlights mechanisms leading to these delays: patient misattribution of symptoms and repeated missed diagnoses by providers. These findings underscore the need to enhance awareness among non-specialist providers who typically first encounter these patients, to improve outcomes and reduce healthcare burden.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.218

P5 - ECE_1585 - Long-term risk of adrenal crisis and hospitalization in chronic adrenal insufficiency—a long-term follow-up study

Irina Chifu[1], Anna Lynn Schreiber[1], Marcus Quinkler[2], Holger S. Willenberg[3], Nicole Reisch[4], Felix Beuschlein[5,6], Olaf Dekkers[7,8], Burger-Stritt Stephanie[1,9] and Stefanie Hahner[1]

[1]Würzburg, Germany; [2]Endocrinology in Charlottenburg, Berlin, Germany; [3]Division of Endocrinology and Metabolism, Department of Internal Medicine, Rostock University Medical Centre, Rostock, Germany; [4]Medizinische Klinik und Poliklinik IV, Klinikum der Ludwig-Maximilians-Universität München, München, Germany; [5]Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, Universitätsspital Zürich (USZ) und Universität Zürich (UZH), Zürich, Switzerland; [6]The LOOP Zurich - Medical Research Center, Zürich, Switzerland; [7]Department of Internal Medicine, Division of Endocrinology, Leiden University Medical Center, Leiden, The Netherlands; [8]Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands; [9]Uppsala Centre of Excellence, Department of Endocrine Oncology, Uppsala University Hospital, Uppsala, Sweden

Background: We evaluated the long-term risk for adrenal crisis (AC) and hospitalization in patients with adrenal insufficiency (AI).

Methods: Patients ($n = 423$) from a previous 2-year prospective study on AC were re-contacted by questionnaire 6 years (FU1) and 14 years (FU2) after study completion (baseline). We collected data on AC, hospitalization, glucocorticoid replacement, stress dosing, co-medication, comorbidities, and patient education on AC prevention. A total of 277 and 203 patients participated at FU1 and FU2, respectively. Incidence rate ratios for AC and hospitalization were determined using Poisson regression.

Findings: Recurrent AC was associated with prior AC ($P < .001$), secondary AI ($P < .001$), glucocorticoid dose ($P = .03$), frequent stress dosing ($P = .009$), DHEA replacement ($P = .003$) and non-endocrine comorbidities ($P < .001$). Recurrent hospitalization was associated with prior hospitalization ($P < .001$), prior AC ($P = .005$), endocrine ($P = .01$) and non-endocrine ($P < .001$) comorbidities. Patients reporting AC or hospitalization received higher glucocorticoid doses at baseline and at each follow-up. Only 44% of patients had ever attended an AC-focused education session. Among 54 reported deaths, 8 were confirmed or suspected to be AC-related, and only 30% of deceased patients possessed an emergency kit at last follow-up.

Interpretation: The persistently increased risk among patients with prior AC despite higher glucocorticoid doses suggests intrinsic vulnerability, which is further amplified with multiple comorbidities. Despite improvements over time, awareness and access to emergency remain suboptimal and require urgent enhancement. Future studies should focus on prospective, long-term assessment of individual AC susceptibility, including biomarker identification and close monitoring of patient-reported outcomes.

Abstract citation ID: lvag096.219

P6 - ECE_2643 - Revisiting composite pheochromocytomas: evidence for a distinct clinical profile from a retrospective dual-center cohort study

Karolina Zawadzka[1,2], Ewelina Rzepka[3], Jan Calissendorf[4,5], C Christofer Juhlin[6], Alicja Hubalewska-Dydejczyk[3] and Henrik Falhammar[4,5]

[1]Doctoral School of Medical and Health Sciences, Jagiellonian University Medical College, Krakow, Poland; [2]Department of Endocrinology, Oncological Endocrinology, Nuclear Medicine and Internal Medicine, University Hospital in Krakow, Krakow, Poland; [3]Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [4]Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden; [5]Department of Endocrinology, Karolinska University Hospital, Stockholm, Sweden; [6]Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden

Background: Composite pheochromocytomas, characterized by the coexistence of pheochromocytoma with additional neural crest–derived components, are considered uncommon, and data on their clinical behaviour and prognosis are limited. This study aimed to determine whether the presence of composite histology in pheochromocytomas is associated with differences in biological features, clinical manifestation, perioperative course, and long-term outcomes compared with conventional pheochromocytomas.

Methods: We conducted a retrospective analysis of 188 patients with histologically confirmed pheochromocytomas from two tertiary centres. Patients with composite and typical tumours were compared with regard to demographic characteristics, clinical presentation, biochemical findings, imaging features, surgical and perioperative data, histopathology, and follow-up outcomes.

Results: Composite pheochromocytomas constituted 15% of all cases ($n = 28$). Patients with composite tumours were older at diagnosis (median age 56 vs 50 years, $P = .04$) and had a higher prevalence of cardiovascular comorbidities (39.3% vs 18.1%, $P = .02$) than those with typical pheochromocytomas. Preoperative systolic blood pressure was higher in the composite group (median 150 mmHg vs 140 mmHg, $P = .03$) and remained significantly elevated following adrenalectomy (130 mmHg vs 123 mmHg, $P = .04$). Laparoscopic adrenalectomy was performed less frequently in patients with composite tumours (67.9% vs 87.5%, $P = .02$), although operative and anaesthesia durations were shorter. On non-contrast CT imaging, composite tumours showed lower attenuation values (median 28 vs 35 Hounsfield units, $P = .01$) and were less commonly identified as adrenal incidentalomas. Ki-67 indices in the range of 3-5% were more frequently observed in composite tumours (23.5% vs 4.6%, $P = .02$), while rates of recurrence and metastatic disease did not differ between groups.

Conclusions: Compared with typical pheochromocytomas, composite tumours present in an older population and are associated with increased cardiovascular morbidity, higher blood pressure, lower CT attenuation values, and distinct perioperative characteristics. Although elevated Ki-67 indices were more common in composite pheochromocytomas, their relevance for long-term prognosis remains unclear.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.220

P7 - ECE_1671 - An ACTH-secreting pheochromocytoma presenting as septic cardiogenic shock

Jaekyung Lee, Sangjun Bae and Dong Jun Lim
Division of Endocrinology and Metabolism, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea

Background: ACTH-secreting pheochromocytoma is an exceptionally rare cause of ectopic Cushing's syndrome. Concurrent catecholamine and cortisol excess can mimic septic shock and induce reversible cardiomyopathy, leading to diagnostic delay. We describe a case presenting with fulminant cardiogenic shock requiring ECMO, characterized by extreme procalcitonin elevation, paradoxical dexamethasone response, and post-operative immune reconstitution with CMV reactivation.

Case: A 42-year-old woman presented with fever and shock (BP 80/73 mmHg, HR 180 bpm). Laboratory tests showed leukocytosis 16 340/μL, CRP 6.09 mg/dL, and procalcitonin 52.29 ng/mL. Echocardiography revealed global akinesia with LVEF 12%. Despite VA-ECMO, CRRT, and broad-spectrum antibiotics, all cultures were negative. Procalcitonin declined rapidly to 1.10 ng/mL while fever and leukocytosis persisted. CT identified a 6.7-cm right adrenal mass. Biochemistry demonstrated dual hormone excess: urine metanephrine 14 306 μg/day (ref <315), ACTH >4000 pg/mL, and cortisol 122.4 μg/dL. High-dose dexamethasone (8 mg) produced a paradoxical ACTH rise from 113.7 pg/mL to 459.8 pg/mL, suggesting an ectopic source. After alpha-blockade and ketoconazole, laparoscopic adrenalectomy was performed. Pathology confirmed pheochromocytoma with positive ACTH immunostaining. Postoperatively, the patient developed pancytopenia and hypotension. CMV PCR revealed 737 534 copies/mL, consistent with viral reactivation during immune recovery after abrupt correction of hypercortisolism. Following ganciclovir and steroid replacement, she recovered completely; LVEF improved to 53.4% and hormonal levels normalized.

Conclusions: ACTH-producing pheochromocytoma may present as apparent septic shock with extreme procalcitonin elevation and reversible cardiomyopathy. Dissociation between declining procalcitonin and persistent inflammation should prompt evaluation for endocrine causes. A paradoxical ACTH rise during dexamethasone testing may represent a useful diagnostic clue. Careful surveillance for opportunistic infections is required after curative treatment due to potential immune reconstitution.

Abstract citation ID: lvag096.221

P8 - ECE_2736 - Phase I, open-label, multiple-ascending-dose study of asedebart, a novel anti-adrenocorticotropic hormone (ACTH) antibody for the treatment of classic congenital adrenal hyperplasia (CAH)

Gudmundur Johannsson[1], Anand Velusamy[2], Alessandro Prete[3,4], Henrik Falhammar[5], Marie Louise Binderup[6], Klaus Groes Larsen[6], Mimi Folden Flensburg[6], Johan Luthman[6] and Umasuthan Srirangalingam[7]
[1]Department of Endocrinology, Sahlgrenska University Hospital, Gothenburg, Sweden; [2]Department of Endocrinology, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; [3]Department of Metabolism and Systems Science, University of Birmingham, College of Medicine and Health, Birmingham, United Kingdom; [4]National Institute for Health and Care Research (NIHR) Birmingham Biomedical Research Centre, Birmingham, United Kingdom; [5]Department of Endocrinology, Karolinska University Hospital, Stockholm, Sweden; [6]H. Lundbeck A/S, Copenhagen, Denmark; [7]Department of Endocrinology, University College London Hospitals NHS Foundation Trust, London, United Kingdom

Introduction: CAH is a rare autosomal recessive disorder predominantly caused by an enzyme deficiency that results in defective cortisol biosynthesis. This impairs negative feedback on the hypothalamus-pituitary-adrenal axis, leading to elevated ACTH and thus an excess of adrenal androgens. Although supraphysiologic glucocorticoids are commonly used to manage hyperandrogenemia, they are associated with long-term adverse effects. Asedebart is a novel, high-affinity, anti-ACTH monoclonal antibody that inhibits ACTH-induced signaling and has been shown to significantly and durably reduce corticosterone and aldosterone concentrations in rats, and cortisol and aldosterone concentrations in cynomolgus monkeys. Here we present preliminary, first-in-human findings on the safety, tolerability, pharmacokinetics, and pharmacodynamics of asedebart from a Phase I trial in adult patients with classic CAH.

Methods: This open-label, multiple-ascending-dose, 2-part trial (NCT05669950) enrolled men and women, aged 18-70 years, with classic CAH and pre-glucocorticoid morning 17-hydroxyprogesterone (17-OHP) concentrations >4 times the upper limit of normal. Participants received up to 6 doses of asedebart at increasing levels, every 28-35 days. Stable glucocorticoids and mineralocorticoid replacement were given. Part A of the trial consisted of a 3 + 3 design: 3 participants received a certain dose level and were escalated to the next dose level, following a 28-day safety observation period. Part B investigated the doses of asedebart which were identified as pharmacologically relevant during Part A, in a larger number of participants. Primary endpoints included adverse events, clinical safety, maximum observed exposure (in a dosing interval), area under the concentration–time curve (in a dosing interval), and relative reductions in morning 17-OHP and androstenedione (A4) concentrations (from baseline to the day following each asedebart dose).

Results: Eleven participants (7 women and 4 men) were enrolled, with a mean age of 37 years (range 21-58 years). At the baseline visit, mean (standard deviation) concentrations were 245.3 nmol/L (2.37 nmol/L) for morning 17-OHP and 10.4 nmol/L (2.28 nmol/L) for morning A4. Clear pharmacodynamic effects were observed in the 11 participants following up to 6 intravenous infusions of asedebart at increasing doses, and morning 17-OHP and A4 concentrations were reduced by 90.5%-98.7% and 66.3%-89.3%, respectively, across all dose levels. There were no safety concerns.

Conclusions: These preliminary Phase I results show that the anti-ACTH monoclonal antibody asedebart is well tolerated and can significantly reduce adrenal androgen production, supporting continued clinical development of asedebart as a promising treatment strategy for classic CAH.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.222

P9 - ECE_3027 - Adrenal vascular events: challenging the hemorrhage-infarction dichotomy

Augustin Maillard[1], Lucas Shorten[1], Vincent Chouraki[1], Fatima Boubziz[1], Arnaud Maillard[2], Alexis Maillard[2], Marine Mallea[1], Arnaud Jannin[1], Douillard Claire[1], Vantyghem Marie Christine[1], Vincent Sobanski[1] and Stéphanie Espiard[1]

[1]CHU de Lille, Lille, France; [2]Institute Imagine, Paris, France

Background: Adrenal hemorrhage (AH) and adrenal infarction (AI) are classically considered distinct entities. However, both share common pathophysiological mechanisms involving the unique "vascular dam" anatomy of the adrenal gland and similar triggers including stress, hypercoagulability, and hemodynamic instability. Clinical comparison between these conditions has never been systematically performed.

Objective: To determine whether adrenal hemorrhage and infarction represent a continuum through comparison of etiologies, laterality patterns, and clinical outcomes.

Methods: Retrospective cohort study of all adrenal vascular events (AVEs) in adults at a University Hospital from 2008-2022, identified through health data warehouse. Patients with underlying adrenal tumors were excluded.

Results: Among 309 patients (263 AH, 46 AI), etiological profiles differed significantly. Trauma dominated AH (62.4% vs 4.3% in AI, $P < .0001$), while prothrombotic contexts dominated AI (73.9% vs 8.7% in AH, $P < .0001$), including pregnancy (AI 30.4% vs AH 1.1%, $P < .0001$), thrombophilia (AI 15.2% vs AH 0.4%, $P < .0001$), antiphospholipid syndrome (AI 15.2% vs AH 3.8%, $P = .006$), and sepsis (AI 13.0% vs AH 3.4%, $P = .014$). Post-operative complications (AH 16.3% vs AI 8.7%, $P = .26$) and anticoagulation (AH 3.8% vs AI 2.2%, $P = 1.00$) showed no significant difference. However, etiological convergence emerged in bilateral presentations: although bilaterality rates differed (AI 56.5% vs AH 9%, $P < .001$), among the 51 bilateral AVEs (25 AH, 26 AI), prothrombotic contexts accounted for 68% overall (56% of bilateral AH, 81% of bilateral AI). Specialized endocrinological evaluation rates differed between unilateral presentations (AH: 22.3% vs AI: 52%, $P < .01$) but were similar in bilateral cases (AH: 60% vs AI: 65%, $P = .78$). Long-term follow-up of bilateral AVEs (median 4.8 years) revealed identical adrenal insufficiency rates (AH: 54% vs AI: 60%, $P = 1.0$), with 56% requiring hydrocortisone and 30% fludrocortisone replacement, irrespective of radiological classification.

Conclusions: Certain adrenal hemorrhages and infarctions represent different manifestations along a common pathophysiological spectrum. Shared prothrombotic etiologies in bilateral presentations and identical clinical outcomes support the unified concept of “adrenal vascular events” where radiological appearance reflects disease mechanism rather than distinct pathophysiology. Clinical management should prioritize systematic endocrinological evaluation based on etiology and bilaterality and not imaging classification.

Abstract citation ID: lvag096.223

P10 - ECE_3261 - Screening for primary aldosteronism with plasma steroids, potassium, and renin: a cross-sectional machine learning study

Wenyu Zhang[1,2], Christina Pamporaki[3], René Jäkel[1,4], Georgiana Constantinescu[3], Mirko Peitzsch[5], Manuel Schulze[1], Jun Yang[6,7], Andrea Horvath[8], Ralph Müller-Pfefferkorn[1], Martin Reincke[9], Felix Beuschlein[9,10,11], Carmina Teresa Fuss[12], Stefanie Hahner[12] and Graeme Eisenhofer[3]

[1]Dresden, Germany; [2]TU Dresden, Dresden, Germany; [3]Department of Medicine III, Technische Universität Dresden, University Hospital Carl Gustav Carus, Dresden, Germany; [4]ScaDS.AI - Center for Scalable Data Analytics and Artificial Intelligence Dresden/Leipzig, Technische Universität Dresden, Dresden, Germany; [5]Institute of Clinical Chemistry and Laboratory Medicine, Technische Universität Dresden, University Hospital Carl Gustav Carus, Dresden, Germany; [6]Centre for Endocrinology and Metabolism, Hudson Institute of Medical Research, Clayton, Australia; [7]Department of Medicine, Monash University, Clayton, Australia; [8]New South Wales Health Pathology, Prince of Wales Hospital, Sydney, Australia; [9]Department of Medicine IV, Ludwig Maximilian University Munich, University Hospital, Munich, Germany; [10]Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich and University of Zurich, Zurich, Switzerland; [11]The LOOP Zurich Medical Research Center, Zurich, Switzerland; [12]Department of Internal Medicine I, Division of Endocrinology and Diabetes, University of Würzburg, University Hospital of Würzburg, Würzburg, Germany

Background: Commonly used screening tests for primary aldosteronism provide suboptimal diagnostic accuracy. Machine learning (ML) models that utilize steroid profiles offer an alternative approach but require improvement.

Methods: Training and validation of ML models—using a panel of 13 plasma steroids, potassium, and renin—involved three patient cohorts, a total of 1380 patients, tested after medication washout. Models were initially trained on one cohort ($n = 352$) to facilitate comparisons of a previous model also trained on that cohort; the second cohort ($n = 849$) was used for external validation. Selected best models were also tested with and without medication washout. Models were subsequently trained on the combined cohorts and externally validated on the third cohort ($n = 179$). Diagnostic performance of best models was then compared to performance of the aldosterone-to-renin ratio (ARR).

Findings: Integration of plasma steroids with potassium using a feedforward neural network (FNN) model provided improved diagnostic performance over a previously established support vector machine model according to areas under ROC curves (AUCs) of 0.940 (CI:0.918-0.963) and 0.917 (CI:0.893-0.937, $P = .0103$). Addition of renin negligibly improved model performance beyond the improvement with potassium. The FNN and other renin-independent models showed similar accuracy before and after antihypertensive medication washout, whereas renin-dependent models exhibited poorer accuracy without medication washout. Paired comparisons of combined-dataset-models with the ARR showed three further optimized renin-independent models outperformed the ARR for screening according to AUCs of 0.948 to 0.954 vs 0.839 for the ARR. Those models, which utilize five selected steroids, minimize need for medication washout

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and at cut-offs for optimal 90% to 95% diagnostic sensitivity reduce false-positives by 53% to 72% to more effectively screen for PA than with the ARR.

Interpretation: The newly developed ML models demonstrate enhanced diagnostic performance compared to the previously established support vector machine model and the ARR. There was no difference in the diagnostic performance of renin-independent compared to renin-dependent models, though the former offer the benefit of screening patients in whom medication washout is not feasible.

Funding: eutsche Forschungsgemeinschaft.

Abstract citation ID: lvag096.224

P11 - ECE_3015 - Validation of the imaging criteria of ESE–ENSAT guidelines on adrenal incidentalomas in a large single-center cohort study

Katharina Kerkau[1], Schlötelburg Wiebke[2], Simon Kloock[3], Esther-Marie Krenig[2], Christine Zecha[2], Patrick Mihatsch[4], Otilia Kimpel[3], Thorsten Bley[4], Andreas Buck[2], Matthias Beissert[4] and Martin Fassnacht[3]
[1]*Clinic: Department of Medicine, Division of Endocrinology and Diabetes, University of Würzburg, University Hospital Würzburg, Würzburg, Germany;* [2]*Department of Nuclear Medicine, University Hospital Würzburg, University of Würzburg, Würzburg, Germany;* [3]*Department of Medicine, Division of Endocrinology and Diabetes, University Hospital Würzburg, University of Würzburg, Würzburg, Germany;* [4]*Department of Radiology, University Hospital Würzburg, University of Würzburg, Würzburg, Germany*

Background: Adrenal incidentalomas occur in about 2% of the adult population. Most lesions are benign and non-functioning or show mild autonomous cortisol secretion. However, malignancy must be reliably identified. In 2023, the European Society of Endocrinology (ESE) and the European Network for the Study of Adrenal Tumors (ENSAT) updated the imaging criteria for risk stratification into four imaging groups based on unenhanced CT, but real-world evidence remains limited. We aimed to validate this ESE/ENSAT algorithm.

Methods: We conducted a retrospective cohort study including all patients with adrenal mass detected by unenhanced CT at the University Hospital Würzburg (2015-2020). Lesion size, mean unenhanced attenuation (HU) and homogeneity were assessed, and lesions were assigned to ESE/ENSAT algorithm groups: group 1 (any size, HU $\leq$10); group 2 (HU 11-20 and tumor <4 cm); group 3 (HU 11-20 and tumor $\geq$4 cm) or (HU >20 and tumor <4 cm); group 4 (tumor $\geq$4 cm and HU >20). Bilateral lesions were evaluated separately. Final diagnosis was defined by histopathology or pre-defined follow-up criteria, including stable tumor size for $\geq$1 year.

Results: We included 1037 patients (580 men, 457 women) with 1308 adrenal lesions (including 271 bilateral, 262 right and 504 left). The median size was 20 mm (range 10-211) and median HU 10 (range −109-+59). 529 were identified as "true incidentalomas" and 729 as part of tumor staging for extra-adrenal malignancies. Up to now, 304/1308 lesions (23.2%) remained indeterminate, mainly due to missing follow-up imaging. According to the guidelines, 161/304 lesions would have required follow-up imaging. Final diagnosis: 672 adenomas, 77 other benign tumors, 162 metastases, 41 ACCs, 14 pheochromocytomas, 38 others. Malignancy rates increased markedly across groups: group 1: 0.2% (1/440); group 2: 5.6% (7/126); group 3: 43.8% (141/322); group 4: 79.3% (92/116). Of note, the malignancy rates were significantly different between "true incidentalomas" and lesions detected during tumor staging: group 1, 0% vs 0.4%; group 2, 0% vs 9.5%; group 3, 24.0% vs 58.4%; group 4, 70.2% vs 83.0%.

Conclusions: In a large real-world cohort, the ESE/ENSAT diagnostic algorithm provided strong malignancy risk stratification. The very low malignancy rate in group 1 supports omission of further diagnostic work-up, while groups 3-4 warrant prompt diagnostic and therapeutic escalation. Notably, malignancy risk within each imaging group was strongly influenced by the initial imaging indication, underscoring the importance of distinguishing true incidentalomas from lesions detected during oncologic staging.

Abstract citation ID: lvag096.225

P12 - ECE_3277 - Effects of modified release hydrocortisone on reproductive function in males with congenital adrenal hyperplasia. insights from CALLIOPE: a multicenter, prospective study

Davide Ferrari[1], Chiara Simeoli[2], Lorenzo Arcolesse[1], Erminio M. Crescenzo[2], Anna Chiara Conflitti[1], Mariangela Piscopo[2], Marta Tenuta[1], Daniele Gianfrilli[1], Carlotta Pozza[1], Davide Menafra[2], Donatella Paoli[1], Riccardo Pofi[1], Rosario Pivonello[2] and Andrea Isidori[1]
[1]*Department of Experimental Medicine, Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy;* [2]*Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione, Università Federico II di Napoli, Naples, Italy*

Background: Patients with congenital adrenal hyperplasia (CAH) frequently experience impaired reproductive function, including altered spermatogenesis and the development of testicular adrenal rest tumors (TARTs). Modified-release hydrocortisone (MR-HC), by mimicking the circadian rhythm of cortisol, has shown benefits in hormonal control and quality of life. However, the specific impact of this new treatment on male reproductive function in CAH patients remains poorly explored.

Purpose: To evaluate the effectiveness of MR-HC on male reproductive function in adult patients with CAH.

Methods: Between July 2024 and May 2025, adult male patients with confirmed CAH were enrolled in the prospective, longitudinal, multicenter CALLIOPE study. Participants were assessed before and approximately 6 months after switching from conventional therapy to an equivalent dose of MR-HC. Assessments included semen analysis, hormonal profiling, and multiparametric testicular ultrasound to evaluate TARTs. Metabolic parameters were also analyzed.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: 32 patients (mean age 29.5 ± 7 years) were enrolled. TARTs were detectable in 20 (62.5%). After 5.7 months of MR-HC treatment (IQR 25-75: 4.11-6.21), a significant increase was observed in sperm concentration [+72.3% (95% CI: +22.79; +121.81, $P = .006$)] and total sperm count in the ejaculate [+71.84% (95% CI: +6.97;+136.72, $P = .032$)], whereas no significant changes were found in qualitative parameters (progressive motility and morphology). Ultrasound analysis showed a trend toward a reduction in total TART volume [−0.24 mL (95% CI: −0.60;+0.12 mL; $P = .055$)]. Hormonal analysis revealed unchanged Testosterone, Androstenedione and 17OH-Progesterone levels, with a significant increase in LH levels ($P = .047$), suggesting reduced suppression of the hypothalamic-pituitary-gonadal axis.

Conclusions: Our findings suggest a beneficial effect of MR-HC therapy on semen parameters and TARTs volume in adult male patients with CAH. These results highlight the need for further studies in larger cohorts with long-term follow-up to fully characterize the efficacy profile of MR-HC on reproductive function.

Abstract citation ID: lvag096.226

P13 - ECE_3363 - Aldosterone/cortisol ratio as a new marker for diagnosing mild autonomous cortisol secretion (Macs). investigating the effects of mild hypercortisolism on the renin-angiotensin-aldosterone system

Filippo Vignali[1], Lucia Zirilli[2], Sara Cerrato[1], Bruno Madeo[2], Laura Roli[3], Maria Cristina De Santis[3], Giulia Canu[3], Tommaso Fasano[3], Sara De Vincentis[1] and Vincenzo Rochira[1,2]

[1]University of Modena and Reggio Emilia, Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, Unit of Endocrinology, University of Modena and Reggio Emilia, Modena, Italy; [2]Endocrinology Unit, Department of Specialty Medicine, Azienda Ospedaliero-Universitaria of Modena, Endocrinology, Department of Specialty Medicine, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [3]Modena, Italy

Introduction: MACS is a frequent finding in patients with adrenal incidentalomas(AI), yet its diagnosis remains challenging due to the limited specificity of the 1-mg overnight dexamethasone suppression test(ONDST) and the lack of reliable complementary biomarkers. In Cushing's syndrome(CS), cortisol excess activates renal mineralocorticoid receptors, causing sodium retention and volume expansion, which suppress aldosterone and renin levels. In MACS, the mild cortisol excess, may exert a partial suppression of the renin–angiotensin–aldosterone system(RAAS), suggesting that aldosterone–cortisol imbalance could help differentiate MACS from non-functioning adrenal incidentalomas(NFAIs).

Objectives: To evaluate the diagnostic accuracy of the ratios of aldosterone/cortisol, renin/cortisol, and aldosterone/urinary free cortisol(UFC) in differentiating MACS from NFAIs. Additionally, to investigate the effects of MACS on the RAAS.

Methods: A retrospective study was conducted on adult patients with AI, referred to the Endocrinology Unit of the AOU-Modena (2013-2025), including patients with MACS and NFAIs according to the ESE-ENSAT guidelines. Patients with CS, primary aldosteronism or major confounders were excluded. Serum cortisol (C), ACTH, aldosterone (A), renin (R), DHEAS, UFC and related ratios(A/C, C/R, A/UFC) were measured. Comparisons were made both overall and after wash-out from interfering therapies affecting the RAAS.

Results: 100 MACS (mean age 67; F/M 57/43) and 214 NFAIs (mean age 62; F/M 114/214) were initially compared without pharmacological wash-out. Serum aldosterone was significantly lower in MACS compared to NFAIs ($P < .001$), while serum cortisol was higher ($P < .001$). Renin showed no significant difference ($P = .125$). The A/C ratio was significantly lower in MACS than in NFAIs ($P < .001$), as was the A/UFC ratio ($P < .001$). ROC analysis of the A/C ratio yielded an area under the curve(AUC) of 0.767(IQR, 0.708-0.825, $P < .001$), with a cut-off <5.88 for MACS (sensitivity 69%, specificity 78.5%, negative predictive value 84.4%). This accuracy improved after wash-out (42 MACS vs 98 NFAIs), reaching an AUC of 0.784(IQR, 0.700-0.870, $P < .001$), with a cutoff <5.88 for MACS diagnosis(sensitivity 78.6%, specificity 74.5%, negative predictive value 89%). A/UFC and C/R showed similar trends, maintaining statistical significance ($P < .001$) but lower accuracy. Interestingly, ACTH, UFC, DHEAS and DHEAS ratio showed lower diagnostic performance than the A/C ratio.

Conclusions: The A/C ratio is a simple, inexpensive, and widely accessible biomarker that reliably differentiates MACS from NFAIs and outperforms other commonly used biochemical tests. A high A/C ratio (>5.88) appears to effectively exclude MACS before ONDST. These findings also provide novel pathophysiological insight, showing that even mild cortisol excess may partially suppress aldosterone secretion without altering renin, indicating RAAS dysregulation in MACS.

Abstract citation ID: lvag096.227

P14 - ECE_3701 - Incidence trends of Primary Aldosteronism in western Sweden 2006-2023

Marsel Koci[1,2], Eleftheria Gkaniatsa[1,2], Penelope Trimpou[1,2] and Oskar Ragnarsson[1,2,3]

[1]Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, Gothenburg, Sweden; [2]Department of Endocrinology, Sahlgrenska University Hospital, Gothenburg, Sweden; [3]Wallenberg Center for Molecular and Translational Medicine, University of Gothenburg, Gothenburg, Sweden

Context: Enhanced awareness of primary aldosteronism (PA) and advances in laboratory diagnostics have improved case detection. Yet population-based studies examining temporal incidence trends of unilateral and bilateral PA are scarce.

Aim: To describe incidence trends of PA and its subtypes in Western Sweden over the period 2006-2023.

Design and Methods: All individuals diagnosed with PA in the Västra Götaland County during the period 2006-2023 were included in the study. Clinical and biochemical data were collected. The annual incidence of PA was calculated by using the total number of inhabitants in Västra Götaland County.

Results: During the study period, 741 individuals were diagnosed with PA. Of these, 670 cases were confirmed by an intravenous saline infusion test, while 68 individuals were diagnosed based on biochemical criteria (aldosterone >550 pmol/L, renin <2.8 mIU/L, and potassium <3.5 mmol/L). Adrenal vein sampling

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(AVS) was performed in 502 individuals (68%). Among those undergoing AVS, 240 were classified as having unilateral PA and 261 as having bilateral PA. Overall, the median incidence of PA was 2.27 (1.41-2.95) cases per 100 000 inhabitants. The total median incidence of PA increased from 1.02 (0.96-1.26) cases per 100 000 during 2006-2011 to 2.27 (2.05-2.56) during 2012-2017, followed by a marked increase to 3.77 (2.81-4.54) during 2018-2023. The median incidence of unilateral PA increased from 0.63 (0.45-0.73) to 0.90 (0.86-1.02) cases per 100 000 and subsequently remained stable at 0.90 (0.80-1.02) across the same time intervals. The median incidence of bilateral PA increased from 0.32 (0.25-0.48) to 0.92 (0.82-1.05), and further to 1.22 (1.19-1.26) cases per 100 000. Higher aldosterone levels at screening ($P < .0001$) and lower serum potassium levels at screening ($P < .0001$) were associated with unilateral PA. There were no significant differences in total defined daily dose (DDD) between the two subgroups ($P = .051$).

Conclusions: The incidence of PA increased markedly over time, with the most pronounced rise in recent years. Unilateral PA was more common in earlier periods, whereas bilateral PA predominated more recently, highlighting improved detection and the importance of accurate subtype classification.

Abstract citation ID: lvag096.228

P15 - ECE_2974 - Does longer preoperative alpha-blockade prevent intraoperative hypertensive crisis in pheochromocytoma surgery? A retrospective cohort study

Karolina Zawadzka[1,2], Magdalena Pisarska-Adamczyk[3], Alicja Hubalewska-Dydejczyk[4] and Michał Pędziwiatr[5]
[1]*Doctoral School of Medical and Health Sciences, Jagiellonian University Medical College, Krakow, Poland;* [2]*Department of Endocrinology, Oncological Endocrinology, Nuclear Medicine and Internal Medicine, University Hospital in Krakow, Krakow, Poland;* [3]*Department of Medical Education, Jagiellonian University Medical College, Krakow, Poland;* [4]*Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland;* [5]*II Department of General Surgery, Jagiellonian University Medical College, Krakow, Poland*

Background: Intraoperative hypertensive crisis remains a major perioperative concern during pheochromocytoma resection and frequently requires urgent pharmacological management. Preoperative α-adrenergic blockade is therefore routinely employed to limit hemodynamic instability. While the choice of α-blocker has been widely discussed, the influence of blockade selectivity, duration of preoperative preparation, and final titrated dose on the occurrence and severity of hypertensive crisis has not been fully elucidated.

Methods: We performed a retrospective cohort study including 110 patients who underwent laparoscopic adrenalectomy for pheochromocytoma. The type of α-adrenergic blockade (doxazosin [DOX] or phenoxybenzamine [PXB]), length of preoperative α-blockade, and final administered dose were analysed in relation to the incidence and duration of intraoperative hypertensive crisis, defined as systolic blood pressure exceeding 200 mmHg.

Results: Patients treated with DOX experienced significantly longer hypertensive crises than those receiving PXB (median 15.0 [10.0-30.0] vs 10.0 [5.0-15.0] minutes, $P = .03$). Intraoperative vasopressor support was required more frequently in the DOX group (39.6% vs 10.9%, $P < .001$), and perioperative hospital stay was longer compared with the PXB group (median 3.0 [2.2-4.0] vs 2.0 [2.0-3.0] days, $P < .001$). Diabetes mellitus, urinary metanephrine levels exceeding ten times the upper limit of normal, and preoperative α-blockade longer than 30 days were identified as independent predictors of hypertensive crisis. Extended α-blockade was associated with prolonged crisis duration and greater vasopressor requirements, particularly among patients receiving DOX. The final titrated α-blocker dose assumed no significant association with hypertensive outcomes.

Conclusions: Selective α-adrenergic blockade with doxazosin was associated with longer intraoperative hypertensive crises, increased need for vasopressor support, and prolonged hospitalization. Moreover, extended preoperative α-blockade exceeding 30 days was linked to a higher frequency and longer duration of hypertensive crises, as well as an increased risk of postoperative vasopressor use.

Abstract citation ID: lvag096.229

P16 - ECE_2390 - Delayed Diagnosis of Pheochromocytoma Presenting with Severe Cardiac Complications in Pregnancy

Naciye Guduk Sirvan[1], Nergis Basmacı[2], Suleyman Nahit Sendur[2], Ali Devrim Karaosmanoglu[3], Cenk Sokmensuer[4], Omer Cennet[5] and Alper Gurlek[2]
[1]*Internal Medicine, Hacettepe University Hospital, Ankara, Türkiye;* [2]*Endocrinology, Hacettepe University Hospital, Ankara, Türkiye;* [3]*Radiology, Hacettepe University Hospital, Ankara, Türkiye;* [4]*Pathology, Hacettepe University Hospital, Ankara, Türkiye;* [5]*General Surgery, Hacettepe University Hospital, Ankara, Türkiye*

Background: Pheochromocytoma is a rare catecholamine-secreting tumor arising from chromaffin cells of the adrenal medulla. Its occurrence during pregnancy is rare but highly dangerous, as it can closely mimic preeclampsia or peripartum cardiomyopathy. This diagnostic overlap often leads to delayed recognition of the disease, causing significant maternal and fetal morbidity and mortality. Recent systematic reviews indicate that, even with modern management, maternal mortality remains between 4%-9% and fetal mortality between 7%-14%. Therefore, timely recognition is essential in pregnant and postpartum patients presenting with paroxysmal hypertension, palpitations, or adrenergic spells that do not respond to standard antihypertensive therapy. Early diagnosis and proper preoperative management with combined α- and β-blockade significantly reduce perioperative risk and improve outcomes for both mother and child.

Case Presentation: A 30-year-old woman at 28 weeks of gestation presented with recurrent headache, palpitations, tremor, sweating, and hypertension. She underwent emergency cesarean section due to a hypertensive crisis, which was complicated by intraoperative cardiac arrest requiring resuscitation. Postoperative echocardiography revealed a left ventricular ejection fraction (LVEF) of 25%-30% and grade 2-3 mitral regurgitation, leading to a diagnosis of peripartum cardiomyopathy. Despite beta-blocker and ACE inhibitor therapy, the patient continued to experience paroxysmal adrenergic symptoms including palpitations and diaphoresis. Abdominal computed tomography (CT) revealed a 42 × 46 mm hypodense mass in the left adrenal gland. Plasma and 24-hour

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

urinary catecholamines were markedly elevated (Table 1): epinephrine 864 ng/L, norepinephrine 1838 ng/L, metanephrine 9262 µg/day, and normetanephrine 4232 µg/day. Preoperative α-adrenergic blockade with doxazosin was followed by β-blockade for heart rate control. Laparoscopic left adrenalectomy was performed, and histopathological analysis confirmed pheochromocytoma (*chromogranin A* and *synaptophysin* positive, Ki-67 3%, PASS 9/20). The postoperative course was uneventful, and the patient's blood pressure normalized. Six months after surgery, cardiac function and symptoms had completely recovered.

Conclusions: Pheochromocytoma in pregnancy represents a rare yet life-threatening etiology of severe hypertension and cardiovascular complications, often clinically indistinguishable from preeclampsia or peripartum cardiomyopathy. A high index of clinical suspicion, prompt biochemical evaluation, and the use of non-ionizing imaging modalities are essential for diagnosis. Proper α- then β-blockade and timely adrenalectomy markedly reduce maternal and fetal morbidity.

Table 1 Laboratory results of the patient.

Parameter	Result	Reference range	Interpretation
Plasma Epinephrine (ng/L)	864	0-140	Markedly elevated
Plasma Norepinephrine (ng/L)	1838	70-750	Markedly elevated
24-h Urinary Metanephrine (µg/day)	9262	52-341	Severely elevated
24-h Urinary Normetanephrine (µg/day)	4232	88-444	Severely elevated

Abstract citation ID: lvag096.230

P17 - ECE_3008 - Operated adrenal tumours: current practice and relevance of the ESE 2023 guidelines

Morgane Mauger[1], François Tariel[2], Agathe Guenego[1], Benjamin Moreau[1], Annabelle Esvant[1], Anne Flore Herrou[1], Christèle Derrien[1], Juliette Hascoet[2], Benoit Peyronnet[2] and Patricia Vaduva[1]

[1]*Endocrinology, Diabetes, and Nutrition, Rennes University Hospital, Rennes, France;* [2]*Urology, Rennes University Hospital, Rennes, France*

Introduction: The incidence of adrenal tumours has risen steadily over the past two decades, while the prevalence of malignant, large, or secretory forms has remained stable. In 2023, the ESE/ENSAT updated recommendations for managing adrenal incidentalomas to improve the identification of patients requiring surgery.

Methods: To assess the clinical relevance of these new criteria, we conducted a retrospective study of patients who underwent adrenalectomy at Rennes University Hospital over a 20-year period. The risk of malignancy was stratified into five groups according to the 2023 guidelines based on imaging features (size, unenhanced CT attenuation, and metabolic activity). We analyzed the distribution of these groups based on histological diagnosis and evaluated the diagnostic performance (sensitivity, specificity, NPV, PPV) of this grading system.

Results: A total of 390 patients were included. Tumours were primarily discovered due to suggestive symptoms (46.6%) or incidentally (29.5%). The most frequent diagnoses were pheochromocytomas (32.8%), adrenal metastases (20.8%)—predominantly of renal origin (48.2%)—and aldosterone-producing adenomas (16.1%). Adrenocortical carcinomas accounted for 5.4% of the cohort. The risk of malignancy could be estimated in 293 patients. Among the 96 malignant tumours, 79 (82.3%) were suspicious on imaging, while 16 (16.7%)—comprising one adrenocortical carcinoma, one metastatic pheochromocytoma, and 14 metastases—were classified as indeterminate. No malignant tumours exhibited strictly benign features on unenhanced CT (≤10 HU). Only one case (a renal cell carcinoma metastasis) was classified as low risk on unenhanced CT and subsequently reclassified as benign due to a lack of ^{18}F-FDG PET/CT uptake. Conversely, only 15.7% (31/197) of benign tumours had reassuring imaging features, while 56.9% (112/197) appeared suspicious. The ESE grading system demonstrated excellent sensitivity (98.7%) and negative predictive value (96.9%) for distinguishing benign from malignant lesions. However, specificity (21.7%) and positive predictive value (41.4%) were low.

Conclusions: The 2023 ESE/ENSAT guidelines appear safe and reliable in our cohort, effectively ruling out malignancy in homogeneous tumours with unenhanced attenuation ≤10 HU, regardless of size. While combined imaging modalities offer excellent sensitivity, caution is required for fat-poor or non-hypermetabolic tumours in patients with a history of extra-adrenal cancer, particularly renal cell carcinoma.

Abstract citation ID: lvag096.231

P19 - ECE_2651 - Potassium status and gender influence steroid profile in Primary Aldosteronism and Non-Primary Aldosteronism-related hypertension: insights from the PROSALDhypO sub-trial

Thomas Uslar[1,2], Soline Bourgeois[3], Christina Pamporaki[4], Carmina Teresa Fuss[5], Stefanie Hahner[5], Jun Yang[6], Martin Reincke[7], Tracy Williams[7], Andrea Horvath[8], Mirko Peitzsch[9], Graeme Eisenhofer[4], Felix Beuschlein[1] and Sven Gruber[1]

[1]*Department of Endocrinology, Diabetology and Clinical Nutrition, University of Zurich, Universitätsspital Zürich, Zürich, Switzerland;* [2]*CETREN-UC, Red de Salud UC-CHRISTUS, Endocrinology, Pontificia Universidad Católica de Chile, Santiago, Chile;* [3]*Department of Endocrinology, Diabetology and Clinical Nutrition, Universitätsspital Zürich, Zürich, Switzerland;* [4]*Medical Clinic III, Medical Faculty and University Hospital Carl Gustav Carus, TU Dresden, Clinic, Dresden, Germany;* [5]*Division of Endocrinology and Diabetes, University Hospital, University of Würzburg, Division of Endocrinology and Diabetes, University Hospital, Würzburg, Germany;* [6]*Clinic, Centre for Endocrinology and Metabolism, Hudson Institute of Medical Research, Clayton, Australia, Melbourne, Australia;* [7]*LMU Klinikum Innenstadt, Medizinische Klinik und Poliklinik IV, Clinic, Medizinische Klinik und Poliklinik IV, München, Germany;* [8]*Department of Chemical Pathology, New South Wales Health Pathology, Prince of Wales Hospital, Sidney, Australia;* [9]*Institute of Clinical Chemistry and Laboratory Medicine, University Hospital Carl Gustav Carus, Technische Universität Dresden, Clinic, Department, Dresden, Germany*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Primary aldosteronism (PA) remains underdiagnosed, even in the context of hypokalemic hypertension. Steroid profiling by liquid chromatography-tandem mass spectrometry (LC-MS/MS) enables comprehensive assessment of adrenal steroidogenesis, but the influence of potassium status and sex on biochemical phenotype and clinical risk remains incompletely defined.

Objective: To assess the impact of potassium status and sex on adrenal steroid profiles and clinical characteristics in patients evaluated for PA, and to determine whether potassium stratification identifies distinct PA phenotypes.

Methods: This cross-sectional analysis was conducted as a predefined subtrial of the PROSALDO study and included 537 patients undergoing evaluation for suspected PA. PA was diagnosed using a combination of prespecified biochemical criteria, incorporating post-saline infusion aldosterone cut-offs measured by LC-MS/MS. Participants were stratified into four groups: hypokalemic PA (HypoPA+, $n = 131$), normokalemic PA (NormoPA+, $n = 56$), hypokalemic non-PA (HypoPA-, $n = 52$), and normokalemic non-PA (NormoPA-, $n = 298$). Steroid profiling covering mineralocorticoid-, glucocorticoid-, and sex-steroid-related pathways was performed by LC-MS/MS. Analyses were conducted overall and stratified by sex, with adjusted multivariable models.

Results: HypoPA+ patients exhibited a distinct and severe clinical phenotype, with higher systolic and diastolic blood pressure and a greater prevalence of stroke (7.6%) and aneurysm of large arteries (2.3%), compared with other groups (both $P \leq .030$). Biochemically, HypoPA+ patients demonstrated markedly elevated mineralocorticoid and hybrid steroids, including aldosterone, 18-oxocortisol, 18-hydroxycortisol and 11-deoxycorticosterone (all $P < .001$). Median 18-oxocortisol concentrations were more than twofold higher in HypoPA+ than in NormoPA+ patients (0.048 vs 0.022 ng/mL; $P < .001$). Glucocorticoid-related hybrid steroids showed a similar pattern. Sex-stratified analyses showed that men had higher blood pressure, higher post-saline infusion aldosterone, 18-hydroxycortisol, 21-deoxycortisol, and 11-deoxycortisol, but lower 11-dehydrocorticosterone and corticosterone than women. Although potassium-dependent group differences were preserved in both sexes, several contrasts in the mineralocorticoid and glucocorticoid hybrid steroids were statistically significant in women but attenuated or absent in men. In multivariable models, potassium/PA stratification independently predicted aldosterone and hybrid steroid concentrations ($P \leq .009$), whereas sex, age, BMI, renin, and cerebrovascular disease were not consistent independent determinants.

Conclusions: Hypokalemia identifies a severe PA phenotype associated with increased cerebrovascular morbidity and amplified autonomous mineralocorticoid steroidogenesis. LC-MS/MS-based steroid profiling robustly characterizes a progressive increase in hybrid steroid production from hypokalemic PA to non-PA. Sex modifies absolute steroid concentrations, while potassium status remains the dominant determinant of PA-specific steroidogenic signatures. Potassium status and sex-related differences should be integrated into interpretative frameworks for steroid-based PA characterization and risk stratification.

Abstract citation ID: lvag096.232

P20 - ECE_1923 - Bioimpedance spectroscopy uncovers extracellular fluid excess in Primary Aldosteronism

Marianna Viukari[1], Antero Ylänen[2,3], Eeva Kokko[2], Niina Matikainen[1], Pasi Nevalainen[3] and Ilkka Pörsti[2,3]
[1]Endocrinology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [2]Helsinki, Finland; [3]Department of Internal Medicine, Tampere University Hospital, Tampere, Finland

Objective: Although primary aldosteronism is characterized by intravascular volume overload, evaluation of volume status is not included in the standard diagnostic workup. Bioimpedance spectroscopy is utilized to assess fluid status and is routinely applied in dialysis patients. However, to our knowledge, this technique has not been used to compare body water balance between patients with primary aldosteronism and essential hypertension. Here we examined whether bioimpedance spectroscopy can distinguish primary aldosteronism from essential hypertension and normotensive controls by quantifying body water distribution.

Design: Patients with confirmed primary aldosteronism ($n = 77$), essential hypertension ($n = 90$), and normotensive controls ($n = 79$) were prospectively recruited for a cross-sectional comparison.

Methods: Total body water, extracellular and intracellular water volumes, and overhydration were measured using bioimpedance spectroscopy. Analyses were adjusted for sex, age, body surface area, estimated glomerular filtration rate, diuretic or spironolactone use, and comorbid diabetes or heart failure. Routine laboratory and hormonal tests were performed. Primary aldosteronism severity classification score was calculated for primary aldosteronism patients.

Results: Extracellular water was 0.69 ± 1.04 and 0.88 ± 1.04 L/m^2 higher, and overhydration 0.76 ± 1.4 and 0.92 ± 1.4 L greater, in primary aldosteronism than in essential hypertension and normotensive controls, respectively ($P < .001$ for all). Primary aldosteronism group also exhibited the highest extracellular water-to-intracellular water ratio (0.84 ± 0.1 vs 0.80 ± 0.1 and 0.73 ± 0.1, respectively; $P < .001$). Total body water indexed to body surface area did not differ significantly among groups (21.3 ± 2.2, 21.0 ± 2.8, and 21.6 ± 2.4 L/m^2, respectively, $P = .083$). Plasma N-terminal pro–atrial natriuretic peptide concentration was highest in primary aldosteronism. Primary aldosteronism severity correlated positively with extracellular water volume ($r = 0.31$), overhydration ($r = 0.43$), and the extracellular-to-intracellular water ratio ($r = 0.36$; $P < .01$ for all).

Conclusions: Bioimpedance spectroscopy detects extracellular volume overload that is pathognomonic in primary aldosteronism. Volume excess correlates with disease severity. This technique may have potential to improve diagnostic accuracy for primary aldosteronism.

Abstract citation ID: lvag096.233

P21 - ECE_2037 - Crinecerfont improves cardiometabolic outcomes associated with chronic supraphysiologic glucocorticoid exposure: 1-year results from CAHtalyst™ adult

Oksana Hamidi[1], Irina Bancos[2], Deborah Merke[3], Nicole Reisch[4], Patrice Rodien[5],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Umasuthan Srirangalingam[6], Maria Vogiatzi[7], Jacques Young[8], Jean Chan[9], Andrea Hartzell[9], Sanjay Keswani[9], Vivian Lin[9], Eiry Roberts[9], Julia Sturgeon[9] and Richard Auchus[10]

[1]University of Texas Southwestern Medical Center, Dallas, United States; [2]Mayo Clinic, Rochester, United States; [3]National Institutes of Health Clinical Center and Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, United States; [4]LMU Klinikum München, Munich, Germany; [5]CHU d'Angers and Labatoire MITOVASC, Université d'Angers, Angers, France; [6]University College London Hospitals, London, United Kingdom; [7]Children's Hospital of Philadelphia, Philadelphia, United States; [8]Bicêtre Hospital, AP-HP, Université Paris-Saclay, Paris, France; [9]Neurocrine Biosciences, Inc., San Diego, United States; [10]University of Michigan Medical School, Ann Arbor, United States

Background: Chronic exposure to supraphysiologic glucocorticoid (GC) doses can adversely impact cardiometabolic health. Crinecerfont is FDA-approved as an adjunct to GC replacement to control androgens in patients with classic congenital adrenal hyperplasia (CAH), enabling GC dose reduction. Changes in GC dose and GC-related outcomes were assessed in adults with CAH who received up to 1 year of crinecerfont.

Methods: Participants from the 24-week double-blind placebo-controlled period of CAHtalyst™ Adult (NCT04490915) continued on crinecerfont 100 mg BID (CFT/CFT) or switched from placebo to crinecerfont (PBO/CFT) in the 6-month open-label (OL) period. At Month 12 (end of OL), mean % change from baseline in GC dose was assessed (1) while maintaining or improving androstenedione (A4), with decreases in GC doses set to 0 if A4 was not ≤120% of baseline or ≤ upper limit of normal; and (2) based on observed dose without imputation of A4, to understand changes in GC-related outcomes that are independent of A4.

Results: At baseline, the 182 randomized participants had a mean GC dose of 17.6 mg/m^2/d (32.3 mg/d) hydrocortisone equivalents (HCe); >70% of participants were overweight or obese; mean homeostatic model assessment of insulin resistance (HOMA-IR) was 3.2 and 43% had insulin resistance (ie, HOMA-IR >2.5). At Month 12, mean % change from baseline in GC dose while maintaining or improving A4 from baseline was −24.6% for CFT/CFT and −29.7% for PBO/CFT. The observed mean % change from baseline in GC dose (without imputation of A4) at Month 12 was −37.4% for CFT/CFT and −36.1% for PBO/CFT, with observed mean GC doses of 10.8 mg/m^2/d (19.9 mg/d) HCe and 11.0 mg/m^2/d (19.7 mg/d) HCe for CFT/CFT and PBO/CFT, respectively. Among participants who were overweight/obese at baseline (BMI ≥25 kg/m^2), 27.4% (23/84) and 38.9% (14/36) in the CFT/CFT and PBO/CFT groups, respectively, achieved >5% reduction in weight at Month 12. Among participants with insulin resistance at baseline (HOMA-IR >2.5), mean change from baseline in HOMA-IR at Month 12 was −1.1 for CFT/CFT ($n = 45$) and −2.0 for PBO/CFT ($n = 22$).

Conclusions: Adults with CAH who received up to 1 year of crinecerfont achieved substantial reductions in GC dose, and participants who were overweight or obese showed remarkable improvements in weight and insulin resistance. These results suggest that crinecerfont can reduce the risk of known complications associated with long-term supraphysiologic GC treatment in patients with CAH.

Abstract citation ID: lvag096.234

P22 - ECE_3241 - The effect of pausing prednisolone 1 or 2 days before an ACTH test in patients on long-term prednisolone treatment—a RESCUE sub-study

Sema Okutan[1], Nanna Thurmann Jørgensen[1,2], Dorte Glintborg[3,4], Lise Sofie Bislev[5], Hajir Al-Jorani[4], Simon Bøggild Hansen[5,7], Victor Brun Boesen[1], Anja Fenger Dreyer[4], Jelena Stankovic[5,7], Louise Lehmann Christensen[3,4], Randi Tei[5], Ulla Feldt-Rasmussen[8], Marianne Klose[1], Jens Otto Lunde Jorgensen[5,7], Marianne Andersen[4] and Stina Willemoes Borresen[1]

[1]Department of Nephrology and Endocrinology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark; [2]Kongens Lyngby, Denmark; [3]Department of Endocrinology, Odense University Hospital, Odense, Denmark; [4]Department of Clinical Research, University of Southern Denmark, Odense, Denmark; [5]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus, Denmark; [6]Department of Endocrinology, Odense University Hospital, Odense, Denmark; [7]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark; [8]Department of Growth and Reproduction, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark

Introduction: Glucocorticoid-induced adrenal insufficiency is a known complication of long-term prednisolone therapy. Current guidelines vary on how long prednisolone should be withheld before assessing adrenal function. This study aimed to quantify how prednisolone withdrawal duration (0, 1, or 2 days) affects ACTH test outcomes, for understanding the potential impact of pause length on the interpretation of adrenal function in patients on long-term prednisolone.

Methods: This study was a sub-study of the ongoing randomized clinical trial RESCUE, investigating glucocorticoid-induced adrenal insufficiency. Forty patients (mean age 73 years ± 7.3) with polymyalgia rheumatica and/or giant cell arteritis treated with prednisolone for ≥3 months, all at a current daily dose of 5 mg, underwent 3 standard ACTH (Synacthen®) tests within median 21 days (range 15-30). The participants underwent the 1-day pause ACTH test at screening and were then alternately scheduled for the 0-day or 2-day visit. It was aimed to include 50% with insufficient ACTH response at the screening visit; defined as 30-minute cortisol <420 nmol/L (local validated cut-off). Plasma cortisol was analysed by Elecsys® Cortisol II. Serum prednisolone was measured after 1 and 2 days of prednisolone pause and analysed by LC-MS/MS, with the lowest detectable concentration limit of 1.0 nmol/l. Concentrations below the limit were listed as 0.5 nmol/L in data analysis. One-factor ANOVA with repeated measurements and paired t-tests were used to compare ACTH test results.

Results: Stimulated 30-minute cortisol increased with increasing time since last prednisolone dose ($F = 127$; $P < .0001$). After 1 vs 2 days of prednisolone pause, mean 30-minute cortisol increased by 71 nmol/L (95% CI: 53-88; $P < .001$), whereas ACTH did not differ (mean difference 0.36 pmol/L; 95% CI: −0.37-1.10; $P = .3$). Stimulated 30-minute cortisol was <420 nmol/L in 30/40 (75%),

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

19/40 (48%), and 14/40 (35%) after 0-, 1- and 2-days prednisolone pause, respectively. Mean ± SD serum prednisolone concentrations were 1.1 ± 0.6 nmol/L after 1 day and 0.9 ± 1.7 nmol/L after 2 days of prednisolone pause.

Conclusions: Extending the prednisolone pause from 1 to 2 days increased stimulated 30-minute cortisol by 71 nmol/L and reduced the proportion of tests <420 nmol/L by 13%. Serum prednisolone concentrations were very low after both 1- and 2-day prednisolone pauses, indicating minimal clinically relevant serum presence. These results characterise the effect of prednisolone withdrawal duration on ACTH test performance; determining the optimal pause may vary depending on the clinical purpose of testing.

Abstract citation ID: lvag096.235

P23 - ECE_3266 - Self-injection matters: behaviours and experiences during adrenal crisis in adults with adrenal insufficiency

Jennie Brown[1], Shashi Hirani[1], Kathleen Mulligan[1], Stanton Newman[1], Stephanie Baldeweg[2], Ashley B. Grossman[3], Philippa Sharman[4], Pat McBride[5] and Sofia Llahana[1]

[1]School of Health and Medical Sciences, City St George's, University of London, London, United Kingdom; [2]University College London Hospital, London, United Kingdom; [3]Royal Free Hospital, London, United Kingdom; [4]Addison's Disease Self-Help Group, Bristol, United Kingdom; [5]The Pituitary Foundation, Bristol, United Kingdom

Background: Adrenal crisis (AC) in patients with adrenal insufficiency has an estimated incidence of 6%-8% per year and is the leading cause of death (mortality rate 0.5 per 100 patient-years). Deaths from AC are potentially preventable by immediate administration of parenteral hydrocortisone. Limited available evidence suggests <25% of patients successfully self-inject or are assisted in the community, while preventative measures and behaviours during AC are underexplored.

Objectives: This cross-sectional study investigated factors associated with hospitalisation due to AC and length of stay.

Method: 561 adults with adrenal insufficiency who had experienced an AC within the previous 12 months completed an online questionnaire about their most recent AC. Recruitment was via 3 patient advocacy groups and 28 endocrine clinics across the UK. Participants were asked whether they: possessed and carried an emergency hydrocortisone injection kit, self-injected or required assistance, needed intervention by an ambulance or attendance at an accident and emergency (A & E) department, and whether hospitalisation due to AC occurred, including length of hospital stay.

Results: During their last AC, 18% of patients self-injected, 39% needed community assistance, 20% were injected in an ambulance/by a paramedic and 23% received their injection in A & E. Of those who self-injected, 58% were hospitalised due to AC compared with those needing assistance within the community (66%) or being injected in an ambulance or A & E (92%). Patients being injected in an ambulance/by a paramedic waited most frequently <30 minutes (49%), however 50% of patients attending A & E waited >60 minutes for their injection. Confidence ratings for self-injecting were higher in people who self-injected, compared with those needing assistance. The most common reasons for participants not self-injecting was being too unwell (57%), preferring a healthcare professional to inject (14%) and being unaware of AC symptoms or that a hydrocortisone injection was needed (11%). No significant differences in hospitalisation rates or length of stay were observed between participants who possessed an emergency steroid card, or carried an injection kit, and those who did not. Confidence in self-injection and prior injection training was also not associated with differences in hospitalisation or length of stay.

Conclusions: Patients who self-injected were around 20% less likely to be hospitalised compared to those who required assistance. These findings highlight the critical importance of early recognition of AC and prompt, independent administration of hydrocortisone in the home or community setting to reduce the need for hospitalisation.

Abstract citation ID: lvag096.236

P24 - ECE_3470 - Diagnostic value of basal and ACTH-stimulated 17-hydroxyprogesterone and 17OHP/cortisol ratio in genetically characterised 21-hydroxylase deficiency

Giordano Paolucci[1,2], Claudio Urbani[1], Luisa Pignata[1], Marianna Scordo[1], Emilio Fiore[1], Luca Manetti[1], Ferruccio Santini[1] and Massimo Tonacchera[1]

[1]Endocrinology Unit, University Hospital of Pisa, Pisa, Italy; [2]Endocrinology, University Hospital Of Pisa, Pisa, Italy

Background: 21-hydroxylase deficiency (21OHD) is the most common cause of congenital adrenal hyperplasia (CAH). Diagnosis relies on basal and ACTH-stimulated 17-hydroxyprogesterone (17OHP) measurements; however, optimal diagnostic thresholds and the utility of derived indices, such as the 17OHP/cortisol ratio, remain uncertain. Whether biochemical testing can reliably identify heterozygous *CYP21A2* carriers is also unclear.

Objective: To evaluate the diagnostic performance of basal and ACTH-stimulated 17OHP, cortisol, and the peak 17OHP-to-peak cortisol ratio (17OHPmax/CORTmax) for identifying genetically confirmed 21OHD, and to assess their ability to discriminate carriers from wild-type subjects. As a secondary aim, we characterized rare *CYP21A2* missense variants using *in silico* and structural tools.

Methods: We retrospectively analyzed 104 patients (83 women) who underwent a standard 250-µg ACTH test and *CYP21A2* genotyping. Based on genotype, 33 subjects had CAH (5 salt-wasting, 1 simple virilizing, 27 non-classic), 30 were heterozygous carriers, and 41 were wild-type. Basal, 30- and 60-minute 17OHP and cortisol were measured by chemiluminescent immunoassays; 17OHPmax, CORTmax, Δ17OHP, and 17OHPmax/CORTmax were derived. ROC curves were constructed using genotype as the reference standard. Three rare missense variants (p.Arg150Pro, p.His204Tyr, p.Leu289Phe) were assessed with prediction scores (CADD, PolyPhen-2, SIFT, GERP), structure-based tools (HOPE, Missense3D), mapping on the CYP21A2 crystal structure, and ACMG/AMP classification (VarSome).

Results: Basal 17OHP discriminated CAH from unaffected subjects (carriers + wild-type) with good accuracy (AUC 0.92); a cut-off >2.815 µg/L yielded 84.9% sensitivity and 85.9% specificity. Diagnostic performance improved for stimulated values: peak 17OHP >9.645 µg/L achieved 93.3% sensitivity and 95.7%

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

specificity, outperforming Δ17OHP and cortisol-based parameters. The 17OHP_max/CORT_max ratio showed the best discrimination (AUC 0.99); a cut-off >0.35 provided 96.6% sensitivity and 94.4% specificity, while raising it to >0.63 increased specificity to 98.6% with 89.7% sensitivity. No basal or stimulated parameter, including 17OHP_max/CORT_max, reliably separated carriers from wild-type subjects (AUCs <0.80). All three rare variants were extremely uncommon in gnomAD and classified as variants of uncertain significance (VUS) by ACMG criteria; structural mapping suggested a potential effect of p.Leu289Phe near the active site, whereas p.Arg150Pro and p.His204Tyr showed only subtle predicted structural impact.

Conclusions: In a genotyped cohort, ACTH-stimulated 17OHP and, particularly, the 17OHPmax/CORTmax ratio provided excellent diagnostic accuracy for 21OHD, outperforming basal 17OHP. However, heterozygous carriers could not be reliably identified biochemically, underscoring the need for *CYP21A2* genotyping in the diagnostic "grey zone." Integrated *in silico* and structural analyses are helpful but not sufficient to definitely classify rare missense variants.

Abstract citation ID: lvag096.237

P25 - ECE_3587 - Ordinary circadian rhythm and physiological variation of diurnal salivary cortisol levels in healthy young adults

Dimitra Adamou[1], Anastasia Evangelatou[2], Evangelia-Georgia Kostaki[3], Angeliki Papapanagiotou[2], Athanasios Kalogeropoulos[4], Charalampos Kalogeropoulos[4], Vasilis Lerakis[4], Eleftherios Pavlou[4], George Chrousos[5,6], Petros Sfikakis[7] and Maria Yavropoulou[8]

[1]Hematology Laboratory, Laiko University Hospital, Athens, Greece; [2]Department of Biological Chemistry, Laiko University Hospital, National and Kapodistrian University of Athens, Athens, Greece; [3]Department of Hygiene, Epidemiology and Medical Statistics, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [4]Medical School, National and Kapodistrian University of Athens, Med-Cort UOA Student Research Team, Athens, Greece; [5]Center for Adolescent Medicine and UNESCO Chair in Adolescent Health Care, First Department of Pediatrics, Medical School, National and Kapodistrian University of Athens, Aghia Sophia Children's Hospital, Athens, Greece; [6]University Research Institute of Maternal and Child Health and Precision Medicine, Athens, Greece; [7]First Department of Propaedeutic and Internal Medicine, Joint Academic Rheumatology Program, Laiko University Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [8]First Department of Propaedeutic Internal Medicine, Joint Academic Rheumatology Program, Endocrinology Unit, Laiko University Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Background: Various associations between health, disease status, stress and cortisol have been inconsistent due to the poor reliability of diurnal cortisol metrics, hindering research in this area. Salivary cortisol is a reliable, non-invasive marker of bioavailable cortisol. Well-defined reference ranges derived from healthy young adults under non-stressful conditions remain limited.

Objective: To characterize the diurnal pattern of salivary cortisol and identify factors influencing daily- cortisol-production in healthy young adults under non-stressful conditions. Reference values for individual Area-Under-the-Curve with respect to ground (AUC-g) were established to define the physiological range of diurnal-cortisol-production.

Study-Design: Cross-sectional study conducted under both controlled (hospital) and home conditions.

Methods: A total of 131 healthy medical students (median age: 19 years; 47 males, 84 females) were included in the final analysis. Salivary cortisol samples were collected at four predefined timepoints (08:00, 12:00, 18:00, and 22:00) across three consecutive weekdays. Morning serum cortisol and plasma adrenocorticotropic hormone(ACTH) levels were obtained on Day-1. Salivary and serum cortisol concentrations were measured using electrochemiluminescence immunoassay (ECLIA)(Cobas-e801analyser). Plasma ACTH levels were determined using chemiluminescence immunoassay(CLIA)(LIAISON-platform). On Day-1, morning salivary sampling was performed in a hospital-setting, whereas all remaining salivary samples, including those collected on Days-2 and 3 and the non-morning samples on Day-1, were obtained by participants at home following standardized instructions. Perceived stress was prospectively assessed using the 14-item Perceived-Stress-Scale (PSS-14) via structured questionnaires. Lifestyle factors and the occurrence of acute stress events were recorded in real-time during the sampling period using a smartphone-based application. Diurnal-cortisol-production was quantified by calculating AUC-g. Linear regression analyses and linear mixed-effects models were applied.

Results: Diurnal-cortisol-production was higher on Day-1 compared with Days-2 and 3 (median AUC-g 3.78 vs 3.34 and 2.96, respectively; $P < .001$). Analysis of Days-2 and 3 together showed a median AUC-g of 3.18, with a 95% reference interval of 1.61-7.14. Day-1 morning saliva cortisol (median 0.74 µg/dl) was higher than Day-2 (median: 0.51 µg/dl) and Day-3 (median: 0.53 µg/dl)($P < .001$), probably reflecting anticipatory stress related to hospital attendance on Day-1. Females exhibited higher morning salivary and serum cortisol levels and greater PSS than males. Lifestyle-factors, including sleep duration, exercise, smoking, alcohol and coffee consumption, were not significantly associated with diurnal-cortisol-production.

Conclusions: In healthy young adults, salivary diurnal-cortisol-production demonstrates modest sex-related differences and limited influence from everyday lifestyle factors. A clear understanding of ordinary cortisol circadian patterns under non-stressful, everyday conditions can enhance the reliability of future research exploring biological, clinical, and psychological associations of cortisol-regulation.

Abstract citation ID: lvag096.238

P26 - ECE_1581 - Salivary cortisone identifies clinically relevant mild autonomous cortisol secretion

Marcus Imamovic, Tommy Olsson and Per Dahlqvist

Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

Objective: Adrenal incidentalomas are frequently detected on imaging. A substantial proportion of these are cortisol secreting adenomas without overt Cushingoid features, ie, mild autonomous cortisol secretion (MACS). MACS is associated with cortisol excess

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

comorbidity, including hypertension, diabetes, and osteoporosis. Current diagnostic criteria rely on serum cortisol after 1 mg dexamethasone suppression testing (DST), although total serum cortisol is influenced by cortisol binding globulin levels and may overestimate biologically active cortisol. Salivary cortisone correlates with serum free cortisol and may represent a more physiological measure. Previous studies have shown that post DST salivary cortisone cut-offs at 2.7-3.5 nmol/L have high sensitivity and specificity for diagnosing Cushing's syndrome. We evaluated whether post DST salivary cortisone is associated with cortisol excess comorbidity in patients with adrenal incidentalomas.

Design and Methods: We performed a retrospective cross-sectional study on patients with newly detected adrenal incidentalomas, ≥10 mm, undergoing post DST salivary cortisone testing at our tertiary centre (February 2016-April 2025). Patients with Cushing's syndrome, primary aldosteronism, pheochromocytoma, adrenal malignancy, and on oral glucocorticoids were excluded. Optimal post DST cut-offs were identified by receiver operating curve analyses using the dichotomous variable of having all three comorbidities: hypertension, diabetes, and osteoporosis [Y/N]. Associations with hypertension, diabetes, osteoporosis, and combined comorbidity outcomes were analysed by logistic regression adjusted for age, sex and smoking.

Results: Ultimately, 254 patients were included. The optimal post DST salivary cortisone cut-off was 3.22 nmol/L (area under the curve 0.80), with 83% sensitivity and 79% specificity. A salivary cortisone cut-off of 6.39 nmol/L was needed to yield a 95% specificity. Patients with post DST salivary cortisone above 3.22 nmol/L were older and had higher prevalence of hypertension (79% vs 58%), diabetes (32% vs 20%), and osteoporosis (25% vs 9%) compared to those below the cut-off. In adjusted regression analyses, salivary cortisone above 3.22 nmol/L was associated with higher odds of osteoporosis (OR 2.46, $P = .05$) and combined morbidity (all three comorbidities OR 12.6, $P < .05$). At >6.39 nmol/L, strong associations were observed for hypertension (OR 8.67, $P < .05$), osteoporosis (OR 7.54. $P < .01$), and multiple comorbidities (≥2 comorbidities OR 3.61, $P < .05$; all three comorbidities OR 29.6. $P < .05$).

Conclusions: Post DST salivary cortisone identifies patients with clinically relevant cortisol excess comorbidity. Salivary cortisone may serve as a physiologically meaningful alternative to serum cortisol in the evaluation of adrenal incidentalomas.

Abstract citation ID: lvag096.239

P27 - ECE_2005 - Macrophage immunometabolic dysfunction in cortisol-producing adenoma patients with mild autonomous and overt cortisol secretion

Ana Crastin[1,2,3], Ezra Leander Onesimu[1], Lorenzo Tucci[1,4], Alessandra Mangone[1,5], Vittoria Favero[1,6], Chiara Parazzoli[1,5], Oskar Podstawka[1,7], Meng Jie Xu[1,8], Alessandro Prete[1,3,9], Rowan Hardy[1,2,3] and Cristina L Ronchi[1,9]

[1]Department of Metabolism and Systems Science, University of Birmingham, Birmingham, United Kingdom; [2]Department of Biomedical Sciences, University of Birmingham, Birmingham, United Kingdom; [3]National Institute for Health and Care Research (NIHR) Birmingham Biomedical Research Centre, University of Birmingham, Birmingham, United Kingdom; [4]Medical and Surgical Sciences Department, Alma Mater Studiorum University of Bologna, Bologna, Italy; [5]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [6]Department of Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [7]Cancer Research UK Clinical Trials Unit (CRCTU), University of Birmingham, Birmingham, United Kingdom; [8]Taihe Hospital, Hubei University of Medicine, Shiyan, China; [9]Department of Endocrinology, Queen Elizabeth Hospital Birmingham NHS Trust, Birmingham, United Kingdom

Background: Cushing's syndrome(CS) is characterised by sustained cortisol excess and profound immune disturbance. However, the direct effects of endogenous cortisol overproduction on macrophage phenotype and cellular metabolism remain incompletely understood. In particular, the immunological consequences of mild autonomous cortisol secretion(MACS) associated with cortisol-producing adrenocortical adenomas (CPA) in the absence of overt CS are poorly defined. We hypothesised that macrophage activation, polarisation, and bioenergetic function are altered in both CPA-CS and CPA-MACS.

Methods: Human macrophages were polarised toward a pro-inflammatory (M1-like) state using TNFα and IFNγ, followed by exposure to 10% serum from 18 patients (12 CPA-MACS, 6 CPA-CS) and 10 age- and sex-matched controls with endocrine-inactive adenomas(EIA). Cytokine secretion and gene expression were measured by ELISA and RT-qPCR. Mitochondrial function, ATP production, glycolytic activity, and phagocytosis were assessed after 48 hours. Associations with cortisol secretion and tumour characteristics were examined.

Results: Pro-inflammatory IL6 secretion was reduced in macrophages treated with CPA-MACS (0.72-fold, $P = .071$) and CPA-CS serum (0.50-fold, $P = .004$) compared with EIA, while IL6 mRNA showed a similar trend. The M2 marker CD163 modestly increased in CPA-CS (1.32-fold, $P = .258$) but not in CPA-MACS, correlating with post-dexamethasone cortisol levels and tumour size. TGFβ concentrations were significantly elevated in CPA-CS ($P = .012$), and the IL6/CD163 ratio increased (2.41-fold, $P = .003$), indicating a cortisol-dependent shift toward an anti-inflammatory phenotype. Mitochondrial viability increased in CPA-MACS ($P = .059$) and CPA-CS ($P = .005$), accompanied by reduced ATP production and maximal respiration ($P < .05$) and enhanced glycolytic activity($P < .01$) in CPA-CS. Phagocytosis was impaired in both CPA-MACS ($P = .014$) and CPA-CS ($P = .076$). Glucocorticoid receptor blockade with RU486 partially restored mitochondrial respiration, spare capacity, and bioenergetic balance.

Conclusions: Serum from patients with CPA-MACS and CS suppresses inflammatory macrophage responses, promotes alternative polarisation, disrupts mitochondrial metabolism, and impairs phagocytosis. These findings demonstrate that mild autonomous cortisol excess significantly modulates macrophage immunometabolism, potentially contributing to systemic immune dysfunction and altered tissue homeostasis.

Abstract citation ID: lvag096.240

P28 - ECE_2507 - Imaging evidence for a continuum from low-renin hypertension to Primary Aldosteronism

Felix Herr[1], Lucia Krüger[2], Júnia Ribeiro De Oliveira Longo Schweizer[2], Friederike Völter[2], Nabeel Mansour[1], Tracy Ann Williams[2], Jens Ricke[1], Max Seidensticker[1],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Martin Bidlingmaier[2], Christine Schmid-Tannwald[1], Clemens Cyran[1], Martin Reincke[2] and Isabel Stüfchen[2]
[1]Department of Radiology, LMU University Hospital, Munich, Germany; [2]Munich, Germany

Background: Primary aldosteronism (PA) is increasingly recognized as a spectrum disorder with recent studies suggesting low-renin hypertension (LRH) as a potential precursor stage. Adrenal morphology across distinct biochemical stages of this spectrum remains insufficiently characterized. This study aimed to systematically define adrenal imaging phenotypes across PA and LRH compared with normal-renin hypertension (NRH) and normotensive controls.

Methods: This retrospective study included 196 patients evaluated for suspected PA with available imaging data. PA was defined by aldosterone-to-renin ratio (ARR) >12 ng/mU with hypokalemia or post-confirmatory aldosterone >42.5 ng/L ($n = 95$). NRH was defined by normokalemia and either a baseline direct renin concentration >12 mU/L or a baseline plasma aldosterone concentration below limit of quantification (28 ng/L) together with an ARR <12 ng/mU ($n = 42$); remaining patients were classified as LRH ($n = 59$). Aldosterone was measured by LC-MS. Fifty age- and sex-matched normotensive individuals served as controls. Imaging features were analyzed on CT or MRI differentiating between diffuse adrenal enlargement, micronodules (<10 mm), adenoma/indeterminate lesions (≥10 mm), and nodular hyperplasia. Image segmentation was performed independently and blinded by two radiologists. Lesions were evaluated by size and attenuation (HU) or MRI signal drop.

Results: Adrenal morphometry, including body and limb width, was comparable across groups including normotensive controls. The overall prevalence of adrenal enlargement was high and similar in all groups, suggesting it to be common and not specific to any hypertension subtype. Imaging pathologies including micronodules, adenoma/indeterminate lesions, and nodular hyperplasia were rare in controls (2.0%), less frequent in NRH (14.3%), and increasingly prevalent in LRH (35.6%) and PA (42.1%) ($P < .001$). The same difference held for lesions ≥10 mm ($P < .001$). Most lesions were unilateral, more often affecting the left adrenal gland, whereas bilateral involvement and nodular hyperplasia were observed exclusively in PA and LRH.

Conclusions: Radiomorphological findings support LRH as an early stage within the PA spectrum, characterized by a progressive increase in adrenal imaging abnormalities preceding overt biochemical PA.

Abstract citation ID: lvag096.241

P29 - ECE_2951 - Modified release hydrocortisone, a new treatment for congenital adrenal hyperplasia due to 21-hydroxylase deficiency: one-year outcomes from a "real-world evidence" study

Erminio M. Crescenzo[1], Chiara Simeoli[1], Angelica Larocca[1], Nicola Di Paola[1], Gennaro Puocci[2], Maria Cimmino[1], Claudia Pivonello[3], Mariarosaria Negri[1,4], Annamaria Colao[1,5] and Rosario Pivonello[1,5]
[1]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione—Università Federico II di Napoli, Naples, Italy; [2]Andrology Unit, Department of Clinical Medicine, Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy; [3]Dipartimento di Sanità Pubblica, Università degli Studi di Napoli Federico II, Naples, Italy; [4]Dipartimento di Psicologia e Scienze della Salute, Università Telematica Pegaso, Naples, Italy; [5]UNESCO Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy

Management of congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21OHD) involves chronic glucocorticoid (GC) replacement in patients with adrenal insufficiency while controlling androgen excess. Treatment with conventional GCs is characterized by regimens with unphysiological peaks and troughs, often associated with GC overexposure and/or poor androgen control. In this scenario, the recently approved twice daily modified-release hydrocortisone (MR-HC) represents a useful tool for a more accurate reproduction of physiological cortisol circadian rhythm, particularly mimicking overnight cortisol increase for better control morning surge of adrenocorticotropic hormone (ACTH) and androgens.The current study aimed at investigating the impact of the switch from conventional GCs to MR-HC on disease control, GC daily dose, hormonal and biochemical profiles in 61 CAH patients treated for 12 months with MR-HC. Thirty-nine (63.9%) females and 22 (36.1%) males, 45 with classic-form [29 (47.5%) with salt-wasting and 16 (26.2%) with simple-virilizing] and 16 (26.2%) with non-classic form, with a median age of 30.9 ± 9.4 yrs, were enrolled. Patients were switched from conventional GC regimens [immediate or dual-release hydrocortisone (IR/DR-HC) or cortisone acetate (CA)] (25.43 ± 8.9 mg/day HC equivalents) to MR-HC (24, 91 ± 8,1 mg/day). The primary outcome was the change from baseline to 12 months of MR-HC in the percentage of patients with good disease control, defined as a morning 17OH-progesterone (17OHP) <12 ng/ml and androstenedione within the reference ranges, according to the phase 3 study. Secondary outcomes included changes in GC total daily dose, hormonal and biochemical parameters. At month 12, the percentage of patients with controlled disease significantly increased: controlled patients were 59% vs 32.8% at baseline ($P = .006$). Particularly, a significant decrease in 17OHP [6.33 ± 11.36 vs 12.77 ± 15.93 ULN at baseline ($P = .002$)] and androstenedione [0.87 ± 1.33 vs 0.95 ± 0.76 ULN at baseline ($P = .025$)] was observed at month 12. Furthermore, a reduction in morning ACTH [10.85 ± 10.3 vs 156 ± 180 pg/mL at baseline ($P = .001$)] was observed at month 12, while morning cortisol increased [10.14 ± 15.35 vs 84.3 ± 49 ng/ml at baseline ($P = .001$)] compared to baseline. Lastly, baseline MR-HC dose was reduced by 4.8% [23.27 ± 8.1 mg/day vs 24.91 ± 8,13 mg/day at baseline ($P = .005$)] at month 12. Data from the current real-world experience showed that MR-HC significantly improved disease control while reducing GC daily dose in 21OHD CAH patients.

Abstract citation ID: lvag096.242

P30 - ECE_3844 - Patients with primary aldosteronism and mild autonomous cortisol secretion (MACS) have increased hybrid steroids compared to patients without MACS: evidence from LC-MS/MS steroid profiling

Georgiana Constantinescu[1,2], Christina Pamporaki[1], Sybille Fuld[1], Manuel Schulze[3], Nicole Bechmann[4], Mirko Peitzsch[4], Jens Passauer[1], Hanna Remde[5], Lydia Kuerzinger[5], Sven Gruber[6], Jimmy Masjkur[7],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Martin Fassnacht[5], Felix Beuschlein[6], Jun Yang[8], Jacques Lenders[9] and Graeme Eisenhofer[1]
[1]Universitätsklinikum Carl Gustav Carus Dresden, Dresden, Germany; [2]Iași, Romania; [3]Center for Information Services and High Performance Computing (ZIH), Technische Universität Dresden, Department of Distributed and Data Intensive Computing, Dresden, Germany; [4]Institute of Clinical Chemistry and Laboratory Medicine, University Hospital "Carl Gustav Carus", Dresden, Germany; [5]Department of Medicine I, Würzburg University Hospital, Würzburg, Germany; [6]Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, University Hospital, Zurich, Switzerland; [7]eSwiss Medical and Surgical Center, Klinik Stephanshorn, St Gallen, Switzerland; [8]Center of Endocrinology and Metabolism, Hudson Institute of Medical Research, Department of Medicine, Monash University, Clayton, Victoria, Australia, Melbourne, Australia; [9]Department of Internal Medicine, Radboud University Medical Center, Nijmegen, The Netherlands

Introduction: Primary aldosteronism (PA) is the most frequent cause of endocrine hypertension, associated with increased cardiovascular and renal risk. Previous studies indicate that approximately 15%-30% of patients with PA have concomitant mild autonomous cortisol secretion (MACS). However, the steroidogenic profile of patients with PA and MACS remains incompletely characterized.

Methods: This study involved analysis of 15 adrenal steroids using liquid chromatography–tandem mass spectrometry (LC-MS/MS) in patients with PA ($n = 96$) with MACS ($n = 18$) and without ($n = 78$), comparing with patients with adrenal adenomas with ($n = 202$) and without MACS ($n = 40$). MACS was defined by a post–1 mg overnight dexamethasone suppression test (DST) serum cortisol concentration >50 nmol/L. Baseline adrenal steroid concentrations were analyzed using linear regression models adjusted for age and sex.

Results: Patients with MACS showed significantly higher baseline concentrations of cortisol ($P = .0003$) than patients with adenomas without MACS. Among mineralocorticoid precursors, the hybrid steroids 18-oxocortisol ($P = .006$) and 18-hydroxycortisol ($P < .0001$) were significantly increased, indicating enhanced hybrid steroidogenesis in this subgroup compared with patients without MACS. 11-deoxycorticosterone levels were also significantly increased ($P = .003$). Patients with MACS exhibited lower concentrations of the adrenal androgen DHEA ($P = .016$). No significant differences were observed for aldosterone ($P = .56$), androstenedione ($P = .29$), 11-deoxycortisol ($P = .75$), or corticosterone ($P = .21$). In the subgroup analysis restricted to patients with PA, those with MACS exhibited significantly higher baseline concentrations of the hybrid steroids 18-oxocortisol ($P = .0088$) and 18-hydroxycortisol ($P = .0003$), as well as increased 11-deoxycorticosterone ($P = .0119$), compared with PA patients without MACS. No significant differences were observed for androstenedione ($P = .332$), 11-deoxycortisol ($P = .952$), corticosterone ($P = .485$), or cortisol ($P = .301$).

Conclusions: Patients with PA and MACS present a distinct steroid profile with selective excess of hybrid steroids and mineralocorticoid precursors, accompanied by reduced adrenal androgen production as compared to PA patients without MACS. LC-MS/MS-based steroid profiling provides additional biochemical information for identification and characterization of cortisol cosecretion in PA beyond the dexamethasone suppression test.

Abstract citation ID: lvag096.243

P31 - ECE_2346 - Adrenal reprogramming after menopause under repeated weight fluctuations

Linghui Kong[1], Coralie Frimat[2], Nicolo Faedda[1], May Fayad[1], Xiaomin Li[1], Isabelle Giscos-Douriez[1], Fabio Fernandes-Rosa[1], Bruno Feve[3,4,5], Antoine Ouvrard-Pascaud[6], Maria-Christina Zennaro[1,7] and Sheerazed Boulkroun[1]
[1]Université Paris Cité, Inserm, PARCC, Paris, France; [2]Inserm U1096, UFR santé, Rouen, France; [3]Centre de Recherche Saint-Antoine UMR_S938, Sorbonne Université-Inserm, Paris, France; [4]Institut Hospitalo-Universitaire de Cardio-Métabolisme et Nutrition (ICAN), Paris, France; [5]Service d'Endocrinologie-Diabétologie, Centre de référence des maladies rares de l'insulino-sécrétion et de l'insulino-sensibilité (PRISIS), Hôpital Saint-Antoine, Assistance Publique Hôpitaux de Paris, Paris, France; [6]Inserm U1096, UFR Santé, Rouen, France; [7]Service de Génétique, Assistance Publique Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Paris, France

Overweight and obesity represent major public health challenges and only 20% of overweight individuals achieve sustainable weight loss, leading to repeated cycles of weight loss and gain. Weight cycling is associated with an increased risk of developing metabolic syndrome. Furthermore, the menopausal transition is associated with a 60% increase in the incidence of metabolic syndrome, which is associated with increased cardiovascular mortality. Aldosterone, produced by the adrenal gland, plays a role in regulating metabolic processes and exhibits a pathophysiological link to visceral adiposity.

Our objective was to investigate the role of the adrenal gland in postmenopausal cardiometabolic complications related to weight cycling.

We developed an experimental model in which female mice were either ovariectomized (OVX, mimicking post-menopause) or not (non-OVX, pre-menopause) and exposed to three cycles of high fat diet/standard diet (Yoyo) or maintained on standard diet throughout. After each dietary phase, blood samples were collected for metabolic profiling and steroid measurements, and multiple tissues (adrenal, heart, adipose tissue …) were collected for further analyses.

Yoyo dieting induced a greater weight gain in OVX mice compared with non-OVX controls. This was accompanied by reduced metabolic adaptability during weight cycling. Adrenal steroidogenic responses to the yoyo diet differed according to ovarian hormone status and evolved progressively across cycles. OVX mice on the yoyo diet displayed increased adrenal gland weight, consistent with dynamic changes in adrenocortical proliferation. Histology and immunofluorescence revealed marked adrenal cortex dysplasia, including loss of zona glomerulosa (ZG) and zona fasciculata (ZF) zonation. OVX triggered a time-dependent gonadal-like transcriptional reprogramming in the adrenal cortex, followed at later stages by structural remodeling and fibrosis. Yoyo diet did not substantially modify OVX-induced adrenal remodeling and triggered only limited transcriptional responses in non-OVX mice.

Collectively, these findings indicate that OVX reprograms adrenal plasticity, compromising normal metabolic and endocrine adaptability. Although repeated dietary cycling does not initiate this remodeling, it induces dysregulation of adrenal steroid hormone production and perturbs adrenocortical proliferative dynamics.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.244

P32 - ECE_3469 - Noninvasive differentiation of adrenal adenomas, pheochromocytomas, and malignant tumors using CT radiomics

Karolina Węgrzyn[1], Anna Grochowska[2], Katarzyna Sitarz[3], Alicja Hubalewska-Dydejczyk[1] and Marta Opalinska[1]
[1]Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [2]University Hospital in Krakow, Krakow, Poland; [3]Department of Clinical Genetics and Rare Diseases, Medical University of Silesia, Katowice, Poland

Background: Non-contrast computed tomography (CT) remains the standard imaging modality for characterizing adrenal lesions and guiding subsequent clinical management. Conventional assessment relies on tumor size, density, and lipid content; however, these parameters may lack sufficient specificity, occasionally resulting in unnecessary surgical interventions or delayed malignancy diagnosis. Radiomics offers advanced quantitative image analysis capable of capturing tumor heterogeneity beyond visual assessment. This study aimed to evaluate whether CT-derived texture features can improve differentiation of adrenal lesions.

Methods: In this single-center retrospective analysis, adrenal incidentalomas from patients treated at the Clinic of Endocrinology, Oncological Endocrinology, and Nuclear Medicine, University Hospital Krakow (2017-2025) were reviewed. Lesions were assessed in a native CT scan and confirmed histopathologically. Eighty-two focal adrenal lesions from 80 patients (58 women, 22 men) were included: 22 adenomas, 35 pheochromocytomas, 16 carcinomas, 3 oncocytomas, 2 borderline oncocytic tumors, and 3 oncocytic carcinomas. Manual segmentation of lesions on native-phase imaging was performed, followed by extraction of first- (GLRLM_GreyLevelNonUniformity) and second-order texture parameters (IntensityBasedRobustMeanAbsoluteDeviation (IBRAMD) and IntensityHistogramEntropyLog10 (IHEL 10) using Local_Image_Feature_Extraction (LIFEx) software. Diagnostic performance was assessed via receiver operating characteristic (ROC) analysis for individual features and multivariable logistic regression for combined models. Statistical analyses were conducted using STATISTICA 13.3.

Results: When integrated with tumor density, selected texture parameters GLRLM, IBRMAD, and Intensity IHEL10 demonstrated significant discriminatory potential. These parameters differentiated adenomas from pheochromocytomas ($P < .01$), adenomas from carcinomas ($P < .01$), and pheochromocytomas from adrenal carcinomas ($P < .01$ for GLRLM; $P = .97$ for IBRMAD; $P = .85$ for IHEL10). For adenomas from pheochromocytomas the texture-based feature HU + GLRLM achieved the highest discriminative ability, with an AUC of 0.95 (SE = 0.03; 95% CI: 0.89-1.00; $P < .001$). For adenomas from carcinomas the texture-based feature HU + GLRLM achieved the highest discriminative ability, with an AUC of 1 (SE = 0.00; 95% CI: 1.00-1.00; $P < .001$). For pheochromocytomas from carcinomas the texture-based feature HU + GLRLM achieved the highest discriminative ability, with an AUC of 0,89 (SE = 0.04; 95% CI: 0,8-0,97; $P < .001$). Diagnostic accuracy remained high across different tumor subtypes, with minimal differences between individual parameters.

Conclusions: Preliminary data suggest that CT texture features, particularly when combined with conventional density metrics, may enhance non-invasive differentiation of adrenal adenomas, pheochoromocytomas, and malignant lesions. These findings support the potential integration of radiomic analysis into routine adrenal imaging workflows and guide clinical decision-making.

Abstract citation ID: lvag096.245

P33 - ECE_1435 - Diagnostic value of hair cortisol in mild autonomous cortisol secretion

Merve Korkmaz Yilmaz[1,2], Semih Tek[3], Aslihan Pekmezci[1], Mutlu Niyazoglu[1] and Esra Hatipoglu[1]
[1]Department of Endocrinology and Metabolism, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye; [2]Endocrinology and Metabolism, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye; [3]Department of Medical Biochemistry, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye

Background: Mild autonomous cortisol secretion (MACS) is a subtle but clinically relevant form of cortisol excess associated with increased cardiometabolic risk. Conventional biochemical tests largely capture short-term hypothalamic–pituitary–adrenal (HPA) axis activity and may not reflect cumulative exposure. Hair cortisol concentration (HCC) has been proposed as a marker of long-term exposure, but evidence in MACS remains limited.

Objective: To compare HCC between MACS and healthy controls, assess diagnostic performance, and examine associations with hormonal and metabolic parameters.

Methods: In this cross-sectional study, 73 MACS patients and 60 rigorously screened controls were included. MACS was defined according to European Society of Endocrinology guidelines. HCC was measured from the proximal 3-cm hair segment. Assessments included the 1-mg overnight dexamethasone suppression test (DST), 2-day low-dose DST, 24-hour urinary free cortisol, and late-night salivary cortisol. Correlation and receiver operating characteristic (ROC) analyses were performed.

Results: HCC was higher in MACS than controls (median 3.6 vs 1.75 ng/g; $P < .01$). In MACS, HCC correlated with waist circumference ($\rho = 0.27$; $P = .02$) and late-night salivary cortisol ($\rho = 0.25$; $P = .03$), but not with DST-based measures or urinary cortisol. ROC analysis showed modest discrimination (AUC = 0.60); the 2.7 ng/g cut-off yielded limited sensitivity and specificity.

Conclusions: HCC is elevated in MACS and reflects aspects of chronic cortisol exposure not captured by conventional testing. Although its standalone diagnostic value is modest, HCC may serve as a complementary biomarker. Prospective studies should clarify its role in risk stratification and disease progression.

Keywords mild autonomous cortisol secretion, hair cortisol concentration, adrenal incidentaloma, chronic cortisol exposure, HPA axis

Abstract citation ID: lvag096.246

P34 - ECE_2194 - Severity-based stratification and its association with lateralization and treatment outcomes in primary aldosteronism

Ju Hee Lee[1], Hayoung Kim[2], Min Jeong Park[3], A Ram Hong[4], Jeongmin Lee[5], Kyong Yeun Jung[6], Eu Jeong Ku[7],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Hyo-Jeong Kim[6], Seung Shin Park[8], Seung Hun Lee[9] and Jung Hee Kim[8]
[1]Department of Internal Medicine, Chungnam National University Hospital, Chungnam National University College of Medicine, Daejeon, South Korea; [2]Department of Internal Medicine, Gangneung Asan Hospital, University of Ulsan College of Medicine, Gangneung, South Korea; [3]Korea University Guro Hospital, Korea University College of Medicine, Seoul, South Korea; [4]Chonnam National University Hwasun Hospital, Chonnam National University Medical School, Gwangju, South Korea; [5]Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea; [6]Nowon Eulji University Hospital, Eulji University School of Medicine, Seoul, South Korea; [7]Seoul National University Hospital Healthcare System Gangnam Center, Seoul National University College of Medicine, Seoul, South Korea; [8]Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Objectives: Lateralization is a key determinant of treatment selection in primary aldosteronism. Although adrenal venous sampling is the reference standard, its use is limited by invasiveness and availability. A primary aldosteronism severity classification has been proposed to reflect integrated biochemical and clinical burden. This study aimed to evaluate the association between disease severity, lateralization results, and treatment outcomes in a large multicenter cohort.

Methods: We conducted a retrospective multicenter cohort study including patients with confirmed primary aldosteronism who underwent adrenal venous sampling at eight tertiary hospitals. Disease severity was classified as mild, moderate, or severe using the primary aldosteronism severity classification. We assessed the relationships between severity category, adrenal venous sampling results, treatment allocation, and clinical and biochemical outcomes based on international consensus criteria. Logistic regression analyses were performed to identify factors associated with complete treatment response.

Results: A total of 848 patients were included, of whom 6.1% were classified as mild, 67.5% as moderate, and 26.4% as severe. Increasing disease severity was associated with a stepwise rise in lateralization indices and a higher prevalence of lateralizing primary aldosteronism on adrenal venous sampling (23.1% in mild, 50.5% in moderate, and 75.9% in severe; $P < .001$). Complete clinical success was observed in 40.0% of patients with moderate disease and 31.7% of those with severe disease, while partial clinical success predominated in severe disease (55.0%). In contrast, biochemical surgical outcomes were consistent across severity categories ($P = .380$), with complete biochemical success achieved in 72.5% and 71.7% of patients with moderate and severe disease, respectively. Among patients with bilateral PA treated medically, clinical outcomes varied by disease severity ($P = .010$), with complete clinical response decreasing from mild to severe disease (35.1%, 26.8%, and 9.1%). Biochemical medical outcomes were comparable across severity groups ($P = .996$).

Conclusions: Disease severity classification demonstrates a strong association with adrenal venous sampling–defined lateralization and treatment selection. Severity-based stratification may provide clinically useful guidance for lateralization assessment and individualized management in primary aldosteronism

Abstract citation ID: lvag096.247

P35 - ECE_2543 - Major adverse cardiovascular events in subjects with CYP11B2-positive aldosterone-producing adrenal lesions: a cross-sectional autopsy study

Antero Ylänen[1,2], Juhani Isojärvi[1], Antti Virtanen[3], Helena Leijon[4], Tiina Vesterinen[4], Eeva Kokko[1], Ilkka Pörsti[1,2], Marianna Viukari[5], Markus Kallio[5], Pasi Nevalainen[1,2] and Niina Matikainen[5]
[1]Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [2]Department of Internal Medicine, Tampere University Hospital, Tampere, Finland; [3]Forensic Medicine Unit, Finnish Institute for Health and Welfare, Helsinki, Finland; [4]HUS Diagnostic Center, HUSLAB, Department of Pathology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [5]Endocrinology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland

Background: In addition to overt primary aldosteronism (PA), mild forms of autonomous aldosterone overproduction are linked to an increased risk for major cardiovascular events (MACE) in population studies. Aldosterone synthase (CYP11B2)–positive adenomas and nodules represent the hallmark of autonomous aldosterone secretion. However, the significance of CYP11B2–positive histopathological features for cardiovascular outcomes remains unclear.

Methods: We analysed the incidence of composite MACE, its components, and histopathological signs of cardiovascular disease using clinical registry and autopsy data from 401 consecutive individuals without known PA who experienced sudden death. Presence of aldosterone-producing adenomas/nodules (APA/APN) was assessed in bilateral adrenal samples with immunohistochemical CYP11B2 staining. This trial was registered at ClinicalTrials.gov (NCT05446779).

Findings: CYP11B2 staining identified APAs or APNs in 25 (6.2%) subjects. Their prevalence was similar in individuals younger than and older than 50 years. The MACE endpoint was identified more frequently in individuals with APA/APN than in those without (19 [76.0%] vs 178 [47.3%], $P = .006$), despite a similar profile of traditional vascular risk factors and biomarkers between the groups. In logistic regression analysis, the presence of APA/APN emerged as an explanatory factor for MACE (OR 4.76, 95% CI 1.61-14.10), alongside moderate or severe coronary artery disease (OR 6.99, 95% CI 3.89-12.53) and higher heart weight (OR 1.08, 95% CI 1.05-1.11). In addition, the presence of APA/APN was an explanatory factor for each MACE component and was associated with autopsy findings of aortic atherosclerosis and myocardial infarction.

Interpretation: Our findings link the presence of an adrenal APA/APN to autopsy–verified vascular disease and MACE, including sudden cardiac death, myocardial infarction, and stroke, in subjects without clinical PA. These associations persisted even after accounting for lifetime cardiovascular risk factors. Our results imply that previously undetected autonomous aldosterone secretion is a clinically relevant risk factor for cardiovascular morbidity and mortality and underscore the importance of adopting screening guidelines for secondary hypertension.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.248

P36 - ECE_3718 - Absorption, metabolism, excretion, and absolute bioavailability of [14C]-labeled atumelnant for treatment of congenital adrenal hyperplasia and adrenocorticotropic hormone-dependent Cushing syndrome

Xiaoli Wang[1,2], Rosa Luo[3], Daria Stypinski[4], Deepak Dalvie[1], Ankita Sharma[1], Mukund Padmanabhan[1], Eduardo De La Torre[1], Alejandro Ayala[1] and Lise Kjems[1]

[1]Princeton, NJ, United States; [2]Crinetics, San Diego, United States; [3]A2-Ai LLC, Ann Arbor, MI, United States; [4]DS Clinical Pharmacology Consulting LLC, Manson, WA, United States

Atumelnant (CRN04894) is a first-in-class, once-daily, oral, selective melanocortin type 2 receptor antagonist. Atumelnant has shown clinical activity in normalizing adrenocorticotropic hormone (ACTH)-mediated pathological elevations of adrenal steroid hormones, demonstrating potential treatment benefits for patients with congenital adrenal hyperplasia (CAH) and ACTH-dependent Cushing syndrome (ADCS). This study characterized the in-human pharmacokinetic (PK) properties (ie, absorption, metabolism, excretion, and absolute bioavailability) of atumelnant to support its clinical development for treatment of CAH and ADCS.

This was an open-label, 2-part, nonrandomized, single-dose study. Part A characterized the absorption, metabolism, excretion, and mass balance of [^{14}C]-CRN04894 in 8 healthy male participants. All participants received a single 85-mg oral dose containing 125 μCi [^{14}C]-CRN04894 and were domiciled for ≤21 days or ≥8 days with early discharge criteria of (1) >90% of radioactive dose recovered in urine and feces and (2) <1% of radioactive dose recovered in combined excreta in 2 consecutive days. Plasma, blood, urine, and feces were collected and analyzed for total radioactivity and atumelnant levels. Metabolite profiling and identification were conducted on plasma, urine, and feces samples.

Part B determined the absolute bioavailability of atumelnant in 7 healthy male participants. All participants received a single 80-mg oral dose of atumelnant in the fasted state, followed by a single intravenous bolus of 22 μg/0.5 μCi [^{14}C]-CRN04894 1 hour later. Plasma was collected for ≤96 hours and analyzed for total radioactivity, [^{14}C]-CRN04894, and atumelnant concentrations.

CRN04894 was the predominant circulating drug-related component in plasma, accounting for 79.2% of total radioactivity. The major circulating metabolite was an oxidative inactive metabolite, M629a, with 14.7% of total radioactivity in plasma. The mean mass balance based on total administered radioactive dose recovered from urine and feces was 87.6%. Fecal excretion was the primary route of elimination, accounting for 76.3% recovered radioactive dose. CRN04894 and its metabolites did not partition into red blood cells (blood/plasma ratio, 0.56). Geometric mean absolute bioavailability after a single 80-mg dose was 56.7%. The mean half-life of oral CRN04894 in plasma was 27.2 hours in Part A and 21.4 hours in Part B. Treatment-emergent adverse events were mild and not considered to be related to atumelnant, indicating a favorable safety profile from both parent and metabolite M629a.

Atumelnant has suitable PK properties for chronic once-daily oral treatment of patients with CAH and patients with ADCS.

Abstract citation ID: lvag096.249

P37 - ECE_3830 - Management of adrenal cysts—a United Kingdom single centre case series

Mariyam Shazra[1], Rathna B. Veerni[2] and Rupa Ahluwalia[1]

[1]Norwich, United Kingdom; [2]Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom

Adrenal cysts are rare, representing 1%-2% of adrenal incidentalomas. Most are benign, non-functional, and asymptomatic. Despite rising incidental detection on cross-sectional imaging, there is limited data on the role of routine radiographic surveillance in management of asymptomatic adrenal cysts.

We report a case series highlighting real world experience of management of adrenal cysts within a U.K. endocrinology centre.

Thirteen patients with adrenal cysts seen within our department over a 32-month period (March 2023-November 2025) were identified following an electronic database search. Mean presenting age at diagnosis was 50 years (range 32-73 years), with 5 patients presenting in their 30s, suggesting a younger age at presentation. Patients were predominantly female (8/13, 61.5%) consistent with published data of 3:1 female-to-male ratio. Initial diagnosis following incidental detection occurred in 10 (76.9%), while remaining 3 patients were symptomatic (abdominal pain or distension). Notably, 61.5% were left-sided adrenal cysts. Cyst sizes ranged from 11-290 mm; 38.4% exceeded 5 cm, yet only 15.3% of large cysts were symptomatic. Two of the largest cysts (160 mm and 290 mm) occurred in patients with bilateral lesions. Among the three symptomatic patients, adrenal cyst sizes at presentation were 15 mm.(pheochromocytoma), 150 mm., and 290 mm.

Median unenhanced CT attenuation was 17 HU, with 61.5% demonstrating non-enhancement. Majority of our patients required secondary imaging to confirm diagnosis (CT adrenals: 23.1%, MRI adrenals: 53.8% or MRI Abdomen: 23.1%). All patients underwent multiple follow up scans as part of radiographic surveillance (range 2-6 scans). Cyst size during follow up imaging increased in five patients, decreased in three, and remained stable in five. Radiological follow up ranged from 2-40 months (mean 14 months) and from 0.07-31 months (mean 10.17 months) from time of endocrinology review. The largest cyst in our cohort had significant spontaneous reduction in size (290 mm to 170 mm). All patients underwent biochemical functional assessment for secretory status (overnight 1mg dexamethasone suppression test, renin & aldosterone studies (for hypertension and/or unprovoked hypokalaemia), 2 × 24 hour urinary metanephrines measurement). Only one patient had a confirmed secretory adrenal cyst (elevated plasma metanephrines in known multiple endocrine neoplasia type 2A mutation) requiring adrenalectomy. One patient requiring surgical intervention was 33-week pregnant with a large retroperitoneal cyst identified during evaluation for shortness of breath; cyst drainage confirmed an adrenal origin. Eleven patients (84.6%) were managed conservatively. At data collection, six patients (46.1%) were discharged, while seven (53.8%) had active endocrinology follow-up.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.250

P38 - ECE_3225 - Ambulatory 24-hr tissue adrenal steroid profiling for personalised hormone replacement in patients with adrenal insufficiency

Ileana R. Botusan[1], Eder Zavala[2], Thomas Upton[3], Katarina Berinder[1], Paal Methlie[4], Katerina Simunkova[4], Dimitra Argyro Vassiliadi[5], Marianne Grytaas[6], Georgina Russell[3], Stylianos Tsagarakis[5], Stafford Lightman[3], Eystein Sverre Husebye[4], Olle Kämpe[1], Marianne Øksnes[6] and Sophie Bensing[1]

[1]Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Solna, Stockholm, Sweden; [2]Division of Diabetes, Endocrinology & Gastroenterology, University of Manchester, Manchester, United Kingdom; [3]University of Bristol, Bristol, United Kingdom; [4]Department of Clinical Science, Faculty of Medicine, University of Bergen, Haukeland University Hospital, Bergen, Norway; [5]Evangelimos Hospital, Athens, Greece; [6]Medicine, University of Bergen, Haukeland University Hospital, Bergen, Norway

Background and Aim: Patients with primary adrenal insufficiency (PAI) lack endogenous corticosteroids and rely on lifelong replacement therapy, which fails to replicate normal circadian and ultradian rhythms. Using the ambulatory U-RHYTHM system, we previously mapped adrenal hormone dynamics in healthy individuals. Here, we characterize tissue corticosteroid profiles in PAI patients on different glucocorticoid therapies and quantify deviations from normal physiological patterns.

Materials and Methods: 41 patients with PAI were included independently of their glucocorticoid replacement therapy (GRT) regime: hydrocortisone, cortisone acetate or modified release hydrocortisone. All were 21 hydroxylase autoantibody positive, confirming an autoimmune cause. The median duration of PAI was 6.5 years (IQR: 3.25-19.75). Data were compared with a previously published cohort of 214 healthy controls. Free steroid hormones were sampled from abdominal subcutaneous tissue by microdialysis in ambulatory settings every 20 minutes over 24 hours, using the novel portable fraction collector U-RHYTHM. Steroid hormones were analyzed by ultrasensitive liquid chromatography tandem mass spectroscopy (LC-MS/MS). Normal cortisol ranges were defined in the healthy cohort using rolling means of cortisol and interquartile variability (25^{th}-75^{th} percentiles). The PAI cohort was then compared against this standard to calculate "time in range." To objectively quantify the differences in hormonal dynamics between the cohorts we further derived computational biomarkers including area under the curve, maximum hormone concentration and rate of increase after dose.

Results: Patients were analyzed according with their GRT regime: hydrocortisone, cortisone acetate, or modified-release hydrocortisone. Mean daily hydrocortisone equivalent doses were 21.6, 27.7, and 17.2 mg, respectively. Across all groups, time in range was low (<35%), with >25% of the day at extreme hormone levels (<5th or >95th percentile). In the early morning, PAI patients showed very low cortisol and cortisone and no pre-awakening rise, whereas healthy controls' levels started to increase 4 hours before awakening. Hormonal peaks in PAI were delayed compared with controls, highlighting marked deviations from normal physiology. Morning hormone surge in PAI showed reduced overall exposure, faster transitions, and altered peak morphology compared with healthy controls.

Conclusions: Here, we show for the first time the full individual 24h hormonal profiles resulting from different glucocorticoid replacement regimes, which we propose as a tool for precision management of GRT in PAI.

Abstract citation ID: lvag096.251

P39 - ECE_2323 - Sensitive diagnostic thresholds in the management of primary aldosteronism

Piotr Kmieć, Jowita Fiszer, Julia Tarnowska, Sonia Zembrzuska and Renata Świątkowska-Stodulska

Department of Endocrinology and Internal Medicine, Medical University of Gdańsk, Gdańsk, Poland

Introduction: The conventional binary approach to primary aldosteronism (PA) work-up has been proven inadequate due to the continuous nature of aldosterone secretion. PA also remains vastly underdiagnosed. Therefore, a sensitivity-oriented approach to PA has been implemented in our tertiary endocrine center in December, 2023. It included a requirement for universal screening of eligible patients, permissive aldosterone-to-renin-ratio thresholds dependent on prescribed medications as well as a low saline infusion test cutoff.

Design and Methods: A single-center, retrospective analysis of two 12-month periods: before and after implementation of a systematic diagnostic approach toward PA. The number of screenings, confirmatory tests, adrenal vein sampling procedures, and therapy outcomes were compared.

Results: In the "before" period (November, 2022 through October, 2023), 61% of normokalemic patients with an indication for screening were tested, which increased to 82% in the second ("after") period (March, 2024 through February, 2025), $P < .001$, see table below. Confirmatory testing almost doubled (37 out of 275 vs 102 out of 432 screened patients, respectively). Among all patients with an indication for PA work-up, confirmed PA cases prevalence increased from 2.9% to 10.9%, whereas among those who underwent work-up: from 4.7% to 13.2%. A shift in suppression test interpretation was evident in higher positivity: 51% vs 29.7%, $P = .03$. In patients with suspected autonomous aldosterone secretion not meeting formal PA criteria mineralocorticoid receptor antagonists (MRAs) were often prescribed. Overall, the rate of newly-prescribed MRAs among patients who underwent work-up more than tripled (Table). Clinical and biochemical outcomes were favorable, however, in the second period, adverse effects occurred in two patients and repeat testing ruled out PA in three others.

Period	Before	After	*P*
Normokalemic patients who had an indication and underwent PA work-up among all	264/433(61%)	402/490 (82%)	<.001
PA suppression tests among all patients who underwent work-up	37/275 (13.5%)	102/432 (23.6%)	<.001
Suppression test positivity	11/37 (29.7%)	52/102 (51%)	.03
PA diagnoses among all	13/275 (4.7%)	57/432 (13.2%)	<.001

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Continued

Period	Before	After	P
patients who underwent work-up			
Newly-initiated MRA among patients off MRA who underwent PA work-up	13/259 (5%)	63/393 (16.1%)	<.001
Planned and performed adrenalectomies in PA patients	3/13 (23.1%)	10/57 (17.5%)	.7
Partial or complete clinical and/or biochemical success in MRA-treated patients	10	50	1
MRA not initiated / discontinued / loss to follow-up	1	9	

Conclusions: This before-and-after study provides real-world data on sensitivity-oriented PA management. The approach significantly improved testing rates and led to a more frequent implementation of targeted pharmacotherapy.

Abstract citation ID: lvag096.252

P42 - ECE_3478 - Variable interferences for aldosterone measured by Liaison and iSYS chemiluminescence immunoassays dictate need for different cut-offs for the seated saline suppression test

Graeme Eisenhofer[1], Carmina Teresa Fuss[2], Stefanie Hahner[2], Jun Yang[3], Tracy Williams[4], Martin Reincke[4], Felix Beuschlein[5], Andrea Horvath[6], Jacques Lenders[7] and Christina Pamporaki[1]

[1]University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [2]University Hospital, University of Würzburg, Wurzburg, Germany; [3]Hudson Institute of Medical Research, Monash University, Melbourne, Australia; [4]Ludwig Maximilian University Munich, Munich, Germany; [5]University Hospital Zurich, Zurich, Switzerland; [6]New South Wales Health Pathology, University of New South Wales, Sydney, Australia; [7]Radboud University Medical Center, Nijmegen, The Netherlands

Background: Protein-based interferences with chemiluminescence immunoassays (CLIA) of plasma aldosterone, particularly at low concentrations during confirmatory tests, are a previously unrecognised problem. We therefore hypothesized that cut-offs for measurements of aldosterone for the seated saline suppression test (SSST) require tailoring according to the particular immunoassay.

Methods: Multicenter study involving 609 patients with suspected primary aldosteronism (PA) who underwent SSSTs with aldosterone measured by liquid chromatography-mass spectrometry (LC-MS/MS) compared to iSYS or Liaison CLIAs in 285 and 286 respective patients and a different LC-MS/MS method in 38 patients. Cut-offs for plasma aldosterone were derived from receiver-operating characteristic curves after classification of patients with ($n = 181$) and without PA ($n = 336$) by methods independent of confirmatory tests. Classifications could not be achieved by methods independent of confirmatory tests in 92 patients.

Findings: Plasma aldosterone measured by the two CLIAs showed considerable differences compared to near identical measurements by the two LC-MS/MS methods. Paired comparisons indicated higher ($P < .0001$) plasma concentrations of aldosterone measured by both Liaison and iSYS CLIAs than by LC-MS/MS for patients with and without PA. Differences were most prominent for suppressed aldosterone measured by the Liaison CLIA in patients without PA in whom concentrations were 130% higher than measured by LC-MS/MS and 40% higher than by the iSYS CLIA. Youden-index derived cut-offs for suppressed aldosterone were 300 and 272 pmol/L for respective Liaison and iSYS CLIAs compared to 169 pmol/L by LC-MS/MS. At those cut-offs, respective diagnostic sensitivities for Liaison and iSYS immunoassays and LC-MS/MS were 90%, 91% and 98% with specificities of 86%, 94% and 90%. Improved disease confirmation according to specificities of 95% for positive predictive values of 87%, 92% and 90% were provided by cut-offs of 436, 297 and 243 pmol/L for respective measurements by Liaison and iSYS CLIAs and LC-MS/MS. At those cut-offs, sensitivities were, however, reduced to 64%, 85% and 78% for those respective measurement methods.

Conclusions: Cut-offs for CLIA-based measurements of aldosterone during the SSST must be established according to the specific immunoassay and are variably higher than those for LC-MS/MS. Severe protein-based interferences with the Liaison CLIA render this method inferior for confirmatory testing than the other methods.

Abstract citation ID: lvag096.253

P43 - ECE_1371 - Hemostasis is altered in patients with mild autonomous cortisol secretion and affected by metyrapone treatment

Helena Niziolek[1], Dino Mehic[2], Tim Dreier[2], Anna Tosin[1], Clemens Baumgartner[1], Paul Fellinger[1], Luise Bellach[1], Alexandra Kautzky-Willer[1], Michael Krebs[1], Peter Quehenberger[3], Michael Leutner[1], Johanna Gebhart[2] and Peter Wolf[1]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria; [2]Division of Hematology and Hemostaseology, Department of Internal Medicine I, Medical University of Vienna, Vienna, Austria; [3]Department of Laboratory Medicine, Medical Unviersity of Vienna, Vienna, Austria

Research Question: Hypercoagulation and impaired fibrinolysis were reported in a state of hypercortisolism, but evidence for patients with mild autonomous cortisol secretion (MACS) is limited. This study aims to characterize hemostasis in patients with MACS compared to patients with non-functional adrenal adenoma (NFA) and to investigate the effects of medical treatment.

Material and Methods: Patients with MACS ($n = 25$, 21 females) were compared to patients with NFA ($n = 25$, 21 females) of comparable age and BMI (median age: 63 (55-67) vs 61 (54-68) years; median BMI: 27 (24.2- 30.5) vs 28.5 (27.5-32.2) kg/m^2). A sub-cohort of 14 patients with MACS was re-investigated prospectively following 12 weeks of treatment with evening doses of metyrapone (500 mg at 6 p.m. & 250 mg at 10p.m.) as part of an exploratory secondary analysis of the AdrenalCLOCK study.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Hemostatic parameters (activated partial thromboplastin time, von Willebrand factor antigen, protein S, plasminogen, α2-antiplasmin, prothrombin time, international normalized ratio, plasminogen activator inhibitor-1, fibrinogen, FVIII, FIX and protein C) were measured by routine laboratory techniques. Dynamics of thrombin and plasmin generation were measured using calibrated fluorescence detection in citrated platelet-poor plasma. Mann-Whitney-U test was applied for cross-sectional analysis, while Wilcoxon signed-rank tests were performed for pre-post metyrapone comparison.

Results: Levels of fibrinogen Clauss [362 (329-414) vs 331 (307-376) mg/dL, $P = .03$], von Willebrand factor antigen [121 (94-170) vs 99(77-128) %, $P = .04$] and factor VIII [109 (78-132) vs 76 (65-101)%, $P = .02$] were increased in MACS compared to NFA. While no differences between MACS and NFA were determined for thrombin generation potential, patients with MACS had a slower plasmin generation reflected by a reduced plasmin velocity in MACS compared to NFA [13.12 (11.59-16.53) vs 16.44 (13.13-18.75) nM/min, $P = .03$]. Treatment with metyrapone increased plasmin peak height [52.69 (47.04-59.61) vs 39.88 (34.49-46.57) nM; $P = .0353$) and endogenous plasmin potential [657.40 (430.26-738.44) vs 454.75 (317.17-524.26) nM/min, $P = .0203$) at follow up compared to baseline, while protein S activity [104 (85.25-109.75) vs 83(79.25-98.25)%, $P = .0035$] decreased.

Conclusions: MACS is associated with changes in hemostasis, which are affected by short-term treatment with evening doses of metyrapone. Future studies are warranted to derive potential clinical implications of medical treatment.

Abstract citation ID: lvag096.254

P44 - ECE_1661 - Salivary 18-hydroxycortisol as a non-invasive biomarker for subtyping Primary Aldosteronism

Seung Shin Park[1,2], Soyeon Park[3], Min Jeong Park[4], Seungho Lee[5], Woochul Kim[5], Su-Jin Kim[5], Man Ho Choi[3] and Jung Hee Kim[1,2]

[1]Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea; [2]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, South Korea; [3]Center for Advanced Biomolecular Recognition, Korea Institute of Science and Technology, Seoul, South Korea; [4]Department of Internal Medicine, Korea University Medical Center, Seoul, South Korea; [5]Department of Surgery, Seoul National University Hospital, Seoul, South Korea

Introduction: Primary aldosteronism (PA) is the most common cause of secondary hypertension, and accurate subtyping into lateralized or non-lateralized disease is essential for optimal management. Although adrenal venous sampling (AVS) remains the gold standard for lateralization, it is invasive, technically demanding, and not widely available. Steroid profiling using liquid chromatography–tandem mass spectrometry (LC–MS/MS) has emerged as a promising alternative, but the potential role of salivary steroid profiling in PA subtyping has not been systematically evaluated. We aimed to investigate whether salivary steroid measurements, particularly 18-hydroxycortisol (18-OHF), could predict lateralization in patients with PA.

Methods: This single-center study included 74 patients with confirmed PA who underwent AVS at Seoul National University Hospital between 2017 and 2023. Lateralized PA was defined by a lateralization index ≥4 or confirmed clinical success after adrenalectomy in indeterminate cases. Morning salivary samples were collected and analyzed using LC–MS/MS. Salivary concentrations of cortisol, cortisone, tetrahydrocortisol, 20α-dihydrocortisol, 18-OHF, and dehydroepiandrosterone sulfate were compared between lateralized and non-lateralized PA. Diagnostic performance was assessed using receiver operating characteristic (ROC) analysis. Incremental value beyond conventional biochemical parameters was evaluated using net reclassification improvement (NRI). Correlations between salivary and serum steroid concentrations were also examined.

Results: Among the 74 patients, 38 had lateralized PA and 36 had non-lateralized PA. Compared with non-lateralized PA, patients with lateralized PA had higher plasma aldosterone (34.9 vs 21.7 ng/dL, $P = .021$), lower plasma renin activity (0.2 vs 0.5 ng/mL/h, $P < .001$), and more frequent hypokalemia (71.1% vs 27.8%, $P < .001$). Among salivary steroids, only 18-OHF differed significantly, with higher levels in LPA (0.66 vs 0.25 ng/mL, $P < .001$). Salivary 18-OHF predicted lateralization with an area under the ROC curve of 0.756 (95% CI, 0.642-0.870). A cutoff value of 0.29 ng/mL yielded a sensitivity of 78.9% and specificity of 69.4%. When added to a conventional model including plasma aldosterone, renin, and serum potassium, salivary 18-OHF significantly improved classification (category-free NRI 0.52, 95% CI, 0.084-0.929 $P = .014$). Salivary and serum 18-OHF levels showed a strong correlation ($\rho = 0.73$, $P < .001$).

Conclusions: Salivary 18-OHF is a promising non-invasive biomarker for subtyping PA. It provides clinically meaningful discrimination of lateralized disease and offers incremental diagnostic value beyond conventional biochemical parameters. Salivary steroid profiling may serve as a practical adjunct to current diagnostic strategies and help reduce reliance on invasive AVS. Larger studies are needed to validate its clinical utility.

Abstract citation ID: lvag096.255

P45 - ECE_2394 - Hypertension in adrenal insufficiency: prevalence, disease specific factors and insights into regulation of the renin-angiotensin-aldosterone system

Irina Chifu[1], Laura Heger[1], Marcus Quinkler[2], Hanna F. Nowotny[3], Georgiana Constantinescu[4,5], Christina Pamporaki[4], Birgit Harbeck[6], Nicole Reisch[3] and Stefanie Hahner[1]

[1]Department of Medicine I, Division of Endocrinology and Diabetology, University Hospital Wuerzburg, Wuerzburg, Germany; [2]Endocrinology in Charlottenburg, Berlin, Germany; [3]Department of Medicine IV, Ludwig Maximilian University, Munich, Germany; [4]Department of Internal Medicine III, University Clinic Carl Gustav Carus at TU Dresden, Dresden, Germany; [5]Grigore T Popa University of Medicine and Pharmacy, Iasi, Romania; [6]III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background: Retrospective analyses consistently show higher cardiovascular (CV) mortality and morbidity in patients with adrenal insufficiency (AI) compared to controls. However, factors driving the increased CV risk remain poorly understood.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Objective: Assess the prevalence of hypertension (HT) by 24-hour blood pressure (24h-BP) measurements and associations with disease-related parameters in patients from our multicentric AI registry.

Methods: We measured 24h-BP in 281 patients (71% primary AI (PAI), 68% female, mean age 50 ± 14 years, 24% under antihypertensive treatment). HT was diagnosed according to ESC/ESH thresholds. Results were correlated with hormone replacement regimens, salivary- and urinary cortisol, key effectors of the renin-angiotensin-aldosterone system (RAAS) (Angiotensin I/II, Aldosterone, angiotensin-converting-enzyme activity (ACE-Q)) and routine clinical and biochemical parameters.

Results: 24h-BP was elevated in 59% of all patients (PAI 57% vs SAI 74%, $P = .006$) and in 52% of patients without antihypertensive treatment (PAI 52% vs SAI 53%, $P = 0.88$). Nighttime-HT was more prevalent than daytime-HT (48% vs 38%) regardless of antihypertensive therapy and 33% of the cohort were non-dippers. Logistic regression in patients not receiving antihypertensive therapy showed significant associations of male sex, BMI, and renal function with 24h-HT, and of higher glucocorticoid (GC) doses with daytime-HT. In the subgroup with available RAAS data, evening GC intake and ACE-Q were additionally associated with 24h-HT and nighttime-HT. Linear regression in patients with 24h-HT demonstrated associations between mean systolic BP and higher 24h urinary cortisol, salivary cortisol AUC, and GC replacement dose.

Conclusions/Outlook: Nighttime hypertension and non-dipping are frequent in our cohort. While classical risk factors appear dominant, the observed associations with GC replacement and cortisol profiles indicate unphysiological steroid exposure under conventional treatment contributes to BP elevations.

Abstract citation ID: lvag096.256

P48 - ECE_1392 - Machine learning model based on preoperative peripheral serum steroids for predicting clinical outcomes after adrenalectomy in primary aldosteronism

Ruyi Li[1,2], Lei Ye[1,2] and Weiqing Wang[1,2]
[1]*Department of Endocrine and Metabolic Diseases, Shanghai Institute of Endocrine and Metabolic Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China;* [2]*Shanghai National Clinical Research Center for metabolic Diseases, Shanghai Key Laboratory for Endocrine Tumor, Shanghai, China*

Background/Introduction: A 2021 study from our research group indicated that *KCNJ5* mutation contributes to complete clinical success after adrenalectomy in aldosterone-producing adenoma (APA). Previous studies have shown that APA patients harboring *KCNJ5* mutations possess a distinct steroid hormone profile. Building on these background, we hypothesize that the subset of APA patients who achieve clinical complete remission after surgery may be characterized by a distinct peripheral blood steroid hormone profiles.

Purpose: We aimed to develop and validate interpretable machine learning (ML) models using peripheral serum steroids to predict surgical outcomes in APA patients and to formulate individualized diagnosis and treatment plans.

Methods: LC-MS/MS was used to detect 24 types of steroid hormones in the preoperative peripheral serum of the enrolled patients with APA. Lasso regression was used to select features and eight ML algorithms such as extreme gradient boosting (XGBoost) were used to construct the model. Model prediction performance was compared using evaluation indicators such as the area under the receiver operating characteristic curve (AUC). The SHapley Additive exPlanation (SHAP) method was used to rank the feature importance and explain the final model.

Results: Among the 338 patients who were followed up for at least six months after surgery, the preoperative peripheral serum levels of 18-oxocortisol (585.00 vs 133.50 pg/mL, $P < .001$), 18-hydroxycortisol (4291.02 vs 1690.50 pg/mL, $P < .001$), and 18-hydroxycorticosterone (875.21 vs 450.00 pg/mL, $P < .001$) in the complete remission group (164 cases) were significantly higher than those in the no complete remission group (174 cases). Among the eight ML models, the XGBoost model performed the best, showing the highest AUC, accuracy, sensitivity, F1 score, and a low Brier score. The XGBoost model accurately predicted the clinical outcomes of surgery in patients with APA in both the training set [AUC: 0.963, 95% confidence interval (CI) (0.944-0.983)] and the test set [AUC: 0.878, 95% CI (0.811-0.946)]. The calibration curve showed high agreement between the predicted and observed probability. SHAP analysis identified variables that contributed to the model predictions. 6 variables were included in the final XGBoost model: 18-oxocortisol, 18-hydroxycortisol, 18-hydroxycorticosterone, sex, cortisone, and deoxycorticosterone.

Conclusions: We developed and validated an explainable ML model by using preoperative circulating steroids for predicting the surgical outcomes in APA patients. The final XGBoost model exhibited excellent prediction ability in both training set and test set validation. The model provides a basis for clinicians to identify individualized treatment plans.

Abstract citation ID: lvag096.257

P49 - ECE_2309 - Bilateral adrenal vein thrombosis and adrenal hemorrhage with acute adrenal insufficiency in a patient with Waldenström's macroglobulinemia

Michał Olejarz[1], Remigiusz Domin[1], Ewelina Szczepanek-Parulska[1] and Marek Ruchala[1]
[1]*Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznan, Poland*

Acute adrenal failure is an endocrine emergency that can be a life-threatening condition if not diagnosed and treated promptly. One of the rare and underrecognized causes of acute adrenal failure is adrenal hemorrhage secondary to adrenal vein thrombosis.

A 66-year-old male presented to the emergency department because of abdominal pain radiating to the left shoulder, nausea, and constipation. His past medical history included Waldenström's macroglobulinemia, depressive disorder, hypothyroidism (following thyroidectomy because of papillary thyroid carcinoma), and two episodes of pulmonary embolism.

Laboratory analysis revealed increased CRP (68 mg/l), hyponatremia (Na 125 mmol/l), thrombocytopenia (108 × 10^3/μl),

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and anemia (11,1 g/dl). Abdominal radiograph revealed moderately distended loops of the descending colon, suggesting subileus. Subsequently, an abdominal CT was performed, which revealed bilateral adrenal vein thrombosis and bilateral adrenal hemorrhage. The distention of the colon was attributed to fecal impaction and did not require surgical intervention.

Because of acute adrenal failure, the patient was started on high doses of intravenous hydrocortisone supplementation, which was subsequently tapered to a standard supplementation dose later.

A week before the admission, the patient had a skin biopsy because of a suspicious skin lesion, which resembled cutaneous vasculitis. Before the biopsy, the patient was switched from oral rivaroxaban to subcutaneous low molecular weight heparin. Thus, we evaluated the patient using the 4T clinical score for heparin-induced thrombocytopenia (HIT), which indicated a high probability of HIT. Heparin was stopped, and rivaroxaban was reintroduced.

The patient's condition improved rapidly after treatment, and the follow-up CT revealed no rebleeding. We tested the patient for anti-platelet factor 4 (anti-PF4) antibodies, which were negative. Eventually, we received the result of the skin biopsy, which was suggestive of monoclonal cryoglobulinemia.

Bilateral adrenal vein thrombosis with secondary bilateral adrenal hemorrhage is potentially life-threatening and needs to be diagnosed and treated promptly. There is a handful of case reports linking it to HIT. Thus, HIT should be considered if heparin was administered recently and the 4T clinical score is high. Anti-PF4 antibodies have an excellent sensitivity and negative predictive value. Thus, a negative anti-PF4 antibody test makes the diagnosis of HIT highly unlikely.

In this case, eventually, the adrenal vein thrombosis was most probably caused by an acquired prothrombotic state associated with the underlying lymphoproliferative disorder and monoclonal cryoglobulinemia.

Abstract citation ID: lvag096.258

P50 - ECE_3013 - What was the cause of recurrent arrhythmogenic syncopes?

Zora Lazurova[1], Adriana Sudzinova[2], Martin Javorsky[1], Kleanthia Efthymiou[1], Jana Katuchova[1] and Peter Bohus[1]

[1]Medical Faculty, Department of Pathology, University of Pavol Jozef Safarik, Kosice, Slovakia; [2]1st Department of Internal Medicine, Institute of Cardiovascular Diseases of East Slovakia, Kosice, Slovakia

We present a case of 32 years old male with no previous history of any diseases. A non obese smoker, without any chronic medication was admitted to the hospital due to recurrent syncopes, without any prodromes. Patient was hemodynamically stable, blood pressure was 120-140/80-90 mmHg, apart from mild systolic murmur, physical examination was unremarkable. ECG revealed atrial flutter with rapid heart rate and short paroxysms of non-sustained ventricular tachycardia. Moreover, signs of left ventricular hypertrophy have been described. In laboratory screening, severe hypokalemia (1.5 mmol/l) and metabolic alkalosis was present, other results were within normal ranges. Transthoracic echocardiography revealed left ventricular hypertrophy (IVS 17 mm) with diastolic dysfunction. After massive potassium replacement and betablocker administration, the conversion to sinus rhythm was noticed. In differential diagnosis of severe hypokalemia, hormonal screening was performed, with identification of severe primary hyperaldosteronism (plasmatic renin activity less then 0.3 ng/ml/hod and aldosterone 2050 g/dl), with no suppression in captopril test. Due to cardiac condition, the saline test was not peformed. On the CT, there was a left adrenal nonhomogenous tumour mass documented with typical features for adrenocortical carcinoma. Furthermore, pathological paraoartic lymph nodes and methastasis in the liver (15 mm) were described. Baseline cotisol levels were normal, however In dexamethasone test there was insignificant suppression, revealing a cortisol cosecretion. Surgical removement was indicated, after preoperative treatment with high doses of spironolactone and potassium surrogation. Histopathology confirmed aldosterone-producing adrenocortical cancer with Ki67 index 35% (in hot spots 50%-60%). After surgery there was normalization of aldosterone levels and the adjuvant therapy by etoposid and cisplatin in combination with mitotan was administered.

Abstract citation ID: lvag096.259

P51 - ECE_2502 - Efficacy and Safety of the clonidine suppression test in identifying false-positive normetanephrine results in the diagnosis of pheochromocytoma and paraganglioma

Alicja Duquenne[1,2,3], Agata Toboła[1], Dorota Leszczynska[1], Małgorzata Waszkiewicz-Hanke[1], Magdalena Ostrowska[1,2], Konrad Kowalski[4], Radosław Samsel[5], Wojciech Zgliczyński[1] and Piotr Glinicki[1,2]

[1]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [2]Centre of Postgraduate Medical Education, EndoLab Laboratory, Warsaw, Poland; [3]Centre of Postgraduate Medical Education, Doctoral School of Translational Medicine, Warsaw, Poland; [4]Masdiag Laboratory, Warsaw, Poland; [5]Department of Surgery, Clinic of Surgical Oncology and Neuroendocrine Tumors, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background: Measurement of free plasma metanephrines using liquid chromatography–tandem mass spectrometry (LC–MS/MS) represents the gold standard for the biochemical diagnosis of pheochromocytoma–paraganglioma (PPGL). However, despite optimal pre-analytical preparation, false-positive results occur in up to 20% of patients.

Purpose: To evaluate the efficacy and safety of the clonidine suppression test (CST) in distinguishing false-positive elevations of plasma normetanephrine.

Methods: The study included 11 patients (median age 59 years; 8 females) with plasma normetanephrine concentrations exceeding age-adjusted cut-offs. Indications for diagnostic evaluation included paroxysmal symptoms, suspected PPGL recurrence, adrenal incidentaloma with unenhanced CT attenuation >10 Hounsfield units, and suspected carotid paraganglioma. All patients received oral clonidine 300 µg. Plasma normetanephrine levels (LC–MS/MS) were measured at baseline and 180 minutes post-administration. Patients were continuously monitored, with vital signs assessed every 30 minutes and adverse events recorded.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: The median reduction in plasma normetanephrine was 42 pg/mL. In all patients, concentrations decreased below age-adjusted cut-offs, and in 10 of 11 patients, levels fell to <80% of the respective cut-off. The most common adverse effects were somnolence, xerostomia, and fatigue. Median reductions in hemodynamic parameters were: systolic blood pressure −48 mmHg, diastolic blood pressure −31 mmHg, and heart rate −15 bpm.

Conclusions: The clonidine suppression test appears to be a safe and effective tool for confirming isolated elevations of plasma normetanephrine in the diagnostic evaluation of PPGL.

Abstract citation ID: lvag096.260

P52 - ECE_1432 - Hair cortisol as a marker of glucocorticoid replacement adequacy in adrenal insufficiency

Merve Korkmaz Yilmaz[1,2], Semih Tek[3], Gizem Karatas Kiliccioglu[1], Aysel Unver Ozkahraman[1], Mutlu Niyazoglu[1] and Esra Hatipoglu[1]

[1]Department of Endocrinology and Metabolism, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye; [2]Endocrinology and Metabolism, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye; [3]Department of Medical Biochemistry, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye

Background: Achieving physiologic glucocorticoid replacement in adrenal insufficiency (AI) remains a major clinical challenge, with both under- and over-replacement contributing to substantial morbidity. Although useful, conventional serum- and urine-based markers reflect mainly short-term cortisol exposure and may not fully capture the patient's clinical status. In contrast, hair cortisol concentration (HCC) integrates long-term cumulative exposure and may address these limitations; however, HCC has been evaluated only sparsely in AI, and its clinical utility remains uncertain.

Methods: In this cross-sectional study, 64 adults with hydrocortisone-treated AI and 64 matched healthy controls were evaluated. HCC was measured from the proximal 3-cm hair segment. Clinical symptoms, anthropometry, metabolic markers, and hydrocortisone dosing parameters were recorded. Group comparisons, Spearman correlations, ROC analyses, and multivariable linear regression were performed. Patients were classified as undertreated based on VAS-fatigue or VAS-pain ≥7, and as overtreated based on SBP ≥140 mmHg, DBP ≥90 mmHg, HbA1c ≥6.5%, FPG ≥126 mg/dL, or ≥5% weight gain.

Results: HCC was higher in AI patients than controls (4.3 vs 1.75 ng/g, $P < .01$) and higher in primary vs secondary AI (6.5 vs 3.8 ng/g, $P = .037$). HCC correlated positively with BMI, waist circumference, systolic and diastolic blood pressure, and hydrocortisone dose, and inversely with fatigue, pain, and total duration of therapy (all $P < .05$). In multivariable models, AI type remained the only independent predictor of HCC. HCC showed strong discrimination for undertreatment (AUC 0.906 for severe fatigue and 0.898 for severe pain; optimal cutoffs 4.9 and 3.5 ng/g). For glucocorticoid excess, the strongest performance was observed for systolic hypertension (AUC 0.837; cutoff 7.9 ng/g). Undertreated patients had markedly lower HCC (2.1 ng/g), whereas overtreated patients exhibited substantially higher levels (14.1 ng/g; $P < .001$).

Conclusions: HCC may serve as a sensitive biomarker of long-term glucocorticoid exposure in adrenal insufficiency, capturing both metabolic strain associated with overtreatment and symptom burden associated with underreplacement. Its strong bidirectional discrimination suggests that HCC may be a practical adjunct to clinical assessment and could support more individualized hydrocortisone titration. Longitudinal studies are warranted to determine whether HCC-informed dosing improves clinical outcomes.

Keywords adrenal insufficiency, hydrocortisone replacement, hair cortisol, biomarker, underreplacement, overreplacement, metabolic outcomes

Abstract citation ID: lvag096.261

P53 - ECE_1519 - Impacts of the use of LC–MS/MS-equivalent chemiluminescent enzyme immunoassay-measured plasma aldosterone concentration in the diagnostic process of unilateral primary aldosteronism

Shoichiro Izawa[1,2], Kazuhisa Matsumoto[1], Kanako Kadowaki[1], Toshifumi Nakamura[3], Norio Wada[4], Takuyuki Katabami[5], Yoichi Nozato[6,7], Ryuji Okamoto[8], Takamasa Ichijo[9], Daisuke Taura[10], Masanori Murakami[11], Miki Kakutani[12], Takashi Yoneda[13], Minemori Watanabe[14], Yutaka Takahashi[15], Shintaro Okamura[16], Katsutoshi Takahashi[17], Hiroki Kobayashi[18], Mitsuhide Naruse[19], Kenichi Yokota[20] and Masakatsu Sone[20]

[1]Division of Endocrinology and Metabolism, Tottori University Faculty of Medicine, Yonago, Japan; [2]Division of Endocrinology and Metabolism, Tottori University Faculty of Medicine, Yonago, Japan; [3]Division of Endocrinology, Metabolism, and Nephrology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan; [4]Department of Diabetes and Endocrinology, Sapporo City General Hospital, Sapporo, Japan; [5]Department of Metabolism and Endocrinology, St. Marianna University Yokohama City Seibu Hospital, Yokohama, Japan; [6]Department of Geriatric and General Medicine, The University of Osaka Graduate School of Medicine, Suita, Japan; [7]Department of Geriatric and General Medicine, Toyonaka Municipal Hospital, Toyonaka, Japan; [8]Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Tsu, Japan; [9]Department of Diabetes and Endocrinology, Saiseikai Yokohamashi Tobu Hospital, Yokohama, Japan; [10]Department of Diabetes, Endocrinology and Nutrition, Kyoto University Graduate School of Medicine, Kyoto, Japan; [11]Department of Molecular Endocrinology and Metabolism, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Tokyo, Japan; [12]Department of Diabetes, Endocrinology and Clinical Immunology, School of Medicine, Hyogo Medical University, Nishinomiya, Japan; [13]Department of Health Promotion and Medicine of the Future, Graduate School of Medical Science, Kanazawa University, Kanazawa, Japan; [14]Department of Endocrinology and Diabetes, Okazaki City Hospital, Okazaki, Japan; [15]Department of Diabetes and Endocrinology, Nara Medical University, Kashihara, Japan; [16]Department of Endocrinology, Tenri Hospital, Tenri, Japan; [17]Division of Metabolism, Showa General Hospital, Kodaira, Japan; [18]Division of Nephrology, Hypertension, and Endocrinology, Department of Internal Medicine, Nihon University School of Medicine, Tokyo, Japan; [19]Endocrine Center, Ijinkai Takeda General Hospital, Kyoto, Japan; [20]Division of Metabolism and Endocrinology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Unilateral primary aldosteronism (UPA) is characterized by a severe clinical phenotype and can be cured by adrenalectomy. Adrenal venous sampling (AVS) is required to distinguish UPA and bilateral primary aldosteronism (BPA). Establishing accurate cutoff values that would warrant AVS is crucial. Recently, new chemiluminescent enzyme immunoassay (CLEIA)-based kits with high level of traceability, close correlation, and equivalent concentration with LC–MS/MS for plasma aldosterone concentration (PAC) are available in Japan. The Japan Endocrine Society Clinical Practice Guideline for the Diagnosis and Management of Primary Aldosteronism 2021 (JES2021) introduced "provisionally positive" range for screening aldosterone-to-renin ratio (sARR), post-captopril challenge test (CCT) aldosterone-to-renin ratio (ARR), and post-saline infusion test (SIT) plasma aldosterone concentration (PAC) to address the concern about the differing PAC values between RIA and LC–MS/MS-equivalent CLEIA. Therefore, we aimed to identify appropriate cutoff values for screening and confirmatory testing to predict UPA by CLEIA-measured PAC.

Methods: A retrospective cohort analysis was conducted as part of the JPAS-II study of 443 patients diagnosed with PA using CLEIA-measured PAC, of whom 179 were confirmed by AVS as having UPA. All patients were diagnosed according to JES2021.

Results: The sARR, screening PAC, post-CCT ARR, post-CCT PAC, and post-SIT PAC were significantly higher in patients with UPA than in those with BPA ($P < .05$). Receiver operator characteristic curve analysis yielded an sARR cutoff value of >183 pg/mL/ng/mL/h (sensitivity: 0.95, specificity: 0.25). The post-CCT ARR (AUC: 0.824 ± 0.022) and post-CCT PAC (AUC: 0.845 ± 0.021) were superior predictors of UPA to post-SIT PAC (AUC: 0.782 ± 0.037). When the cutoff values were designed to maximize sensitivity without a significant reduction in specificity, cutoff values for post-CCT ARR of >153 pg/mL/ng/mL/h (sensitivity: 0.85, specificity: 0.55), post-CCT PAC of >69 pg/mL (sensitivity: 0.85, specificity: 0.67) and for post-SIT PAC of >48 pg/mL (sensitivity: 0.80, specificity: 0.61) were obtained. The cutoff values determined for sARR, post-CCT ARR, and post-SIT PAC were within the "provisionally positive" range defined in JES2021. Importantly, these cutoff values contributed to a diagnosis of UPA when the presence of hypokalemia or adrenal tumor was also considered.

Conclusions: LC–MS/MS-equivalent CLEIA-measured cutoff values for post-CCT ARR of >153 pg/mL/ng/mL/h, for post-CCT PAC of >69 pg/mL and for post-SIT PAC of >48 pg/mL are considered to indicate AVS. Among patients with "provisionally positive" test results on sARR, post-CCT ARR, and post-SIT PAC in JES2021, AVS should be considered when clinical features suggest PA, such as hypokalemia and adrenal tumor.

Abstract citation ID: lvag096.262

P55 - ECE_2714 - Role of CACUL1/ARMC5 complex in primary bilateral macronodular adrenal hyperplasia

Rania Nait Challal, Isadora Pontes Cavalcante, Oriane Genard, Alexandre Quesnoy, Lamia Sefraoui, Anna Vaczlavik, Karine Perlemoine, Fidéline Bonnet-Serrano, Marthe Rizk, Annabel Berthon, Jérôme Bertherat and Bruno Ragazzon
Institut Cochin, Institut Cochin, INSERM U1016, Université Paris Cité, Paris, France

Introduction: Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a rare cause of ACTH-independent hypercortisolism. Inactivating mutations of the tumor suppressor gene *ARMC5* have been identified in approximately 25% of cases. ARMC5, an armadillo repeat–containing protein with a BTB domain, interacts with Cullin-3 (CUL3) and acts as its adaptor for ubiquitination and degradation of specific substrates involved in several cellular processes. Using a proximity-dependent biotinylation approach (APEX2) in living cells coupled with mass spectrometry, we identified CACUL1 (CDK2-associated and Cullin domain-containing protein 1) as an interacting partner of ARMC5. CACUL1 is a nuclear protein involved in chromatin organization and transcriptional regulation, but its function in adrenal cortical cells has not been defined. The aim of this study was to characterize the ARMC5/CACUL1 interaction and to investigate its impact on ARMC5 subcellular localization, cAMP/PKA signaling pathway and steroidogenic gene expression.

Materials and Methods: Protein interactions and subcellular localization were investigated by co-immunoprecipitation and immunofluorescence after modulation of CACUL1 and/or ARMC5 expression using different constructs (wild-type, PBMAH-associated pathogenic missense variants and fragments of ARMC5) in two cellular models (HEK293 and H295R cells). Effects of ARMC5/CACUL1 modulation (siRNA/overexpression) on cAMP/PKA/steroidogenesis were assessed using CREB phosphorylation analysis, CRE-luciferase reporter assays and RT-qPCR of steroidogenic genes.

Results: We show that CACUL1 is insensitive to ARMC5/CUL3 ubiquitination. Moreover, ARMC5 interacts with CACUL1 through its BTB domain as CUL3, supporting that CACUL1 is not a target of the ARMC5/CUL3 complex. Interestingly, CACUL1 overexpression induced a nuclear translocation of ARMC5 wild-type but not ARMC5 pathogenic missense identified in PBMAH patients, which remain cytoplasmic. As CACUL1 is a partner of ARMC5, we wonder whether CACUL1 modulation could alter cAMP/PKA pathway and steroidogenic gene expression. Accordingly, we observed modification of CREB phosphorylation and CRE-luciferase activity depending on CACUL1.

Discussion: CACUL1 appears to be involved in the development of PBMAH, in association with *ARMC5* alterations and through the cAMP/PKA pathway activity and transcriptional control of steroidogenesis. Further characterization of the ARMC5/CACUL1 complex will be required to better understand the pathophysiological mechanisms underlying PBMAH.

Abstract citation ID: lvag096.263

P56 - ECE_2749 - Modified-release hydrocortisone impact on metabolism and hormonal control in patients with congenital adrenal hyperplasia: an observational cohort study

Pierluigi Mazzeo, Irene Tizianel, Giulia Bovo, Chiara Sabbadin, Filippo Ceccato and Mattia Barbot
Endocrinology unit, Padova University Hospital, Department of Medicine—DIMED, Padova, Italy

Background: Congenital adrenal hyperplasia (CAH) is a genetic disorder characterized by impaired cortisol secretion and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

androgen excess. The mainstay of CAH treatment is glucocorticoid (GC) replacement, necessary to avoid adrenal crises and manage androgen excess. The delicate balance between GC under- and overtreatment is crucial to prevent metabolic and cardiovascular (CV) complications. The new modified-release hydrocortisone (MRHC) formulation improves hormonal control compared to conventional GC; however, there are few data on its metabolic impact.

Aim of the Study: to evaluate the hormonal control and metabolic impact of MRHC treatment in patients with CAH.

Patients and Methods: 38 patients with CAH due to 21OH-deficiency (33 patients with classic form and 5 with non-classic CAH, median age 31years) were included; clinical, metabolic and hormonal data were analyzed at baseline, after 12 and 18 or 24 months after switching to MRHC. At baseline, 15 patients were previously treated with long-acting GC, while 23 with immediate-release or dual-release hydrocortisone.

Results: During MRHC treatment, hormonal control improved, with a significant reduction in 17-OH-progesterone (median values 418 nmol/L vs 38 nmol/L at 18/24 months, $P = .001$) and androstenedione levels (19.5 nmol/L vs 8.5 nmol/L, $P = .003$). Additionally, we observed a decrease in total testosterone levels in women (2.9 nmol/L vs 0.6 nmol/L, $P = .001$) and a significant increase of the proportion of patients with good disease control (28% at baseline vs 62% at 18/24 months, $P = .014$). Furthermore, we reported a slight but significant worsening in lipid profile, with increases of total cholesterol (165 mg/dL vs 176 mg/dL, $P = .004$), and LDL-cholesterol levels (90 mg/dL vs 107 mg/dL, $P = .008$); in addition, there was also a slight elevation of homocysteine levels (10.2 µmol/L vs 12.1 µmol/L, $P = .017$). However, after performing a subgroup analysis, we observed that only patients previously treated with immediate or dual-release hydrocortisone had a worsening of lipidic profile; instead, it remained stable in patients who took long-acting GC at baseline. In addition, we noticed a slight improvement of SCORE2 and VAI scores, which were used to evaluate the CV risk profile of our patients. During MRHC treatment no adrenal crises were reported, and it was discontinued only in two cases due to insomnia and polyuria.

Conclusions: MRHC treatment showed an improvement in hormonal control, while maintaining a good safety profile. Nevertheless, a potential negative effect on metabolic parameters was observed. Although these changes do not appear to affect negatively the CV risk profile, clinicians should carefully assess the overall impact of available therapeutic options to optimally personalize treatment for each patient.

Abstract citation ID: lvag096.264

P57 - ECE_3262 - Distinctive dynamic adrenal steroid fingerprints in Liver Cirrhosis

Min Jeong Park[1,2], Soyeon Park[3], Seung Shin Park[4], Hyewon Yang[5], Man Ho Choi[3], Eun Ju Cho[4] and Jung Hee Kim[4]

[1]*Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea;* [2]*Korea University College of Medicine, Seoul, South Korea;* [3]*Center for Advanced Biomolecular Recognition, Korea Institute of Science and Technology, Seoul, South Korea;* [4]*Department of Internal Medicine, Seoul National University College of Medicine, Seoul, South Korea;* [5]*Department of Internal Medicine, Nowon Eulji Medical Center, Eulji University, Seoul, South Korea*

Introduction: Adrenal insufficiency is often overestimated when assessed by immunoassay in patients with liver cirrhosis (LC) due to reduced cortisol-binding globulin and hypoalbuminemia, which lower total serum cortisol concentration. Steroid profiling using liquid chromatography tandem mass spectrometry (LC-MS/MS) enables accurate and simultaneous quantification of multiple adrenal steroids. We aimed to characterize serum and salivary adrenal steroid phenotypes in patients with LC compared to non-LC controls using LC-MS/MS methods.

Methods: Between 2023 and 2024, patients with LC ($n = 33$) and controls ($n = 34$) were prospectively enrolled, and serum and salivary samples were collected during short Synacthen tests at a single center. LC–MS/MS was applied for the analysis of serum and saliva samples. We measured a panel of 27 serum and 13 salivary steroids, including cortisol (F), cortisone (E), 11β-hydroxy androstenedione (11-OHA4), 11-ketoandrostenedione (11-KA4), and 18-hydroxycorticosterone (18-OHF).

Results: Patients with LC had a higher percentage of male (72.7 vs 47.1%, $P = .04$) and were of similar age (58 vs 60 years, $P = .12$) than controls. Serum and salivary peak F/E were lower in patients with LC compared to control (serum F/E: 6.40 [5.37-8.11] vs 8.98 [7.25-10.31], $P < .001$; salivary F/E: 0.25 [0.20-0.34] vs 0.37 [0.24-0.43], $P = .043$), which indicated decreased 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) in LC. In contrast, concentrations of 11-OHA4 (7.29 [5.34-10.02] vs 3.13 [2.18-5.88], $P < .001$) and 11-KA4 (1.05 [0.69-1.24] vs 0.45 [0.07-0.67], $P < .001$), which are metabolites of androgen pathways, were higher in patients with LC than in controls. Elevation of 18-OHF (1.08 [0.65-1.59] vs 0.65 [0.45-0.93], $P = .001$) was observed in patients with LC compared to controls, which may reflect renin-angiotensin-aldosterone system activation secondary to cirrhosis.

Conclusions: Patients with LC exhibited a distinctive inactivation of cortisol to cortisone along with an elevation of 11-oxygenated and mineralocorticoid pathway metabolites, indicating cirrhosis -associated remodeling of adrenal steroidogenesis. Accurate diagnosis of adrenal insufficiency in LC requires consideration of cirrhosis-specific alterations of steroid metabolism.

Abstract citation ID: lvag096.265

P58 - ECE_2848 - Comprehensive mapping of steroid metabolism across biological matrices using a novel high-coverage LC-MS/MS steroidomics platform

Federico Ponzetto[1], Samuele Scurati[2], Laura Leoni[1], Alessia Melis[1], Giulia Montesano[3], Fabio Settanni[4], Mirko Parasiliti Caprino[3], Giulio Mengozzi[1] and Gianluca Aimaretti[3]

[1]*Department of Medical Sciences, University of Turin, Clinical Biochemistry Laboratory, Turin, Italy;* [2]*DASP s.r.l., Milan, Italy;* [3]*Department of Medical Sciences, University of Turin, Endocrinology, Diabetes and Metabolism, Turin, Italy;* [4]*Clinical Biochemistry Laboratory, City of Health and Science University Hospital, Turin, Italy*

Background-Aim: Steroid hormones and their metabolites play a central role in endocrine physiology and disease. Although several hundred steroidal compounds have been described in human biological fluids, routine clinical and research assays still focus on

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

limited subsets, providing only a partial view of steroid metabolism. Advances in LC-MS/MS have expanded analytical capabilities; however, comprehensive steroid profiling across multiple biological matrices remains challenging. The aim of this study was to develop and validate a novel high-coverage LC-MS/MS targeted steroidomics platform enabling an integrated assessment of steroid metabolism across different biological matrices.

Methods: A novel LC-MS/MS platform was developed for the detection and relative quantification of 210 steroidal compounds, including 147 free steroids and 64 phase II metabolites, across serum, saliva, and 24-hour urine. Distinct sample preparation workflows were optimized for free and conjugated steroids using supported liquid extraction and solid phase extraction, respectively. Enzymatic hydrolysis was applied for the analysis of total urinary steroids. Chromatographic separation was optimized by testing six LC columns with different stationary phase chemistries and by using ammonium fluoride as an aqueous mobile phase modifier to enhance ionization efficiency and improve chromatographic performance, particularly for sulfated compounds.

Results: The platform was applied to samples from healthy individuals, including paired serum, saliva, and 24-hour urine collections. In serum, up to 92 free steroids in males and 83 in females were detected, together with 33 and 31 conjugated metabolites, respectively. Saliva showed a lower but still informative coverage, with up to 53 free steroids in males and 42 in females, accompanied by a limited number of conjugated compounds. Urine provided the broadest steroidal coverage. In non-hydrolyzed 24-hour urine, up to 87 free steroids in males and 91 in females were detected, together with 42 conjugated metabolites in both sexes. Following enzymatic hydrolysis, the number of detectable free steroids increased to 107 compounds in both males and females, highlighting the contribution of phase II metabolism to urinary steroid excretion.

Conclusions: This novel high-coverage LC-MS/MS platform enables an unprecedented and integrated mapping of steroid metabolism across multiple biological matrices. By markedly expanding the detectable steroid repertoire, this approach provides a more complete representation of steroid biosynthesis, metabolism, and clearance. Clinically, the combined analysis of serum, saliva, and urine may improve phenotypic characterization and diagnostic accuracy in disorders of steroid metabolism, supporting the implementation of targeted steroidomics in endocrinology and enabling the development of matrix-specific analytical panels for clinical and translational research.

Abstract citation ID: lvag096.266

P59 - ECE_3327 - Anastomosing hemangioma mimicking a paraganglioma: a case of false positive finding on 68Ga-DOTATOC PET/CT

Athanasios Fountas[1], Aikaterini Themis Vyllioti[1], Dimitra Zerva[1], Akrivi Kostopoulou[2], Ioannis Karoumpalis[3], Sofia Chatziioannou[4], Pinelopi Lampropoulou[5], Kostas Lymperopoulos[6], Chrysanthi Aggeli[7], Giorgos Zografos[7] and Athina Markou[1]

[1]Unit of Endocrinology and Diabetes Center, "G. Gennimatas" General Hospital of Athens, Athens, Greece; [2]Department of Pathology, "G. Gennimatas" General Hospital of Athens, Athens, Greece; [3]Department of Gastroenterology, "G. Gennimatas" General Hospital of Athens, Athens, Greece; [4]Department of Nuclear Medicine and Molecular Imaging, Attikon NTUA University Hospital, Athens, Greece; [5]Department of Radiology and Medical Imaging New imaging methods, "G. Gennimatas" General Hospital of Athens, Athens, Greece; [6]Department of Radiology and Medical imaging CT/MRI/US, "G. Gennimatas" General Hospital of Athens, Athens, Greece; [7]First Department of Surgery, "G. Gennimatas" General Hospital of Athens, Athens, Greece

Introduction: In recent years, ^{68}Ga-DOTATOC/DOTATATE PET/CT has become paramount in the diagnostic localization of paragangliomas. Despite its enhanced affinity and sensitivity, this imaging method is not without challenges. Herein, we present a case of a presumed paraganglioma, based on ^{68}Ga-DOTATOC PET/CT finding, but proven to be an anastomosing hemangioma.

Case Presentation: A 50-year-old man, with a history of arterial hypertension, Crohn's disease and a 3 cm left retroperitoneal lesion, presented to the Emergency Department with palpitations and pallor. Atrial fibrillation with rapid ventricular response was found and treated appropriately. An abdominal CT scan was performed revealing a 4 cm mass next to the celiac trunk and the superior mesenteric artery, in contact with the left adrenal and the left renal artery. Further imaging with MRI showed a 3.8 cm retroperitoneal lesion with increased T2 signal intensity and no signal suppression on T1 out-of-phase sequence. Differential diagnosis included a left renal vein aneurysm and a paraganglioma. Renal vein ultrasound did not confirm the presence of an aneurysm while endoscopic ultrasound showed a highly vascular lesion with increased contrast uptake in the arterial phase, being contiguous with the celiac ganglia making paraganglioma the most likely diagnosis. However, 24hour urine metanephrine and normetanephrine levels were normal. In order to exclude the possibility of a biochemically silent paraganglioma a ^{68}Ga-DOTATOC PET/CT was performed which showed significant radiotracer uptake (SUVmax 12.8) by the lesion. Taking into account the PET/CT, MRI and ultrasound findings an endoscopic resection of the abdominal mass was decided and performed after preparation with hydration and α-blockade. The surgery and the peri-operative period were uneventful. Surprisingly, the histology was indicative of an anastomosing hemangioma.

Conclusions: Anastomosing hemangiomas are rare benign vascular lesions, often discovered incidentally, and, on imaging, they may mimic other vascular lesions and neuroendocrine tumors. Hemangiomas may, scarcely, express somatostatin receptors 2 leading to false positive uptake on somatostatin receptor functional imaging. To our knowledge, our patient is the second reported case of anastomosing hemangioma showing significant radiotracer uptake on ^{68}Ga-DOTATOC PET/CT.

Abstract citation ID: lvag096.267

P62 - ECE_3790 - Overnight Dexamethasone in Primary Aldosteronism Screening (ODEPRASC): initial results of a diagnostic interpretability study

Piotr Kmieć[1], Dominika Okroj[1], Małgorzata Zdrojewska[1], Ewa Zalewska[1], Jowita Fiszer[1], Sonia Zembrzuska[1] and Renata Świątkowska-Stodulska[1]

[1]Department of Endocrinology and Internal Medicine, Medical University of Gdańsk, Gdańsk, Poland

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: The recommendation to withdraw medications that interfere with the renin–angiotensin–aldosterone system (RAAS) prior to work-up partially underlies the underdiagnosis of primary aldosteronism (PA). Research by others showed that:

1. an aldosterone (Ald)-to-renin ratio (ARR) of 10 pg/uIU in patients on RAAS-interfering medications was equivalent to 20 pg/uIU in those switched to non-interfering drugs,
2. PA work-up accuracy among HT patients off interfering drugs improved significantly when 48-hour cosyntropin suppression was combined with objective diagnostic cutoffs.

The current study aims to generate thresholds offering a 25% higher interpretability in PA screening than baseline ARR determination despite RAAS-interfering medications by applying overnight cosyntropin suppression.

Methods: In this prospective, single-center, cross-sectional study development and confirmatory cohorts are recruited among patients with an adrenal incidentaloma. ARRs are determined before and after overnight intake of 1 mg dexamethasone (DXM) on and off interfering medications. Exclusion criteria include renin above the upper reference limit (chemiluminescence immunoassay).

Results: So far, data of 67 patients have been available for initial analyzes (39 women and 28 men, mean age 61.5+-10.2 years) out of 511 screened for participation. Possible mild autonomous cortisol secretion was recorded in eleven patients (highest post-DXM cortisol: 88.3 nmol/l). Baseline PA screening was negative in 22, positive in 19, and equivocal in 26 patients (39%). Post-DXM measurements allowed classifing the basally equivocal ARRs as positive in 12 more patients (for a total of 31 out of 67, ie, 46%), negative in 24 (36%), and equivocal in 12 (18%). One positive ARR pre-DXM shifted to a negative result post-DXM (eplerenone therapy), the opposite was observed in two patients. Among the recruited patients, the presence of PA could be verified in 61 patients: by ARR re-testing off interfering medications ($n = 33$) or by PA suppression tests (27 saline infusion tests, one oral salt loading test). PA was diagnosed in 21 patients (34.4%) and ruled out in 40 patients (65.6%). The definitive diagnosis status allowed comparing diagnostic accuracy measures, which revealed clear clinical benefit of applying overnight DXM intake on ARR interpretation, in particular a 24.5 percentage point reduction in equivocal ARR rate (from 24 to 9 out of 61 patients).

Conclusions: The 2025 Endocrine Society guideline places greater emphasis on ARR in the PA work-up while restricting the use of suppression tests. The approach proposed here could be highly advantageous as demonstrated in a 24.5% reduction in equivocal ARR results among patients on interfering medications (ClinicalTrials.gov ID NCT06740838).

Abstract citation ID: lvag096.268

P63 - ECE_2054 - Diagnostic accuracy of 68Ga-pentixafor PET/CT in identifying functional Primary Aldosteronism Lesions with different features in CT images

Shiman Li[1], Fan Yang[2], Yuxing Lou[1], Wei Zhang[2], Chuanjiang Chen[1] and Ping Li[2]

[1]*Department of Endocrinology, Endocrine and Metabolic Disease Medical Center, Nanjing Drum Tower Hospital Clinical College of Nanjing University of Chinese Medicine, Nanjing, China;* [2]*Nanjing, China*

Background: Numerous studies have confirmed the value of ^{68}Ga-pentixafor PET/CT for PA subtyping. However, some diagnostic errors remain. The features of adrenal lesions on CT images vary across patients with PA. To date, no study has investigated whether the diagnostic performance of PET/CT varies among adrenal lesions with different imaging features.

Aim: To define the features of the adrenal lesions in CT images of patients with PA associated with better ^{68}Ga-pentixafor PET/CT diagnostic performance.

Methods: This single-center, retrospective study was conducted at a tertiary hospital in China. Consecutive PA patients who underwent both adrenal CT and ^{68}Ga-pentixafor PET/CT imaging were included. PET/CT image interpretation involved visual analysis, and semiquantitative parameters, including the SUVmax, liver-to-lesion ratio (LLR), and lesion-to-adrenal ratio (LAR), were recorded. According to the outcome after surgery or the results of AVS, patients were classified as having unilateral PA or bilateral PA, and their lesions were categorized as functional or nonfunctional. Based on adrenal CT imaging features, the lesions were classified as adenomas or nonadenomas. ROC curve analysis was performed to evaluate the accuracy of PET/CT for identifying adrenal lesions with different imaging features.

Results: A total of 93 patients with postoperative follow-up data or successful AVS were analyzed (45.2% female; mean age 49.3 ± 11.6 years). A total of 136 adrenal lesions, including 81 typical adenomas and 55 nonadenomas, were detected by CT. Visual analysis yielded a positivity rate of 90.1% in the adenoma group, which was significantly higher than the 18.2% for in the nonadenoma group ($P < 0.001$). Semiquantitative analysis revealed that all the parameters were significantly greater in the adenoma group than in the nonadenoma group ($P < .001$). Furthermore, the AUCs of the four PET/CT indices for identifying functional lesions in the adenoma group ranged from 0.828 to 0.915, which were consistently greater than those in the nonadenoma group (0.541-0.613). Notably, visual analysis demonstrated superior diagnostic efficacy within the adenoma group, yielding a sensitivity of 97.3%, specificity of 85.7%, and accuracy of 96.3%. In contrast, the diagnostic sensitivity of visual analysis in the nonadenoma group was only 33.3%.

Conclusions: The diagnostic performance of ^{68}Ga-pentixafor PET/CT is better for PA patients with adenomas than for those with nonadenomas by CT. Therefore, ^{68}Ga-pentixafor PET/CT could serve as a primary subtype modality in patients with adenoma lesions on CT. Further multicenter prospective studies are warranted to validate these findings.

Abstract citation ID: lvag096.269

P65 - ECE_3078 - Glucocorticoids: hub between infection susceptibility and inflammation

Samira Kaziakhmedova[1,2] and Charlotte Steenblock[1,2]

[1]*Technical University of Dresden Medical School, Dresden, Germany;* [2]*University Clinic Dresden, Dresden, Germany*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Infections represent the second leading cause of mortality in patients with Cushing's syndrome, highlighting a clinically significant consequence of chronic endogenous hypercortisolism. While it is well established that sustained glucocorticoid excess induces a generalized immunosuppressive state, current understanding is largely based on descriptive immunophenotyping, with limited mechanistic insight into how prolonged glucocorticoid exposure alters immune competence and host-pathogen interactions. In particular, the effects of chronic hypercortisolism on innate immunity, pathogen recognition pathways, and immune responses to viral and bacterial infections remain poorly defined. This study aims to establish and translationally characterize a murine model of chronic hypercortisolism that faithfully recapitulates the metabolic, endocrine, and immune alterations observed in patients with Cushing's syndrome. Such a model is essential for elucidating the mechanisms underlying infection susceptibility in these patients. Seventeen-week-old mice were administered dexamethasone in drinking water (0.0167 mg/mL) for 14 or 21 days. Metabolic assessments included glucose and insulin tolerance tests performed prior to study termination. At the experimental endpoint, plasma was collected for measurement of adrenocorticotropic hormone (ACTH), corticosterone, and circulating cytokines. Lung and spleen tissues were analyzed by flow cytometry to quantify innate immune populations, focusing on monocytes and neutrophils using Ly6C and Ly6G markers. Adrenal glands were harvested for histological evaluation of tissue atrophy and for quantitative PCR analysis to assess transcriptional changes within the hypothalamic-pituitary-adrenal (HPA) axis. Prolonged dexamethasone exposure resulted in significant metabolic impairment, including reduced glucose tolerance, closely resembling metabolic abnormalities observed in patients with hypercortisolism. Endocrine profiling revealed high ACTH levels after 21 days of dexamethasone treatment. Flow cytometric analysis did not demonstrate glucocorticoid-dependent changes in lung innate immune cell composition, though further investigation is warranted. Histological and molecular analyses confirmed glucocorticoid-induced adrenal suppression. In conclusion, this translational murine model successfully reproduces key clinical features of Cushing's syndrome, including metabolic dysregulation and alteration of the HPA axis. As such, it provides a valuable bridge between experimental endocrinology and clinical practice. Insights gained from this in vivo model will be validated in human samples, with the ultimate goal of identifying immune biomarkers for infection risk stratification and developing targeted interventions to reduce infectious morbidity in patients with chronic hypercortisolism.

Abstract citation ID: lvag096.270

P66 - ECE_3926 - Adrenal crisis in pre-hospital and emergency care: healthcare professionals' knowledge, attitudes and practices, and implications for endocrine nursing

Heather Reid[1,2], Charlotte Rowe[1] and Sofia Llahana[1]
[1]City St George's University, London, United Kingdom; [2]Emergency Department, King's College Hospital, London, United Kingdom

Background: Adrenal crisis is a life-threatening endocrine emergency requiring rapid symptom recognition and prompt treatment with parenteral hydrocortisone. Effective management across pre-hospital and emergency department settings relies on timely triage, patient prioritisation and coordination of care, clinical assessment, prompt recognition of deterioration, and escalation for hydrocortisone administration and intravenous fluids. However, adrenal crisis often presents with non-specific features such as hypotension, vomiting, or confusion. In high-pressure emergency environments, limited familiarity with adrenal insufficiency, inconsistent protocols, and uncertainty around management may contribute to delayed or suboptimal care. Understanding current knowledge, attitudes, and practices across professional groups is essential to inform interventions that support patients with adrenal insufficiency and healthcare professionals to navigate emergency settings safely.

Aim: To explore the knowledge, attitudes, and clinical practices of pre-hospital and emergency department healthcare professionals in recognising and managing adrenal crisis.

Methods: A cross-sectional online survey was distributed to paramedics, nurses, medical doctors, and advanced clinical practitioners working in pre-hospital and emergency care settings across the United Kingdom. Participants were recruited through professional networks and social media between October and December 2025. The survey examined knowledge of adrenal crisis, clinical experience, perceived confidence in recognition and management, and learning needs.

Results: A total of 211 emergency care clinicians (89 paramedics, 85 nurses and 37 medical doctors) completed the survey. General awareness of adrenal crisis was high; however, gaps were identified in applied treatment knowledge. Most participants (75.1%; $n = 139/185$) correctly identified intravenous or intramuscular as the appropriate route for hydrocortisone administration in an AC. Knowledge of hydrocortisone dosing varied: 88.0% ($n = 125/142$) identified the correct initial hydrocortisone dose, but only 55.6% ($n = 45/81$) identified the recommended ongoing dose over 24 hours. Confidence in recognising and managing adrenal crisis was low to moderate overall, with paramedics reporting higher confidence than nurses and medical doctors. Perceived competence in medication administration and the adequacy of training were also higher among paramedics and differed significantly by role (all $P < .01$). There was strong agreement that greater awareness of the NHS Emergency Steroid Card is needed, although fewer respondents felt it is routinely recognised in practice.

Conclusions and Implications for Practice: Despite good general awareness of adrenal crisis, significant gaps remain in applied knowledge and clinical confidence among pre-hospital and emergency clinicians. Targeted, multidisciplinary education and clearer clinical pathways are needed to support timely, guideline-concordant management of adrenal crisis across acute care settings.

Abstract citation ID: lvag096.271

P67 - ECE_3676 - A single centre audit on the Adrenal Lesion service in Serbia

Dijana Jankovic[1], Aldons Chua[2], Sara Odalovic[1], Kristina Saravinovska[1,3], Antoan Stefan Sojat[1,3], Natalija Antic[1], Boban Stepanovic[4], Jana Vujnovic[1], Dragana Mitrovic[1], Jelena Vujovic[1], Miomira Ivovic[1,3], Svetlana Vujovic[1,3] and Ljiljana Marina[1,3]
[1]Clinic of Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Belgrade, Serbia; [2]Endocrinology, St

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Bartholomew's Hospital, London, United Kingdom; [3]Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [4]Clinic of Endocrine Surgery, University Clinical Centre of Serbia, Belgrade, Serbia

Introduction: Studies have shown a wide range between the time of initial CT finding of adrenal lesions (AL) until the final diagnosis. Such discrepancies affect treatment outcomes, potentially adding to healthcare system burden. Service models in other countries, such as the United Kingdom, where nurses have expanded competencies by running nurse-led clinics, have shown positive outcomes. In Serbia, there is currently no nurse-led clinics and the role of endocrine nurses in AL is not yet structured.

Aim: The aim of this audit is to review the current effectiveness of the diagnostic pathway for patients with AL, managed at tertiary endocrine unit, and to identify potential gaps in the service where specialist nurse involvement could improve coordination and the diagnostic process.

Method: A retrospective audit was conducted using the endocrine unit database over the past 10 years and randomly selected 23 patients with non-functioning adrenal lesions (NAL) and non-randomly 27 patients with functioning confirmed AL on CT imaging. Data was collected anonymously: age, sex, date of the incidental finding, diagnostic tests performed, confirmed diagnosis and treatment received.

Results: Fifty patients, 12 males and 38 females, aged 21-77, had an incidental AL finding on imaging (MRI, CT) except for two with overt signs and symptoms of Cushing's syndrome and Primary hyperaldosteronism. All patients underwent diagnostic tests-overnight dexamethasone test, 24-hour urine metanephrines and cortisol, plasma renin and aldosterone, and cortisol profile. Final diagnoses included NAL-23, phaeochromocytoma-10, adrenocortical carcinoma (ACC)-6, Cushing's syndrome-4, mild autonomous cortisol secretion-4, and primary hyperaldosteronism-3. The median time from initial AL visualization to tertiary center referral was 5.9 months, whereas the median time from tertiary care assessment to final diagnosis was 1.6 months. The total median time from initial AL visualization to final diagnosis in our cohort was 7.5 months. For ACC, the median time from AL visualization to final diagnosis was 13.4 months. This is comparable to international data for ACC, where reported median diagnostic intervals span from 8.7 months to 4 years in some cases.

Conclusions: Our findings place Serbia close to the international median for ACC but still highlight significant delays, predominantly before tertiary referral, which is particularly important as delayed diagnosis may negatively affect outcomes. Our results reflect the gaps in primary care recognition and referral pathways. Targeted primary care education, combined with nurse-led AL clinics at the tertiary level, could lead to earlier triage, and a more efficient diagnostic pathway, thus improving patient outcomes.

Abstract citation ID: lvag096.272

P68 - ECE_3385 - "Out in no man's land": illness perceptions and diagnostic experiences in adults with adrenal insufficiency

Charlotte Rowe, Shashi Hirani, Kathleen Mulligan, Stanton Newman and Sofia Llahana
London, United Kingdom

Background: Adrenal insufficiency is a rare, chronic endocrine condition requiring lifelong treatment with glucocorticoids replacement and effective self-management. Delayed diagnosis and challenges for daily treatment and Illness perception refers to patients' belief and expectations about their illness, encompassing physical, cognitive and emotional representations, and can be described within the Common Sense Model (CSM) theoretical framework (Leventhal, 2012). The CSM differentiates between cognitive and emotional illness representations, and captures the individual's overall understanding and global sense of coherence around their illness. Cognitive representations are described across five classes 1) identity, 2) consequences, reflecting an individual's beliefs about illness severity and its impact on physical, mental and social functioning, 3) timeline, relating to temporal expectations of the illness duration, 4) control-cure, referring to beliefs about whether the illness can be cured, or controlled by treatment, and 5) cause, reflecting beliefs about the underlying mechanisms of the illness.

Objective: To explore the dimensions of illness perception amongst adults with adrenal insufficiency and how these perceptions map onto the CSM.

Methods: This qualitative study investigated illness perceptions of adults with adrenal insufficiency. Semi-structured focus group interviews were conducted with 61 participants from the UK, USA and Canada, across 13 groups of 3-6 participants (10 from UK and 3 from USA and Canada). The sample included 13 males, 46 females and 2 non-binary, mean age 46.26; 20 participants were diagnosed with secondary adrenal insufficiency, 32 with primary, and 9 with tertiary. Data were transcribed verbatim, de-identified, and analysed using deductive thematic analysis and mapped onto CSM domains.

Results: Participants frequently described their identity in relation to the physical symptoms they experienced, as well as the type of adrenal insufficiency, and associated comorbidities. A wide range of perceived consequences were reported, including physical, social, and emotional.

The journey to diagnosis was often described as complex and prolonged, and participants reported experiences of misdiagnosis, and symptom misattribution by healthcare professionals. Participants often described emotional reactions when considering their diagnosis and many reported a feeling of unfairness. Treatment was largely perceived as unpredictable, unreliable and not fully effective and long-lasting.

Conclusions: This study highlights the need for access to training and support for individuals with adrenal insufficiency and their families, particularly around medication management and responding to an adrenal crisis. While support is available via patient advocacy groups these findings emphasised that clinical information and peer support should be integrated across services throughout the lifespan.

Abstract citation ID: lvag096.273

P69 - ECE_3364 - Bone health in patients with pituitary adenomas: a multicenter retrospective cohort study

Romy van der Groef[1], Claudia Campana[1,2], Els van Zaanen[1], Diego Ferone[2], Federico Gatto[2], Julie Celine Refardt[1], Evert van Velsen[1] and Sebastian Neggers[1]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Section Endocrinology, Erasmus MC, Internal Medicine, Rotterdam, The Netherlands; [2]Section Endocrinology, Università di Genova, Internal Medicine and Medical Specialties (DIMI), Genova, Italy

Introduction: Patients with pituitary adenomas are thought to have an increased risk of vertebral fractures (VFs), due to either hormone excess or hypopituitarism. However, evidence comparing bone health across different pituitary adenoma types is scares. We aimed to assess the differences in associations between bone mineral density (BMD) and bone quality, measured by Trabecular Bone Score (TBS), and their relationship with fracture prevalence across various pituitary adenomas.

Methods: This retrospective, multicenter cohort study included patients with acromegaly, Cushing's disease, prolactinomas, and non-functional pituitary adenomas (NFPA). BMD at the femoral neck (FN) and lumbar spine (LS, L1-L4), TBS, fracture prevalence and incidence were analyzed. Moderate-severe VFs (Genant grade ≥2) were considered as clinically significant. Bone quantity, quality and VFs were compared between adenoma types and assessed with univariable and multivariable regression models.

Results: Our combined Italian and Dutch cohort included 335 patients (133 acromegaly, 69 Cushing's disease, 83 prolactinomas, 50 NFPAs; mean age 60 years (SD 13.8); 53.1% female). VFs were observed in 35 patients (10.5%, 12 acromegaly, 12 Cushing's disease, 1 prolactinomas, 10 NFPAs), of which 6 VFs were incident. After adjusting for FN BMD (T-score), age, prolactinomas showed significantly lower odds of VFs (OR 0.05, 95% CI: 0.002-0.31) compared to the other pituitary adenomas. Secondary hypogonadism was similar across pituitary adenoma types, except in NFPAs, where nearly all patients (96%) had secondary hypogonadism. FN BMD was strongly associated with VFs in most groups, except for acromegaly. Here, TBS was more strongly associated with fracture risk (log odds: TBS −5.03 vs FN BMD −4.73). Overall TBS and LS BMD had a weak correlation (rho = 0.28) independently of pituitary adenoma type. In all patients, age negatively affected bone health, with each 10-year increase associated with a 0.186 decrease in BMD T-score and a 0.346 decrease in TBS T-score. Additionally, higher baseline TBS was linked to better BMD, while higher baseline vitamin D levels were positively associated with improved TBS.

Conclusions: In this large cohort of pituitary adenoma patients, vertebral fracture (VF) prevalence and incidence were lower than previously reported, and similar across most pituitary adenoma types. TBS proved to be a valuable marker for assessing fracture risk in acromegaly, while age and vitamin D levels were key factors influencing bone health in all pituitary adenoma patients. Our results highlight the importance of incorporating TBS, age and Vitamin D levels into the bone health assessment of pituitary adenoma patients.

Abstract citation ID: lvag096.274

P71 - ECE_1542 - Beneficial for weight, detrimental for bone: semaglutide and PYY3-36 exacerbate metabolic osteoporosis (MetOP) in a novel two-hit MetOP rat model

Simon Kloock[1], Palina Zytner[1], Niklas Geiger[1], Vasco Sequeira[2], Angelika Schmitt-Böhrer[3], Jasmin Felker[1], Humma Sarwar[4], Anita Ignatius[4], Martin Fassnacht[1], Melanie Haffner-Luntzer[4] and Ulrich Dischinger[1]

[1]Department of Internal Medicine, Division of Endocrinology and Diabetes, University of Wuerzburg, University Hospital Wuerzburg, Wuerzburg, Germany; [2]Comprehensive Heart Failure Center, University of Wuerzburg, University Hospital Wuerzburg, Wuerzburg, Germany; [3]Department of Psychiatry, Psychosomatics and Psychotherapy, Center of Mental Health, University of Wuerzburg, University Hospital Wuerzburg, Wuerzburg, Germany; [4]Institute of Orthopaedic Research and Biomechanics, University of Ulm, Ulm, Germany

Background: Metabolic syndrome–associated osteoporosis (MetOP) arises from the convergence of metabolic, vascular, and stress hormone disturbances. Modern gut hormone–based therapies are beneficial in the treatment of the metabolic syndrome, but the skeletal consequences remain poorly understood. This study (1) establishes and sex-specifically characterizes a "two-hit" rat model of MetOP combining a Western diet (WD) with nitric oxide synthase inhibition (L-NAME), and (2) evaluates the effects of semaglutide, peptide YY3-36 (PYY3-36), and their combination on bone health in this model.

Methods: (1) Male and female Wistar rats were fed WD and treated with L-NAME for 16 weeks to induce MetOP. Femoral trabecular bone architecture was assessed by micro-computed tomography and histomorphometry. Bone RNA-sequencing, alongside serum analyses of bone turnover markers and steroid hormones (LC/MS-MS) were performed. (2) Female MetOP rats (treated with WD and L-NAME for eight weeks) were randomized to receive semaglutide, PYY3-36, or semaglutide+PYY3-36 for another eight weeks. The read-out was similar to (1) but also included gene-expression analysis of the hypothalamus to describe alterations of the hypothalamus-pituitary-adrenal (HPA) axis as an indicator of metabolic stress.

Results: (1) WD+L-NAME induced a robust osteoporotic phenotype in both sexes, characterized by significantly reduced bone-volume-to-tissue-volume-ratio (BV/TV) in the distal femur, altered osteoclast numbers, and transcriptional suppression of bone formation pathways. While WD predominantly affected extracellular matrix–related gene expression, male rats exhibited markedly elevated circulating sclerostin, implicating Wnt-signaling inhibition. (2) Semaglutide and semaglutide +PYY3-36 significantly reduced body weight. Semaglutide monotherapy caused a modest decline in BV/TV, whereas PYY3-36 and especially semaglutide+PYY3-36 exacerbated trabecular deterioration, including significantly increased trabecular separation. Osteoclast numbers increased under semaglutide and PYY3-36, while osteoblast numbers showed a trend towards reduction across treatments. Transcriptomic analyses revealed downregulation of osteoblast and cell cycle genes with semaglutide, and upregulation of angiogenesis and extracellular matrix pathways with PYY3-36. Hypothalamic analyses suggested modulation of the NPY2 receptor and a trend towards reduced HPA-axis activity with semaglutide+PYY3-36.

Conclusions: A WD+L-NAME "two-hit" model reliably induces MetOP and reveals sex-specific molecular signatures involving Wnt-signaling and extracellular matrix regulation. In this vulnerable context, semaglutide further reduced bone-mineral content, especially in combination with PYY3-36. These findings may limit the progression of PYY3-36 to clinical application and underscore the importance of evaluating long-term bone safety of gut hormone–based therapies in patients with osteoporosis.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.275

P72 - ECE_1568 - Autosomal dominant hypocalcemia type 1 and Type 2: baseline quality of life measures in adult participants in the CLARIFY disease monitoring study

Heide Siggelkow[1,2], Brigitte Decallonne[3], Lars Rejnmark[4], Cardot Catherine[5], Roderick Clifton-Bligh[6,7], Steven Ing[8], Outi Mäkitie[9], Tariq Ahmad[10], Stefano Mora[11], Evert Van Velsen[12], Ana Paula Barbosa[13], Erik Imel[14], Aliya Khan[15], Lemoine Sandrine[16], Nina S. MA[17,18], Peter Tebben[19], Mark Warren[20], Nobuaki Ito[21], Agnès Linglart[22], Giovanna Mantovani[23,24], Halley Wasserman[25], Jessica Chen[26], Mary Scott Roberts[26] and Andrea Palermo[27,28]

[1]MVZ Endokrinologikum Göttingen, Göttingen, Germany; [2]Department of Trauma, Orthopedics and Reconstructive Surgery, University Medical Center Göttingen, Göttingen, Germany; [3]Department of Endocrinology, University Hospitals Leuven, Leuven, Belgium; [4]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus, Denmark; [5]Department of Endocrinology and Metabolism, Lille University Hospital, Lille, France; [6]Department of Endocrinology, Royal North Shore Hospital, Sydney, Australia; [7]Faculty of Medicine and Health, University of Sydney, Sydney, Australia; [8]Ohio State University Wexner Medical Center, Columbus, United States; [9]Pediatric Research Center, University of Helsinki and Helsinki University Hospital, Children's Hospital, Helsinki, Finland; [10]Division of Pediatric Endocrinology, University of California San Francisco—Benioff Children's Hospital, Oakland, United States; [11]Pediatric Endocrinology, IRCCS Ospedale San Raffaele, Milano, Italy; [12]Department of Internal Medicine, Erasmus University Medical Center, Erasmus MC Bone Center, Rotterdam, The Netherlands; [13]Department of Endocrinology Diabetes and Metabolism, ULS Santa Maria Lisboa and Faculty of Medicine, Lisboa, Portugal; [14]Department of Medicine and Pediatrics, Indiana University School of Medicine, Indianapolis, United States; [15]Divisions Endocrinology and Metabolism and Geriatrics, McMaster University, Ontario, Canada; [16]Department of Nephrology and Physiology, Université de Lyon, Edouard Herriot Hospital, Hospices Civils de Lyon, Lyon, France; [17]University of Colorado School of Medicine, Aurora, United States; [18]Pediatric Endocrinology, Children's Hospital Colorado, Aurora, United States; [19]Division of Endocrinology and Metabolism, Yale University School of Medicine, New Haven, United States; [20]Physicians East, Greenville, United States; [21]Division of Therapeutic Development for Intractable Bone Diseases, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo, Tokyo, Japan; [22]Paris Saclay University, AP-HP Hopital Bicetre, Le Kremlin-Bicêtre, France; [23]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [24]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [25]Department of Pediatric Endocrinology, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, United States; [26]BridgeBio, San Francisco, United States; [27]Unit of Metabolic bone and thyroid disorders, Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy; [28]Unit of Endocrinology and Diabetes, Campus Bio-Medico University, Roma, Italy

Autosomal dominant hypocalcemia type 1 (ADH1) and type 2 (ADH2) are rare disorders caused by activating variants of the calcium-sensing receptor (*CASR*) and G-protein subunit alpha-11 (*GNA11*) genes, respectively. The CaSR and its signal transducer GNA11 play a critical role in calcium homeostasis by regulating parathyroid hormone secretion and urinary calcium reabsorption in response to variations in blood ionized calcium. Activating variants in *CASR* or *GNA11* increase signaling sensitivity to calcium, leading to hypocalcemia and hypercalciuria.

The CLARIFY disease monitoring study [NCT05227287] is an ongoing global, multicenter, longitudinal, observational study to characterize disease burden, management, and progression in children and adults with ADH1/2 over a 5-year period. Of 95 participants enrolled, 74% (70) were adults (≥18 years; 65 ADH1, 5 ADH2). Adult participants had a mean ± SD age of 44 ± 16 years (median 41; range 18-80); 53% (37) were female. We report baseline (Day 1), self-reported quality-of-life (QoL) findings from adult participants assessed by a sponsor-developed ADH1/2 questionnaire and the 36-Item Short Form Health Survey (SF-36 v2). The ADH1/2 questionnaire captured data on clinical manifestations, symptoms, and treatment. Responses indicated that neuromuscular symptoms most frequently affected QoL ([percentage of participants (n)]: muscle cramps/spasms [76% (53)], paresthesia [70% (49)], joint pain [57% (40)], followed by chronic fatigue [50% (35)]). Symptoms reported to have greatest overall impact on daily functioning were muscle cramps/spasms [44% (31)], paresthesia [37% (26)], chronic fatigue [30% (21)], and joint pain [23% (16)]. The most impaired activities of daily living were exercising regularly [36% (25)], climbing stairs [21% (15)], and performing house cleaning and home maintenance [20% (14)]. Compared with the US general population for SF-36 assessment, ADH1/2 negatively affected all physical and mental domains [mean ± SD physical (47.2 ± 9.7) and mental component scores (47.1 ± 10.1)]. Burden of disease was further emphasized by 42% (29) of participants ever requiring hospitalization for treatment of hypocalcemia [16% (11) with 1-2 hospitalizations; 26% (18) with ≥3 hospitalizations] and 28% (19) ever requiring intravenous calcium to manage ADH1/2 [6% (4) with 1-2 infusions; 22% (15) with ≥3 infusions]. This study represents the largest cohort of adults with ADH1/2 described to date. Baseline findings reveal major and underrecognized disease burden driven by chronic neuromuscular symptoms, physical limitations, and symptomatic hypocalcemia. Continued follow-up of these QoL measures aims to elucidate factors contributing to disease burden and inform improved monitoring and management strategies for ADH1/2.

Abstract citation ID: lvag096.276

P73 - ECE_1859 - Sarcopenia and circulating GDF15 levels in severe osteoporotic individuals: effects of 18 months treatment with teriparatide

Chiara Verdelli[1], Veronica Sansoni[1], Chiara Degradi[2], Silvia Carrara[3], Romina Mirsepanj[4], Giovanni Lombardi[1,5] and Sabrina Corbetta[3,6]

[1]Laboratory of Experimental Biochemistry & Advanced Diagnostics, IRCCS Ospedale Galeazzi-Sant'Ambrogio, Milan, Italy; [2]Centro Obesità, Centro Disturbi Alimentari e della Nutrizione, IRCCS Istituto Auxologico Italiano, Milan, Italy; [3]Bone Metabolism Diseases and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Milan, Italy; [4]Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [5]Department of Athletics, Strength and Conditioning, Poznań University of Physical Education, Poznan, Poland; [6]Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Sarcopenia is associated with aging and osteoporosis contributing to the risk of falls and fragility fractures. Circulating myokines has been proposed as muscle-related biomarkers. The myokines growth differentiation factor 15 (GDF15), a stress-induced signaling molecule, and follistatin-like 1 (FSTL1) were measured in severe osteoporotic patients, investigated by lumbar spine, femur and total body DXA and handgrip test. Eighty-nine severe osteoporotic patients [84 females, 5 males; aged 74 (71-79) years, BMI 24.5 (22.9-27.6) kg/m^2] were prospectively enrolled; all experienced at least one fracture (total 356 fractures, 277 vertebral fractures, 17 femur fractures). All individuals were vitamin D repleted [96.5 (79.5-116.7) nmol/L]. Low muscle mass, evaluated as appendicular skeletal muscle index (ASMI), was diagnosed in 34 individuals (38.2%), while sarcopenia, defined as reduced ASMI and low muscle strength by handgrip test, was diagnosed in 14 individuals (15.7%). Dynapenia was detected in 26 individuals (29.2%). In the analyzed series, serum GDF15 and FSLT1 positively correlated with each other and with sclerostin levels suggesting a bone-muscle crosstalk. Serum GDF15 levels, but not FSTL1, positively correlated with ASMI ($r = 0.249$, $P = .021$), while handgrip values did not correlate with any myokines levels. Similarly, GDF15 levels, but not FLST1, showed a trend to positively correlate with lumbar spine T-scores ($r = 0.202$, $P = .071$) and with the bone mineral content (BMC) at dorsal spine ($r = 0.264$, $P = .019$) and pelvis ($r = 0.219$, $P = .052$). Moreover, GDF15 levels emerged as a marker of frailty as they positively correlated with the number of fractures in each individual ($r = 0.202$, $P = .057$), in particular with pelvis and lower limb fractures. Twenty-two individuals were evaluated after 18 months treatment with teriparatide 20 mcg/day (TPT). TPT increased lumbar spine T-score (-3.39 ± 1.17 vs -2.92 ± 1.14, $P < .0001$), while it did not prevent the reduction of ASMI (5.64 ± 0.58 vs 5.35 ± 0.63 kg/m^2, $P = .0033$), though handgrip values remained unchanged. Moreover, TPT induced significant increases of GDF15 levels by a mean of 29% ($P < .0001$), while FSTL1 levels were unaffected. TPT-induced GDF15 levels positively correlated with ASMI ($r = 0.592$, $P = .0047$). Considering that TPT did not prevent the 5% aging-related reduction of skeletal muscle mass, the TPT-increased GDF15 levels might come from osteoblasts/osteocytes stimulation.

In conclusion, in severe osteoporotic patients, low skeletal muscle mass and dynapenia are common, and sarcopenia occurs in about 1 out of 6 individuals. GDF15 emerges as a marker of frailty but osteoporosis and sarcopenia are associated with lower levels and anabolic TPT treatment increases GDF15 levels. GDF15 role in bone-muscle crosstalk deserves further investigation.

Abstract citation ID: lvag096.277

P74 - ECE_2384 - Epidemiology of low bone density and osteoporosis in chronic hypoparathyroidism: baseline prevalence and medication usage from National US claims

David Vizcaya[1], Aliya Khan[2], Ying Kong[3], Yingqi Gu[4], Ellen Colman[3], Sigridur Björnsdottir[5,6] and Luke McGuinness[4]

[1]Epidemiology and Real-World Science, Alexion, AstraZeneca Rare Disease, Barcelona, Spain; [2]Division of Endocrinology and Metabolism, McMaster University, Hamilton, ON, Canada; [3]Global Medical Affairs, Alexion, AstraZeneca Rare Disease, Boston, MA, United States; [4]Epidemiology and Real-World Science, Alexion, AstraZeneca Rare Disease, Dublin, Ireland; [5]Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden; [6]Department of Endocrinology, Metabolism and Diabetes, Karolinska University Hospital, Stockholm, Sweden

Background: Bone health is compromised in chronic hypoparathyroidism (cHypoPT). Recent clinical guidance recommends skeletal assessment, notably in postmenopausal women and men aged ≥50 years. This study aims to report low bone density and osteoporosis prevalence at baseline and real-world osteoporosis drug usage in cHypoPT.

Methods: This is a retrospective study using the US claims database IQVIA PharMetrics Plus. Disease diagnoses were determined by ICD-10-CM codes. cHypoPT was defined by meeting ≥1 of the following criteria during 2018-2024: (1) 2 HypoPT codes separated by 30-365 days, with no prior neck surgery; (2) 1 HypoPT and 1 hypocalcemia code separated by 30-365 days, with no prior neck surgery; or (3) 1 HypoPT or 1 hypocalcemia code and ≥365 days after neck surgery. The baseline was any time prior to or on index date. In the cHypoPT cohort, low bone density was identified by the presence of ≥1 of selected M85 codes and osteoporosis by the presence of ≥1 code of M80 or M81 lists. Osteoporosis medication exposure at baseline was obtained from pharmacy claims. Recent treatment usage covers 365 to 31 days before the index date, and current usage spans 30 days before to 90 days after the index date. Analyses were stratified by age, sex, and postmenopausal status (including natural and induced ones), which was determined by menopause code or age ≥50 years.

Results: Out of 33 311 patients with cHypoPT, 76% (25 306) were female with a median age of 57 years (interquartile range of 44-65 years) at index. Among 17 407 postmenopausal women, 16% (2761) and 24% (4167) had low bone density and osteoporosis, respectively. In 7897 premenopausal women, 3% (202) had low bone density, and 2% (159) had osteoporosis. In 5290 men aged ≥50 years, 8% (440) had low bone density, and 10% (541) had osteoporosis. In 2460 men aged <50 years, 4% (94) had low bone density, and 4% (99) had osteoporosis. Though 15% of the total cohort had concomitant osteoporosis, the use of osteoporosis medication around the index date was low; 7% and 0.1% had exposure to ≥1 class of antiresorptive and anabolic therapies, respectively.

Conclusions: This large cHypoPT cohort shows notable prevalence of concomitant low bone density and osteoporosis, especially in postmenopausal women and men aged ≥50 years, and limited osteoporosis medication use despite substantial disease burden, underscoring the need for skeletal health awareness and assessment in cHypoPT.

Abstract citation ID: lvag096.278

P75 - ECE_2530 - Bone microarchitecture, density and turnover 5 years after gastric bypass vs sleeve gastrectomy in people with severe obesity and type 2 diabetes: a post-hoc analysis from the Oseberg RCT

Jostein Wågen Hauge[1,2], Jøran Hjelmesæth[1,2], Heidi Borgeraas[1], Jens Kristoffer Hertel[1], Morten Lindberg[1], Rune Sandbu[1], Marius Svanevik[1], Karen Hind[3], Mikkel Pretorius[4] and Dag Hofsø[1]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Vestfold Hospital Trust, Tønsberg, Norway; [2]University of Oslo, Oslo, Norway; [3]Medimaps, Geneva, Switzerland; [4]Oslo University Hospital, Oslo, Norway

Introduction: Greater bone mineral density (BMD) reduction and higher bone turnover after gastric bypass (GB) compared with sleeve gastrectomy (SG) may partly explain the increased fracture risk after GB. Trabecular bone score (TBS), a marker of bone microarchitecture, correlates with fracture risk. However, the long-term comparative effect of GB vs SG on TBS in people with obesity (PwO) and type 2 diabetes (T2D) is unknown.

Methods: Post-hoc analysis of a two-armed RCT conducted at Vestfold Hospital Trust (Norway). Adults with BMI ≥35 kg/m^2 and T2D were randomised (1:1) to GB or SG and followed for 5 years. Blood-tests were obtained at all visits; DXA at baseline, 1 and 5 years for participants <150 kg. This analysis reports DXA-derived areal BMD, TBS (Medimaps v4.0, valid for tissue thickness <30 cm) retrospectively analysed from lumbar scans obtained from DXA, and bone turnover markers (Procollagen type 1 N-terminal propeptide [P1NP] and C-telopeptide of type I collagen [CTX-1]). Outcomes were assessed according to intention-to-treat principles utilising generalised linear mixed models for repeated measures. Statistical analyses were performed using Stata (version 18).

Results: A total of 109 participants (mean (SD) age 47.7 (9.6) years, BMI 42.3 (5.3) kg/m^2, 66% women) were randomised to GB ($n = 54$) and SG ($n = 55$). Ninety-three (85%) completed 5-year check-up. Available DXA-scans and valid TBS were 97 and 78 at baseline, 94 and 93 at 1-year and 73 and 71 at 5-year, respectively. GB resulted in greater reduction in BMD in the femoral neck (estimated treatment difference = ETD (−4.7% [95% CI −6.7 to −2.7]), the total hip (−4.5% [−6.5 to −2.5]), and the lumbar spine (-6.0% [−8.0 to −4.0]), and greater increase in P1NP (11.7 µg/L [3.1 to 20.4] and CTX-1 (0.17 µg/L [0.09 to 0.25] than SG. Compared with baseline, TBS was 14.7% [12.6 to 16.7] and 15.9% [13.9 to 17.9] higher at 1-year, ETD (1.2% [−1.6 to 4.1], and 6.7% [4.4 to 9.0] and 7.2% [4.9 to 9.4] higher at 5-year, ETD (0.5% [−2.8 to 3.7], after GB vs SG, respectively.

Discussion: GB was, compared with SG, associated with greater reduction in BMD, larger increase in bone turnover, but similar increase in TBS in PwO and T2D suggesting different effects of the procedures on bone density vs microarchitecture. Our findings should be interpreted with caution and require confirmation in future studies using other bone microarchitecture assessment techniques.

Abstract citation ID: lvag096.279

P76 - ECE_3978 - Denosumab or Zoledronate in primary hyperparathyroidism with osteoporosis: two-year calcium and skeletal outcomes

Katarina Mlekus Kozamernik and Tomaz Kocjan
Endocrinology, Department of Endocrinology, Diabetes and Metabolic Diseases, Univerzitetni Kliničnі center Ljubljana, Ljubljana, Slovenia

Background: Primary hyperparathyroidism (PHPT) is associated with reduced bone mineral density (BMD). In patients managed conservatively, antiresorptive therapy is used, but its effects on calcium homeostasis and skeletal outcomes remain incompletely characterized.

Objective: To assess two-year changes in serum calcium and BMD with denosumab or zoledronate in postmenopausal women with PHPT and osteoporosis.

Methods: In this randomized, open-label pilot study, 40 postmenopausal women with PHPT and osteoporosis (mean age 73.0 ± 7.8 years) received either zoledronate 5 mg intravenously once yearly (ZOL) or denosumab 60 mg subcutaneously every six months (DMAB) (ClinicalTrials.gov NCT04085419). Serum total calcium was measured at 3, 6, 12, 18, and 24 months. BMD at the lumbar spine (LS), total hip (TH), femoral neck (FN), and one-third radius (1/3R) was assessed at baseline, 12 months, and 24 months.

Results: Serum calcium declined early, remaining below baseline at 3 and 6 months, before returning to baseline levels thereafter, with no sustained between-group differences. BMD changes did not differ between therapies at any site. Over the first year, denosumab increased BMD at the lumbar spine and total hip, whereas zoledronate increased BMD at the lumbar spine only. No additional BMD gains were observed during the second year, and FN and 1/3R BMD remained unchanged.

Conclusions: In conservatively managed postmenopausal women with PHPT and osteoporosis, two years of treatment with zoledronate or denosumab produced similar, modest, transient reduction in serum calcium and site-specific BMD gains that were largely limited to the first year of treatment.

Abstract citation ID: lvag096.280

P77 - ECE_2395 - Bone metabolism and body composition two years after Roux-en-Y Gastric bypass and sleeve gastrectomy among women—the BARIATRIC BONE study

Fernando Mendonça[1,2], Ana Rita Leite[2], Pietra Soares[3], Mafalda Maia[4], João Neves[2], Carla Luís[5,6], Ilda Rodrigues[4], Liliana Carvalho[4], Joana Alves[4], Beatriz Fonseca[4], Beatriz Pinto[4], Beatriz Silva[4], Joana Barbosa[4], Luísa Couto[4], Telma Moreno[2], Marta Borges Canha[2], Jorge Pedro[2], Diana Alexandra Festas Silva[2], Ana Varela[2], Teresa Faria[2], Ana Fernandes[7], Sónia Vieira[2], Altin Ndrio[2], João Tiago Guimarães[4], Eduardo Lima Da Costa[2], Raquel Soares[4] and Paula Freitas[2]
[1]*Departamento de Endocrinologia, Diabetes e Metabolismo, Unidade Local de Saúde de S. João, Porto, Portugal;* [2]*Unidade Local de Saúde de S. João, Porto, Portugal;* [3]*Unidade Local de Saúde de Matosinhos, Matosinhos, Portugal;* [4]*Faculdade de Medicina da Universidade do Porto, Porto, Portugal;* [5]*FMUP—Faculdade de Medicina Universidade do Porto, Porto, Portugal;* [6]*EMCB/ UFP—Escola de Medicina e Ciências Biomédicas/ Universidade Fernando Pessoa, Gondomar, Portugal;* [7]*Universidade Fernando Pessoa, Porto, Portugal*

Introduction: Despite the benefic impact on weight management and obesity-related complications, metabolic/bariatric surgery (BS) presents deleterious effects on bone health. The differential outcomes of the two main bariatric techniques on bone metabolism and body composition still need to be clarified.

Methods: Prospective single-centre study of female participants who underwent BS between November/2019 and December/2022, followed between one and two years after surgery. We

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

compared the impact of Sleeve gastrectomy (SG) and Roux-and-Y gastric bypass (RYGB) on the variation of bone mineral density (BMD), body composition (evaluated with DEXA) and bone metabolism markers [such as osteocalcin and beta-crosslaps (CTX)] after BS. Linear regression analysis adjusted for age, surgery type, diabetes mellitus status, BMI, and femoral neck BMD at baseline, were performed to find predictors of BMD variation after surgery. Logistic regression analysis was adjusted for the same variables, being conducted to find predictors of osteopenia or osteoporosis 2 years after surgery.

Results: Of the 162 included women, 99 (61.1%) underwent RYGB and 63 (38.9%) SG. Total femur BMD significantly decreased one and two years after BS, with a steeper reduction in the RYGB group. Two years after surgery, RYGB led to a greater BMD decline in femoral neck (-0.09 ± 0.07 vs -0.12 ± 0.07 g/cm^2, $P = .049$). RYGB group also presented more fat loss at both time points, with no differences in lean mass reduction at one (-6.3 ± 3.4 vs -6.3 ± 2.9 kg, $P = .38$) and two years (-7.4 ± 3.4 vs -7.4 ± 3.0 kg, $P = .11$). Urinary calcium in 24hour urine increased after SG and decreased after RYGB, one and two years after BS. Osteocalcin and CTX increased at both time points, with a significantly higher increase in RYGB group. RYGB was predictor of BMD reductions in total femur and femoral neck. Logistic regression revealed a trend for RYGB to be a predictor of osteoporosis/osteopenia 2 years after BS [OR 2.97 (0.89-9.89), $P = .077$] and for higher BMC at baseline to be a protective factor [OR 0.09 (0.01-1.45), $P = .089$]. Five patients developed fragility fractures after BS (two in the radius, one in the proximal humerus, another in the fibula and the last one fractured two ribs). Nine patients developed osteoporosis after BS, with 8 of them presenting ≥50 years at diagnosis.

Conclusions: RYGB showed a greater impact in bone metabolism and body composition than SG, with noticeable effects in the hip bone and fat mass reduction, even after adjustments. This reinforces the importance of proper calcium and vitamin D supplementation after BS.

Abstract citation ID: lvag096.281

P78 - ECE_2391 - The effects of eneboparatide vs PTH(1-34) delivered by daily injection or continuous infusion on blood calcium levels and bone metabolism in thyroparathyroidectomized (TPTX) rats

Cagri Aksu[1,2], Xavier Gaume[3], Xueyi Zhang[4], Myriam Aouadi[3] and Thomas Gardella[1,2]

[1]Endocrine Unit, Massachusetts General Hospital, Boston, MA, United States; [2]Harvard Medical School, Boston, MA, United States; [3]Alexion, AstraZeneca Rare Disease, Discovery Biology, Écully, France; [4]Alexion, AstraZeneca Rare Disease, Bioinformatics and Data Science, Boston, MA, United States

Background: Eneboparatide is a long-acting parathyroid hormone (PTH) in development for the treatment of chronic hypoparathyroidism. Eneboparatide binds with higher affinity to the R0 conformation of the PTH 1 receptor vs PTH(1-34), producing sustained elevations in blood calcium in vivo despite a short circulating half-life. Here, we present further statistical analyses of previously presented data assessing whether repeated injection of eneboparatide into thyroparathyroidectomized (TPTX) rats at doses normalizing serum calcium produces different effects on bone than PTH(1-34) administered intermittently or continuously.

Methods: Male Sprague-Dawley rats aged 9 weeks (2 weeks after TPTX surgery) received daily subcutaneous (sc) injections of eneboparatide at doses of 1.0, 2.0, or 4.0 nmol/kg, daily sc injections of PTH(1-34) at 50, 100, or 150 nmol/kg, or continuous infusion of PTH(1-34) via ALZET minipump at 1.5, 2.0, or 3.0 nmol/kg/day ($n = 8$/group) for 16 days. TPTX controls received vehicle injections or infusion. Tail vein blood ionized calcium (Ca^{++}) was analyzed pre- and postinjection on days 1, 7, 14, and 15. Rats were euthanized 24 hours post-last injection, and blood and femurs were collected for analysis of bone turnover biomarkers and microcomputed tomography parameters. Differences between the effective dose of each treatment and vehicle were analyzed using *t* tests. Equivalency of eneboparatide and vehicle was analyzed using the two one-sided tests (TOST) procedure.

Results: Doses normalizing blood Ca^{++} to baseline values expected in non-TPTX rats were 1.0 nmol/kg for eneboparatide daily injection, 50 nmol/kg for PTH(1-34) daily injection, and 3.0 nmol/kg/day for PTH(1-34) continuous infusion. Continuous infusion of 3.0 nmol/kg/day PTH(1-34) significantly increased bone turnover biomarkers CTX1 ($P = .014$), TRAP5b ($P = .025$), and P1NP ($P = .035$) and reduced trabecular bone volume/tissue volume (BV/TV; $P = .003$), number ($P = .005$), and thickness ($P = .004$) and cortical thickness ($P = .012$). Daily injection of 50 nmol/kg PTH(1-34) significantly increased TRAP5b ($P < .001$), P1NP ($P < .001$), trabecular BV/TV ($P < .003$), and trabecular thickness ($P < .001$). Daily injection of 1.0 nmol/kg eneboparatide did not change the thickness of trabecular bone (TOST: P's $< .001$) or cortical bone (TOST: P's $< .01$) but significantly reduced cortical bone porosity ($P = .003$). No significant differences were observed on TRAP5b, P1NP, or CTX1 (P's $> .05$), although equivalency tests were inconclusive.

Conclusions: Our analyses confirm that at doses similarly normalizing blood Ca^{++} levels in TPTX rats, continuous infusion of PTH(1-34) was bone catabolic, daily injection of PTH(1-34) was bone anabolic, and daily injection of eneboparatide was bone neutral. The unique mechanism of eneboparatide may lead to less detrimental impact on bone when used as treatment for hypoparathyroidism.

Abstract citation ID: lvag096.282

P79 - ECE_2596 - Predicting permanent postoperative hypoparathyroidism using preoperative and intraoperative PTH dynamics

Miguel Paja[1,2,3], Leire Pérez de Azpeitia[3], Cristina Moreno[2], Josune Rodríguez-Soto[2], Aitzol Lizarraga[2,3], Eider Etxeberria[2], Natalia Covadonga Iglesias Hernandez[2], Ana Izuzquiza[2], Javier Espiga Alzola[2], Iñigo Hernando[2,3], María Ausín[2], Jon Garai[2], Jon Portu[2], Alejandra Santamaría[2], Amelia Oleaga[1,2,3], Teresa Gutierrez[2,3] and Aitziber Ugalde[2]

[1]Endocrinology & Nutrition, Biobizkaia Health Research Institute, Bilbao, Spain; [2]Osakidetza, Basurto University Hospital, Bllbao, Spain; [3]EHU, Basque Country University, Bllbao, Spain

Background: Permanent postoperative hypoparathyroidism (PpoHypoPT) is a clinically significant complication of total thyroidectomy, associated with renal morbidity and long-term deterioration in quality of life. Early identification of patients at risk among those who initially develop postoperative hypoparathyroidism (poHypoPT) may enable optimized management strategies. This

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

study investigates preoperative, intraoperative, and early postoperative determinants of progression to PpoHypoPT.

Methods: We conducted a retrospective analysis involving 295 patients who developed poHypoPT following total thyroidectomy between 2015 and 2022. PpoHypoPT was defined as persistent dependence on calcitriol to maintain asymptomatic normocalcaemia or failure to achieve serum PTH >15 pg/mL at any point during follow-up, despite supplementation with calcifediol and calcium. Patients recovering PTH >15 pg/mL without calcitriol were classified as having transient poHypoPT (TpoHypoPT). Clinical characteristics, perioperative biochemical parameters, intraoperative findings, and postoperative PTH kinetics (immediate and 24-hour values) were compared. Independent predictors were identified using multivariate logistic regression.

Results: Of the 295 patients with poHypoPT, 52 (17.6%) progressed to PpoHypoPT, corresponding to an overall incidence of 6.8% among 767 total thyroidectomies. PpoHypoPT was associated with older age, lower postoperative calcium levels and reduced immediate and 24-hour postoperative parathyroid hormone (PTH) concentrations. It was also associated with the identification of fewer than three parathyroid glands during surgery. Central neck dissection did not increase risk. In multivariate analysis, age, number of identified parathyroid glands, preoperative PTH, and the 24-hour PTH/baseline PTH ratio were independent predictors. Identification of fewer than three parathyroid glands was the strongest predictor of PpoHypoPT (OR 4.81). PTH at 24 hours showed the highest diagnostic performance (AUC 0.798). A 24-hour PTH threshold of 6.5 pg/mL optimally predicted PpoHypoPT (with a sensitivity of 56.3% and a specificity of 89.2%). Conversely, a PTH24h decline of less than 86.3% from baseline predicted the recovery of parathyroid function (sensitivity: 54.3%; specificity: 86.5%).

Conclusions: The incidence of PpoHypoPT after total thyroidectomy was 6.8%, occurring in 17.6% of patients with poHypoPT. Intraoperative identification of fewer than three parathyroid glands was found to be the most powerful predictor of permanent dysfunction. Higher preoperative PTH levels were also associated with increased risk, underscoring the potential relevance of preoperative vitamin D optimization. Early postoperative PTH dynamics, particularly PTH24h below 6.5 pg/mL or a reduction of over 86% from baseline, provide robust markers of the progression to permanent hypoparathyroidism.

Abstract citation ID: lvag096.283

P80 - ECE_3377 - Phenotyping hypercalciuria in primary hyperparathyroidism before and after parathyroidectomy: a large single-center study

Sara Capra[1,2], Nicolò Bisceglia[1,2], Anna Piazza[1,2], Cristiana Cantone[1,2], Virginia Samaritani[1,2], Matteo Malagrinò[1,2], Enrico Saudelli[1,2], Giulia Vandi[1,2], Andrea Repaci[1], Uberto Pagotto[1,2] and Guido Zavatta[1,2]

[1]*Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy;* [2]*Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna, Italy*

Introduction: Hypercalciuria is a common complication of primary hyperparathyroidism (PHPT) and represents an indication for parathyroidectomy. However, the rate and extent of hypercalciuria remission after surgery remain unclear.

Objective: To evaluate the remission of hypercalciuria after parathyroidectomy.

Design: Single-center, longitudinal, retrospective study.

Methods: Among 390 hypercalcaemic PHPT patients undergoing parathyroidectomy (1989-2025), after excluding persistent disease, missing biochemical data, and malignancy, 272 patients with preoperative and 12 ± 6-month postoperative laboratory evaluation were selected. Patients were stratified into four groups by baseline biochemistry: mild hypercalcemia (10.5-11.0 mg/dL) with hypercalciuria (A) or normocalciuria (B), and significant hypercalcemia (>11 mg/dL) with hypercalciuria (C) or normocalciuria (D). Hypercalciuria was defined as ≥250 mg/day in women and ≥300 mg/day in men.

Results: Study population was: mean age at parathyroidectomy 60 ± 12 years, 83.5% women ($n = 227$), 24% ($n = 56$) with BMI ≥30 kg/m^2 and 9.6% ($n = 26$) with eGFR<60 mL/min. At diagnosis, 43.7% ($n = 119$) had nephrolithiasis, of whom 20.2% ($n = 55$) had bilateral lithiasis. At baseline, patients with hypercalciuria had lower serum phosphate levels (2.48 ± 0.04 vs 2.74 ± 0.06 mg/dL; $P < .0001$) and higher BMI (27 vs 25 kg/m^2, $P = .026$), but similar PTH levels ($P = .534$), serum calcium levels ($P = .254$) and prevalence of nephrolithiasis ($P = .130$). Postoperatively, a significant reduction in urinary calcium was observed exclusively in patients with baseline hypercalciuria (group A: 389 ± 113 to 202 ± 92 mg/day, $P < .0001$; B: 164 ± 50 to 187 ± 178 mg/day, $P = .462$; C: 475 ± 143 to 190 ± 139 mg/day, $P < .0001$; D: 176 ± 62 to 162 ± 114 mg/day, P = .333), with the maximum variation in group C ($P < .0001$). We found a significant increase in the proportion of patients with normocalciuria at 12 months (70.7% group A and 76.8% group C, $P = .501$ between groups). Mean postoperative calciuria did not differ among groups ($P = .882$). On multivariate regression analysis, baseline serum calcium was inversely associated with postoperative calciuria (β = −29.3, 95% CI −54.1 to −4.5; $P = .021$), whereas sex, nephrolithiasis, baseline PTH, baseline calciuria, serum phosphate levels, BMI, and eGFR showed no significant associations. In patients with persistent hypercalciuria, urinary calcium remained unchanged (Δ = 1.34 mg/day, $P = .971$); no differences were observed between patients with persistent vs normalized postoperative calciuria in preoperative nephrolithiasis prevalence ($P = .463$), histological diagnosis ($P = .438$), age ($P = .546$), eGFR ($P = .103$) or sex ($P = .653$).

Conclusions: Parathyroidectomy significantly reduces urinary calcium excretion in PHPT with hypercalciuria, particularly in patients with more severe disease. Further studies are needed to explain why one in four patients remain hypercalciuric and to identify biomarkers that predict persistent hypercalciuria. Lower baseline serum calcium emerged as the sole independent predictor.

Abstract citation ID: lvag096.284

P81 - ECE_2466 - Parathyroid carcinoma and atypical parathyroid tumor: surgical management and germline genetics

Magdalena Matejkova Behanova[1], Josef Vcelak[2], Marcela Linhartová[3], Renata Chmelová[1], Jan Schovanek[4], Olivia Cillikova[2], Klára Hovorková[1] and Petr Libánský[1]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Motol and Homolka University Hospital, Prague, Czech Republic; [2]Institute od Endocrinology, Prague, Czech Republic; [3]University Hospital Brno, Brno, Czech Republic; [4]University Hospital Olomouc, Olomouc, Czech Republic

Introduction: Parathyroid carcinoma (PC) is an extremely rare malignant disease, while atypical parathyroid tumor (APT) represents a neoplasm of uncertain malignant potential. Preoperative differentiation between PC, APT, and benign parathyroid adenoma remains challenging. Suspicion of malignancy is based on imaging modalities, biochemistry, and intraoperative findings. Radical *en bloc* resection with ipsilateral hemithyroidectomy is considered the gold standard for PC. Hereditary forms have been reported in up to 30% of PC cases, predominantly associated with pathogenic variants in *CDC73*, and in approximately 7%-36% of APT cases. The aim of the study was to compare clinical presentation, surgical management, and germline genetic background in patients with PC and APT, with a particular focus on hereditary forms.

Methods: We retrospectively evaluated patients with PC or APT who underwent parathyroid surgery between 2010 and 2025. Diagnoses were established by expert endocrine pathologists according to the 2022 WHO classification. The extent of surgery, including concomitant thyroid resection, was determined by preoperative imaging, biochemistry, and/or intraoperative findings. Germline genetic testing was performed postoperatively from peripheral leukocytes using whole-exome sequencing.

Results: The cohort included 30 patients with PC (14 men, 16 women) and 20 patients with APT (9 men, 11 women). Age at diagnosis (PC: 63.4 ± 14.3 years; APT: 59.9 ± 14.0 years), tumor size (PC: 2.89 ± 0.93 cm; APT: 2.88 ± 1.15 cm), and calcium levels (PC: 3.6 ± 0.5 mmol/L; APT: 3.3 ± 0.7 mmol/L) were comparable between groups. Concomitant thyroid surgery was performed significantly more often in patients with PC than in those with APT (76% vs 25%, $p < 0.01$). Postoperative germline genetic testing was available for 27 patients (17 PC, 10 APT). Pathogenic germline variants in *CDC73* were identified in two patients (one PC, 6%; one APT, 10%). No pathogenic or likely pathogenic variants were detected in other selected genes (*CASR, CCND1, CDKN1B, CDKN2B, FLCN, GCM2, MEN1, PIK3CA, PTEN, RB1, RET,* and *TP53*). Several variants of uncertain significance were identified.

Conclusions: Concomitant thyroid surgery was performed significantly more often in patients with parathyroid carcinoma than in those with atypical parathyroid tumor, reflecting a higher perioperative suspicion of malignancy. The prevalence of hereditary disease was lower than expected in both entities, suggesting that vast majority of cases in our cohort were sporadic. Larger multicenter studies are needed to further define the clinical impact of hereditary forms.

Abstract citation ID: lvag096.285

P82 - ECE_2073 - Parathyroidectomy and risk of diabetes progression in primary hyperparathyroidism patients comorbid with diabetes: a target trial emulation in a population-based cohort

Xiaodong Liu[1], Lanlan Li[2], Xi Xiong[3], Chenhao Pan[4], Yan Luk[5], Paul Chi-Ho Lee[2], Carlos Wong[6], Brian Lang[5], Matrix Fung[5] and David Lui[2]

[1]Surgery, The University of Hong Kong, Hong Kong, Hong Kong; [2]Division of Endocrinology and Metabolism, Department of Medicine, The University of Hong Kong, Hong Kong, Hong Kong; [3]Department of Non-communicable Disease Epidemiology, The London School of Hygiene & Tropical Medicine, London, United Kingdom; [4]Department of Orthopaedics and Traumatology, The University of Hong Kong, Hong Kong, Hong Kong; [5]Division of Endocrine Surgery, Department of Surgery, The University of Hong Kong, Hong Kong, Hong Kong; [6]Department of Infectious Disease Epidemiology & Dynamics, London School of Hygiene and Tropical Medicine, London, United Kingdom

Background: Primary hyperparathyroidism (PHPT) was reported to increase diabetes risk due to insulin resistance. However, it is not known if parathyroidectomy could reduce the progression of diabetes among PHPT patients who already had diabetes. This study aimed to estimate the impact of parathyroidectomy on diabetes progression in PHPT patients comorbid with diabetes.

Methods: Patients diagnosed with PHPT who had coexisting diabetes were retrieved from a territory-wide electronic health database in Hong Kong between January 2006 and December 2023. The primary outcome was the risk of diabetes progression (defined by the occurrence of acute hyperglycemic crises, HbA1c increase ≥0.5% from baseline, or intensification of glucose-lowering therapy). We adopted the framework of target trial emulation and fitted marginal structural models with inverse probability of treatment weighting, modelling surgery as a time-varying exposure. Differences in cumulative incidence between patients with and without surgery were estimated. The Cox proportional hazards model was used to assess the association between parathyroidectomy and diabetes progression. Estimates of hazard ratios (HR) with 95% confidence intervals (CI) were calculated.

Results: A total of 2051 patients with a median follow-up period of 3.4 years were included. 1213 cases with diabetes progression were identified, including 162 in surgical patients and 1051 among non-surgical patients.The 10-year cumulative incidence of diabetes progression demonstratrd a lower incidence in surgical group compared with non-surgical group. Compared to non-surgical management, parathyroidectomy was associated with a lower risk of diabetes progression (HR 0.61; 95% CI, 0.47-0.79, $P < .001$). Results were consistent in subgroup and sensitivity analyses. There was no association between parathyroidectomy and the negative controls, including gastrointestinal bleeding, chronic obstructive pulmonary disease, pneumonia, and urinary tract infection. Parathyroidectomy was associated with lower risks of positive controls: chronic kidney disease (HR 0.59; 95% CI: 0.44-0.78; $P < .001$) and fractures (HR 0.49; 95% CI: 0.28-0.87; $P = .001$). Furthermore, we found that the impact of parathyroidectomy on lowering risk of diabetes progression was more prominent in PHPT patients with abnormal eGFR levels (≤60 mL/min/1.73 m^2 vs >60 mL/min/1.73 m^2: HR, 0.42 [95% CI, 0.25-0.72] vs HR, 0.74 [95% CI, 0.56-0.99]; interaction $P = .005$) and insulin use (with vs without: HR, 0.34 [95% CI, 0.16-0.73] vs HR, 0.73 [95% CI, 0.55-0.98]; interaction $P = .001$).

Conclusions: Parathyroidectomy was associated with a lower risk of diabetes progression in PHPT patients comorbid with diabetes, adding to the list of metabolic benefits for PHPT patients comorbid with diabetes for treatment decisions.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.286

P83 - ECE_2243 - Detection of osteitis fibrosa cystica in hyperparathyroidism using [18F]fluorocholine PET/CT

Aida Orois[1], Manel Mateu-Salat[1], Mireia Mora[1], Amparo Cobo[2], Oscar Vidal[3], Martí Manyalich[3], Maite Rodrigo[4], Nerea Anton[1], David Fuster[2] and Felicia Alexandra Hanzu[1]

[1]Endocrinology and Nutrition, Hospital Clínic de Barcelona, Barcelona, Spain; [2]Nuclear Medicine, Hospital Clínic de Barcelona, Barcelona, Spain; [3]Surgery, Hospital Clínic de Barcelona, Barcelona, Spain; [4]Pathological Anatomy, Hospital Clínic de Barcelona, Barcelona, Spain

Background: Osteitis fibrosa cystica (OFC) is a rare skeletal manifestation of hyperparathyroidism, characterized by osteolytic lesions known as brown tumours. Although its prevalence has declined with early detection of hyperparathyroidism, OFC remains clinically relevant in severe or delayed cases.

Objective: To evaluate the role of [18F]fluorocholine PET/CT in detecting OFC and describe its clinical and imaging features.

Methods: A retrospective review of 274 patients who underwent [18F]fluorocholine PET/CT for hyperparathyroidism at Hospital Clínic de Barcelona (2020-2024) was performed. Clinical, biochemical, and imaging data were analysed, focusing on patients with OFC lesions.

Results: Six cases of OFC were identified. Lesions were located in the jaw, skull, humerus, iliac bone, femur, and ribs, showing characteristic uptake patterns on PET/CT. Compared to patients without OFC, those with OFC had significantly higher PTH levels (median 600 vs 154 pg/mL, $P = .0226$) and worse renal function (median eGFR 54.2 vs 86 mL/min/1.73 m^2, $P = .0256$). None of the OFC patients had osteoporosis, contrasting with its high prevalence in non-OFC cases. Follow-up imaging revealed variable timelines for lesion resolution after parathyroidectomy.

Conclusions: [18F]fluorocholine PET/CT is a valuable tool for detecting OFC in hyperparathyroidism, enabling differentiation from malignant bone lesions and guiding management. OFC appears associated with severe biochemical derangements and distinct skeletal phenotype, underscoring the need for early recognition and tailored follow-up.

Abstract citation ID: lvag096.287

P84 - ECE_2846 - Clinical and pathological significance of oxyphil cells content in sporadic parathyroid adenomas: a double center study

Anna Dal Lago[1], Elena Ruotolo[2], Liborio Torregrossa[3], Andrea Satta[4], Paolo Piaggi[5,6], Laura Pierotti[1], Simone Della Valentina[1], Giacomo De Leo[1], Chiara Sardella[7], Romina Mirsepanj[2], Silvia Carrara[8], Sabrina Corbetta[8,9] and Filomena Cetani[1,7]

[1]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [2]Department of Clinical and Community Science, University of Milan, Milan, Italy; [3]Department of Surgical, Medical and Molecular Pathology and Critical Area, University Hospital of Pisa, Pisa, Italy; [4]Pathology Unit, Istituto di Ricerca e Cura a Carattere Scientifico (IRCCS) Istituto Auxologico Italiano, Milan, Italy; [5]Department of Information Engineering, University of Pisa, Pisa, Italy; [6]NIDDK, National Institutes of Health, Phoenix, Arizona, Phoenix, United States; [7]Endocrine Unit 2, University of Pisa, Pisa, Italy; [8]Bone Metabolism Disorders and Diabetes Unit, Istituto di Ricerca e Cura a Carattere Scientifico (IRCCS) Istituto Auxologico Italiano, Milan, Italy; [9]Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder and is caused in over 90% of cases by chief cell adenoma (CCA), while up to 8.4% are attributable to oncocytic parathyroid adenomas (OPA). The significance of oxyphil cells (OCs) remains incompletely understood, with limited evidence regarding differences in presentation, biochemical severity, and outcomes between OPA and CCA.

We conducted a retrospective, bicentric case–control study including patients with sporadic PHPT who underwent selective parathyroidectomy for single-gland disease between 2019 and 2024 at the Universities of Pisa and Milan. Patients with OPA (>75% OCs at histology) were compared with control groups of CCA with different percentages of OCs content (0%; ≤75%; 1%-50% and 51%-75%). All histopathological slides were systematically reviewed.

A total of 213 parathyroid tumors (PAds) from 166 females and 47 males (mean age 58.9 ± 11 years) with PHPT were included; all tumors were diagnosed as single adenoma according to the WHO 2022 classification. OCs were frequent in PAds showing a heterogenous distribution among the analyzed samples. The distribution of OCs content was as follows: 0% in 42 PAds, 1%-50% in 81, 51%-75% in 28, and 76%-100% in 62 cases.

Across all analytical approaches, a significant association was observed between OCs percentage and adenoma size. PAds with >75% OC, identified as OC-PAds, were significantly larger than those without OCs (2.12 ± 0.89 cm vs 1.74 ± 0.67 cm, $P = .018$). Also, the continuous correlation 0-100% of OCs underlined a size increase (Spearman $r = 0.200$, $P = .003$). Consistently, OC-PAds were larger than those with ≤75% OCs (2.12 ± 0.89 vs 1.84 ± 0.74 cm, $P = .021$). These results indicate that PAds with higher OC content are approximately 15%-22% larger.

No significant associations were found between OCs percentage and age, body mass index, dietary calcium intake, clinical manifestations of PHPT (including nephrolithiasis, fractures, and osteoporosis), or biochemical severity (PTH, serum total and ionized calcium, 25-hydroxyvitamin D, phosphate, 24-h urinary calcium and bone turnover markers). Only a significant difference in 24-hour urinary phosphate excretion was observed across groups ($P = .006$), with highest values in tumors containing 50%-75% OCs. Moreover, a higher rate of postoperative recurrence was observed in patients with OC-PAds compared with those with ≤75% OC ($P = .045$).

In conclusion, OC-rich PAds appear to represent a morphological variant associated with increased tumor size but not with greater clinical or biochemical severity of PHPT. The association with postoperative recurrence suggests a potential prognostic relevance that merits further investigation.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.288

P85 - ECE_3433 - Should vitamin D supplementation be recommended in hypoparathyroidism? preliminary results from a routine care trial on cellular and humoral immunity in patients with hypoparathyroidism

Christina Berr[1], Henrike Buchschuster[2], Jakob Wieke[2], Phillip Löhr[2], Christian Pfob[3], Thomas Pusl[1], Andreas Rank[2] and Mathias Lutz[2]

[1]Department of Endocrinology, I. Medical Clinic, University Hospital; University of Augsburg, Augsburg, Germany; [2]Hematology and Oncology, Department of Medicine II, Faculty of Medicine, University of Augsburg, Augsburg, Germany; [3]Nuclear Medicine, Faculty of Medicine, University of Augsburg, Augsburg, Germany

Background: Patients with hypoparathyroidism demonstrate increased infection susceptibility and hospitalization rates compared to the general population. In hypoparathyroidism, reduced parathyroid hormone levels impair renal 1-alpha-hydroxylase activity, limiting conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D. While cholecalciferol modulates humoral and cellular immunity in healthy individuals, its therapeutic efficacy may be compromised in this setting. Although current guidelines on hypoparathyroidism recommend cholecalciferol supplementation for vitamin D deficiency, the added value of its addition to active vitamin D remains still unclear. This ongoing prospective trial investigates the impact of guideline-based cholecalciferol supplementation on immune cell profiles and infection rates in hypoparathyroid patients with vitamin D deficiency. Here, we present preliminary findings from this study.

Methods: Patients with hypoparathyroidism and simultaneous vitamin D deficiency are receiving guideline-based colecalciferol supplementation. Before and after three months of colecalciferol supplementation aiming at mid-normal 25-hydroxyvitamin D serum levels. Humoral immunity is assessed by measuring immunoglobulin levels and cellular immunity is evaluated using a comprehensive flow cytometry (FACS) panel. Clinical, endocrinological and functional parameters are recorded and infection frequency is assessed via a standardized questionnaire at both time points mentioned above.

Results: Up to now, fifteen patients have been enrolled in our trial. Preliminary FACS results in a small subcohort show trends towards changes in immune cell markers following colecalciferol supplementation. The expression of CD366 (TIM-3) on conventional CD4+ and CD8+ T cells decreased, suggesting reduced T cell exhaustion. Additionally, the activation marker CD226 on regulatory T cells and conventional CD4+ T cells increased, indicating potential enhanced immune activation. These results suggest a possible improvement in immune function following colecalciferol supplementation, with the results of the entire trial cohort still to be awaited.

Discussion: Preliminary FACS results suggest that colecalciferol supplementation may lead to improved immune function in patients with hypoparathyroidism and simultaneous vitamin D deficiency. The decrease in T cell exhaustion and increase in T cell activation markers point to a potential restoration of immune responsiveness. However, these findings are based on a small subcohort and sample evaluation and patient recruitment is ongoing.

Abstract citation ID: lvag096.289

P86 - ECE_3759 - Levels of serum inflammation markers before and after parathyroidectomy in patients with primary hyperparathyroidism

Lingqiong Meng[1] and Xiangbing Wang[2]

[1]Internal medicine, University of Arizona, Phoenix, United States; [2]Department of Medicine, Rutgers University-Robert Wood Johnson Medical School, New Brunswick, United States

Background: Our previous studies suggest that patients with primary hyperparathyroidism (PHPT) are accompanied by increased cardiovascular risk factor (CRF). Vitamin D binding protein (DBP) and inflammation markers, including interleukin-6 (IL-6) and monocyte chemoattractant protein-1 (MCP-1) are reported to be associated with elevated CRF. Yet, the association of levels of DBP and inflammation markers and CRF in PHPT patients remains not clear.

Objective: To investigate the effects of PTX on levels of CRF, DBP and inflammatory cytokines in patients with PHPT.

Methods: Seventy patients with PHPT and 70 age and BMI-matched healthy subjects were included as controls. Forty patients had minimally invasive PTX, and 28 patients returned 3 months after PTX. Biochemical markers, blood pressure and body weight were measured before and after PTX.

Results: Patients with PHPT had lower serum DBP and higher IL-6, C-reactive protein (CRP), and MCP-1 ($P < .05$) than controls. And their circulating levels of IL-6 and MCP-1 were positive correlated with iPTH (intact parathyroid hormone). Multiple regression analysis indicated that the preoperative iPTH explained a significant portion of the variance of IL-6 and MCP-1 ($P < .05$). The levels of MCP-1 and iPTH decreased by 20% and >50%, respectively, 15-20 min after removal parathyroid adenoma ($P < .05$). Three months after PTX, levels of DBP and MCP-1 became normalized ($P < .05$) to the similar level of normal controls ($P > .05$). Serum IL-6 was also markedly reduced ($P < .01$) but remained higher than controls ($P < .05$). The systolic blood pressure was 5 mm lower after PTX, but not significant ($P > .05$), while BMI and diastolic blood pressure remained no change ($P > .05$).

Conclusions: These findings confirmed that PTX decreases levels of inflammatory cytokines, MCP-1 and IL-6, and increases DBP in patients with PHPT. We suggest that besides its benefits on calcium and bone metabolism, PTX may also decrease CRF by reducing levels of MCP-1, IL-6 and increasing levels of DBP in patients with PHPT. Further long-term follow up study of effect of PTX on CRF including BMI, blood pressure, HDL and LDL are under investigation.

Abstract citation ID: lvag096.290

P89 - ECE_1227 - Fracture incidence in patients with toxic nodular goiter: a population-based long-term follow-up study

Sorena Abbaszadeh[1,2], Ruzan Udumyan[3], Gabriel Sjölin[3], Jan Calissendorff[4], Helena Filipsson Nyström[5], Mats Holmberg[6], Hallengren Bengt[7], Tereza Planck[7], Göran Wallin[8], Östen Ljunggren[9] and Selwan Khamisi[10]

[1]Department of Medical Sciences, Uppsala University, Uppsala, Sweden; [2]Department of medical science, Uppsala, Sweden; [3]Clinical Epidemiology and Biostatistics, School of Medical Sciences, Faculty

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

of Medicine and Health, Örebro University, Örebro, Sweden; [4]Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden; [5]Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [6]ANOVA; Karolinska University Hospital, Stockholm, Sweden; [7]Department of Endocrinology, Skåne University Hospital, Malmö, Sweden; [8]Faculty of Medicine and Health, Örebro University Hospital, Örebro, Sweden; [9]Department of Endocrinology and Diabetes, Uppsala University Hospital, Uppsala, Sweden; [10]Department of Endocrinology and Diabetes, Uppsala University Hospital, Uppsala, Sweden

Hyperthyroidism, including toxic nodular goiter (TNG), adversely affects bones and is a recognized cause of osteoporosis. However, the extent to which it contributes to fractures remains uncertain, as studies have yielded conflicting results. This study aimed to determine whether TNG is associated with a higher incidence of fractures than controls.

Methods: We followed 621 patients with overt hyperthyroidism due to TNG for a median of 13.8 years and searched for fractures in national registries. For each case with TNG, up to 10 controls without hyperthyroidism from the general population were matched for sex, age, and county of residence. We used Cox regression stratified on the matching sets to compare rates of fragility fractures as well as osteoporosis and corticosteroid treatments between case and control groups. Analyses were performed in all as well as stratified by sex and by age (≤52 and >52 years).

Results: Higher rates of total fragility fracture were observed in women ≤52 years (2.15 (1.11-4.15). In women aged >52 years, patients with TNG had higher hip fracture rates (1.41 (1.08-1.84)). When considering all patients in both the case and control groups, total fragility fracture rates did not differ significantly (HR 1.08; 95% CI 0.89-1.32).

Conclusions: In women >52 years with TNG, hip fracture rates were higher than in the reference population. Furthermore, younger women with TNG had higher rates of all fractures. These data suggest that TNG might be a more prominent risk factor for osteoporotic fractures than previously thought.

Abstract citation ID: lvag096.291

P90 - ECE_2619 - Age-related decline in bioelectrical phase angle exhibits nonlinear midlife accelerations across the human lifespan

Michail Savvas Magklis[1,2,3], Maria Chrysoula Tatarida Palla[1,2,3], Myrsini Chamakioti[1,2,3], Mina Koutrouli[1,2,3], Galateia Stathori[1,2,3], Katerina Firfilioni[1,2,3], Dimitra Siori[1,2,3], Dario Boschiero[4], Eleni Papanikolaou[1,2] and George Chrousos[1,2,3]

[1]National and Kapodistrian University of Athens, Athens, Greece; [2]Clinical and Translational Research Endocrine Unit, National and Kapodistrian University of Athens, Athens, Greece; [3]National and Kapodistrian University of Athens, University Research Institute of Maternal and Child Health and Precision Medicine, University Research Institute of Maternal and Child Health and Precision Medicine, Athens, Greece; [4]BioTekna, Venice, Italy

Background: Human aging involves progressive loss of cellular integrity and homeostatic capacity, ofter preceding disease. Bioelectrical impedance–derived phase angle (PhA) is a integrative, noninvasive marker of cell membrane integrity, hydration distribution, and tissue quality. In parallel, published multi-omics and plasma proteomics evidence suggest that major molecular shifts occur with age in a nonlinear fashion, with discrete midlife and later-life inflection periods.

Objective: To characterize the age- and sex-specific trajectory of PhA across the lifespan in a very large cohort and to contextualize its nonlinear pattern against reported midlife accelerations in DNA stability loss.

Methods: Cross-sectional PhA at 50 kHz was analyzed in 184 830 individuals (121 403 women; 63 427 men), spanning 10-89 years, using standardized bioelectrical impedance procedures. Mean PhA was evaluated across 5-year age strata and modeled as a nonlinear function of age with sex stratification.

Results: PhA showed a marked age-related decline with evident nonlinearity. In men, PhA increased from early adolescence to a peak in early adulthood (approximately ~7.1-7.2° at 20-29 years), followed by a progressive decline; in women, values reached a lower early-adulthood plateau (approximately ~6.1° across 15-29 years) before declining. The downward slope appeared to steepen across two midlife-to-late-life transitions centered around ~40-44 years and ~60-64 years, consistent with a two-step acceleration pattern. Sex differences were largest from adolescence through midlife (men higher), narrowed progressively with age, and converged in the eighth decade, with near-equal values around 80-84 years (~4.6°) and a small sex-dependent divergence in the oldest stratum (85-89 years, ~4.2-4.3°).

Conclusions: In a large lifespan cohort assessed within a predictive health framework, PhA exhibits a nonlinear age-related decline with midlife accelerations that conceptually parallel reported nonlinear deterioration in multi-omics-determined physiologic stability. These convergent trajectories support PhA as a practical functional biomarker of biological aging and highlight midlife as a critical window for interventions aimed at preserving cellular integrity and resilience.

Abstract citation ID: lvag096.292

P91 - ECE_2885 - Cardiovascular safety of Romosozumab therapy in men with osteoporosis

Hadar Duskin-Bitan[1,2,3], Doron Netzer[3,4], Lilach Dolev[3], Arnon Cohen[2,3], Doron Comaneshter[3] and Gloria Tsvetov[1,2]

[1]Rabin Medical Center, Endocrinology & Metabolism Institute, Petah Tiqva, Israel; [2]Gray Faculty of Medicine, Tel Aviv University, Petah Tiqva, Israel; [3]Clalit Health Services, Division of Community Medical Services, Tel Aviv, Israel; [4]Ariel University, Adelson School of Medicine, Ariel, Israel

Aims: Romosozumab is an osteo-anabolic treatment for patients with severe osteoporosis. A signal for increased cardiovascular risk was observed in patients receiving romosozumab, especially in male patients. Real-world safety data in men is currently limited. The aim of our study was to evaluate the cardiovascular risk in patients treated with romosozumab compared to teriparatide in men and women.

Methods: A retrospective cohort study using Clalit Health Services database, to assess the incidence of major adverse cardiovascular events (MACE) in patients with severe osteoporosis using osteo-anabolic medications.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: The cohort included 6063 patients: 1794 patients received romosozumab (66, 3.7% men), and 4269 patients received teriparatide (404, 9.5% men). In the romosozumab group, the mean age was 73 and 73 for women and men, respectively. In the teriparatide group, the mean age was 71 and 74 for women and men, respectively. At baseline, men in both the romosozumab and teriparatide cohorts had higher proportions of smoking compared to women (26% and 19% vs 13% and 14%, $P < .001$), ischemic heart disease (IHD, 26% and 32% vs 7% and 13%, $P < .001$), and congestive heart failure (CHF, 11% and 9% vs 3% and 5%, $P < .001$) respectively. In the teriparatide group, men had significantly higher proportions of diabetes mellitus (DM) and cerebrovascular accidents (CVA). BMI was lower in men compared to women treated with romosozumab. During the follow up period, we observed an increased risk for IHD CHF and CVA in men treated with romosozumab compared to other patients' groups. Men patients treated with romosozumab had higher risk for hospitalization and death compered to women treated with romosozumab. In a multivariate analysis, adjusted for age, obesity, DM, hypertension, dyslipidemia, renal function, smoking, recent steroid use, and previous bisphosphonates treatment, we observed an increased hazard ratio for IHD (2.2, 95%CI 1.5-3.3), hospitalization in cardiovascular departments (1.6, 95%CI 1.1-2.3) and death (1.4 95% 1-1.9) in men vs women, treated with romosozumab compared to teriparatide.

Conclusions: We observed an increased risk for IHD and death in men vs women, treated by romosozumab compared to teriparatide.

Abstract citation ID: lvag096.293

P93 - ECE_3738 - Elevated parathyroid hormone due to macro-PTH: a diagnostic trap

Agata Rzepecka[1,2], Sonia Kaniuka-Jakubowska[2,3] and Renata Świątkowska-Stodulska[2,4]
[1]*Department Endocrinology and Internal Medicine, Medical University of Gdansk, Poland, Gdansk, Poland;* [2]*Department of Endocrinology and Internal Medicine, University Clinical Centre, Gdansk, Poland, Faculty of Medicine, Medical University of Gdansk, Gdansk, Poland;* [3]*Gdansk, Poland;* [4]*Department Endocrinology and Internal Medicine, Medical University of Gdansk, Poland, Gdansk, Poland*

Introduction: Parathyroid hormone (PTH) is a key regulator of calcium and phosphate homeostasis and an essential marker in the evaluation of hyperparathyroidism and chronic kidney disease. In routine practice, PTH is measured using immunometric assays together with serum calcium, phosphate, and vitamin D concentrations. However, circulating PTH includes not only the biologically active intact hormone but also inactive immunoreactive forms, which may lead to falsely elevated results. Despite improved analytical specificity of modern assays, immunoassay interference remains an underrecognized diagnostic problem. Macro-parathyroid hormone (macro-PTH) is a rare high-molecular-weight complex formed by PTH bound to immunoglobulins. It is biologically inactive and not associated with clinical or biochemical features of primary hyperparathyroidism, yet it may closely mimic this condition in routine laboratory testing. Failure to recognize macro-PTH may therefore result in misdiagnosis and unnecessary additional diagnostic procedures. Polyethylene glycol (PEG) precipitation is a simple laboratory technique that enables identification of macro-hormone complexes by selectively removing high-molecular-weight proteins from serum samples. Despite its low cost and diagnostic value, it is not routinely used in the evaluation of discordant PTH results.

Case Presentation: A 47-year-old woman was referred for evaluation of long-standing suspected primary hyperparathyroidism. For over ten years, persistently elevated PTH concentrations were documented, while total serum calcium remained within the normal range. PTH values ranged from 85 to 563 pg/mL, whereas serum calcium ranged between 8.8 and 9.6 mg/dL. Renal function was preserved, phosphate levels were normal or mildly reduced, and vitamin D deficiency was corrected. PTH was measured using a second-generation chemiluminescent immunoassay (DiaSorin) on the LIAISON XL analyser. The patient had no nephrolithiasis, fragility fractures, or symptoms of hypercalcaemia. Her medical history included autoimmune hypothyroidism treated with levothyroxine. Neck ultrasonography intermittently showed small hypoechoic lesions near the lower pole of the left thyroid lobe, while repeated 99mTc-MIBI scintigraphy with SPECT-CT revealed no pathological uptake. Fine-needle aspiration with PTH measurement in needle washout was negative. Given the marked biochemical–clinical discrepancy, PEG precipitation was performed, resulting in a marked reduction in PTH concentrations (recovery 8%-10%), confirming macro-PTH and excluding primary hyperparathyroidism.

Conclusions: Macro-PTH is an important diagnostic pitfall. PEG precipitation should be considered in cases of persistent PTH elevation inconsistent with clinical and biochemical findings to avoid misdiagnosis and unnecessary interventions

Abstract citation ID: lvag096.294

P94 - ECE_3841 - Kidney function trajectories and incremental therapeutic benefit of Palopegteriparatide after rhPTH(1-84) exposure in chronic hypoparathyroidism: a real-world cohort

Dimitra Lygerou[1], Ariadni Androvitsanea[1], Grigoria Betsi[2], Maria Sfakiotaki[2], Vasiliki Daraki[2], Ioannis Petrakis[1], Andreas Antonakis[1], Konstantina Kydonaki[1], Georgios Alexandros Kavvadias[1], Konstantinos Stylianou[1] and Paraskevi Xekouki[2]
[1]*Nephrology, University Hospital of Heraklion, Heraklion, Greece;* [2]*Endocrinology, University Hospital of Heraklion, Heraklion, Greece*

Background: In chronic hypoparathyroidism (HypoPT), long-term mineral management raises concerns regarding renal outcomes. We evaluated (i) eGFR trajectories in the full cohort and stratified by CKD status, and (ii) whether Palopegteriparatide provided incremental therapeutic benefit beyond an intermediate rhPTH(1-84) phase in rhPTH(1-84) -exposed patients.

Methods: Single-center real-world cohort of adults with chronic HypoPT treated with Palopegteriparatide. Outcomes were assessed at three phases: baseline, rhPTH(1-84) (pre-Palopegteriparatide), and last follow-up on Palopegteriparatide. eGFR (CKD-EPI) was analyzed overall and by CKD status (defined as eGFR <60 mL/min/1.73 m^2). In the rhPTH(1-84) -exposed

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

subgroup ($n = 11$), elemental calcium, alfacalcidol, serum phosphate, and eGFR were analyzed across all three phases to assess incremental Palopegteriparatide effects. Friedman tests (3 timepoints) and paired Wilcoxon tests (pairwise contrasts) were used.

Results: Part 1 (eGFR trajectories, whole cohort): All patients had complete 3-phase eGFR data ($N = 20$). Median eGFR was 71.5 (53.5-97.8) at baseline, 72.5 (57.5-98.7) on rhPTH(1-84), and 70.5 (56.0-89.0) on Palopegteriparatide (Friedman $P = .0753$). In CKD patients ($n = 7$), eGFR increased from 40.0 (37.0-53.0) at baseline to 40.0 (37.0-57.0) on rhPTH(1-84) to 56.0 (49.2-56.5) on Palopegteriparatide (Friedman $P = .0062$; baseline vs Palopegteriparatide $P = .0156$). In non-CKD patients ($n = 13$), eGFR remained stable (Friedman $P = .4006$). Part 2 (incremental therapeutic effect after rhPTH(1-84), $n = 11$): Elemental calcium decreased from 3000 (3000-4250) to 500 (0-1250) on Natpar and to 0 (0-500) mg/day on Palopegteriparatide (Friedman $P = .0001$). Alfacalcidol decreased from 3.00 (1.50-3.00) to 0.50 (0.12-0.50) and to 0.00 (0.00-0.12) µg/day (Friedman $P = .0004$). Serum phosphate decreased from 5.70 (4.60-6.10) to 4.50 (4.20-4.75) and further to 3.70 (3.40-4.20) mg/dL (Friedman $P = .0003$; rhPTH(1-84) vs Palopegteriparatide $P = .0217$). eGFR did not significantly change across phases in this subgroup (Friedman $P = .1146$).

Conclusions: Overall kidney function remained stable across phases, supporting renal safety. Importantly, patients with baseline CKD showed an increase in eGFR after transition to Palopegteriparatide, while non-CKD patients maintained stable eGFR. In rhPTH(1-84) -exposed patients, Palopegteriparatide was associated with further optimization of mineral management—near-complete withdrawal of conventional supplementation and additional phosphate improvement—suggesting incremental therapeutic benefit beyond rhPTH(1-84) in selected patients.

Abstract citation ID: lvag096.295

P95 - ECE_1772 - Optimizing post-thyroidectomy care through a PTH and calcium–guided algorithm

Ana Gheorghe Milea[1,2,3], Johannes H.W. de Wilt[4], Han J. Bonenkamp[4], Antonius van Herwaarden[5], Carmen Emanuela Georgescu[1,2] and Romana Teodora Netea-Maier[3]

[1]*Department of Endocrinology, Clinical County Emergency Hospital Cluj-Napoca, Cluj-Napoca, Romania;* [2]*Department of Endocrinology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania;* [3]*Department of Internal Medicine, Radboud University Medical Center, Nijmegen, The Netherlands;* [4]*Department of Oncological Surgery, Radboud University Medical Center, Nijmegen, The Netherlands;* [5]*Department of Laboratory Medicine, Radboud University Medical Center, Nijmegen, The Netherlands*

Introduction: Thyroidectomy is a fundamental therapeutic intervention in the management of a broad spectrum of both benign and malignant thyroid disorders. However, it entails significant risks, including iatrogenic hypoparathyroidism, the most frequent complication associated with bilateral thyroid surgery.[1] Since 2019, our institution has implemented a standardized post-thyroidectomy protocol using parathyroid hormone (PTH) and calcium measurements to stratify hypocalcemia risk and guide calcium and alfacalcidol supplementation.

Objective: This study aimed to assess the effectiveness of this structured approach in reducing the incidence of unscheduled referrals due to hypocalcemia within three weeks after total thyroidectomy and evaluate the utility of early postoperative PTH levels in predicting the development of permanent hypoparathyroidism (PhP).

Methods: A retrospective observational cohort study was conducted at Radboud University Medical Center Nijmegen, including 373 adult patients who underwent total/ completion thyroidectomy between January 2014 and April 2025. Patients were assigned to either the post-protocol cohort (PPC) ($n = 154$) or the historic cohort ($n = 219$), depending on whether surgery occurred after or before protocol implementation, and subsequently compared.

Results: Unscheduled referrals were significantly more frequent in the historic cohort than in the PPC (19.2% vs 11% respectively, $P = .034$), and the introduction of the protocol was associated with a significant reduction in the odds of these referrals. Early postoperative PTH levels were a significant predictor of unscheduled referrals ($P = .003$), postoperative hypocalcemia ($P < .001$) and PhP ($P < .001$). A postoperative PTH cutoff of 1.7 pmol/L was identified as a clinically meaningful threshold for PhP prediction, demonstrating 100% sensitivity.

Conclusions: Subject to assay availability and workflow efficiency, these findings support the widespread implementation of this standardized protocol to mitigate post-thyroidectomy emergency consultations and readmissions.

Reference

1. McMurran AEL, Blundell R, Kim V. Predictors of post-thyroidectomy hypocalcaemia: a systematic and narrative review. *J Laryngol Otol*. 2020;134(6):541-552. https://doi.org/10.1017/S0022215120001024

Abstract citation ID: lvag096.296

P96 - ECE_2118 - Clinical, biochemical, and histopathological features of CDC73 mutation carriers in pediatric and young-adult (≤21 years) patients with sporadic primary hyperparathyroidism

Simone Della Valentina[1], Alfredo Scillitani[2], Sabrina Corbetta[3,4], Anna Dal Lago[1], Laura Pierotti[1], Chiara Sardella[5], Silvia Carrara[4], Elisa Cairoli[4], Cristina Eller Vainicher[6], Serena Palmieri[6], Rosaria Maddalena Ruggeri[7], Bruno Madeo[8], Massimo Procopio[9], Marco Barale[10], Laura Gianotti[11], Elena Castellano[12], Andrea Gerardo Antonio Lania[13,14], Marco Pitea[15], Roberto Lanzi[16], Riccardo Maggiore[17], Cristiana Cipriani[18], Jessica Pepe[18], Alessandro Rossini[19] and Filomena Cetani[1,5]

[1]*Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy;* [2]*Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy;* [3]*Dipartimento di Scienze Biomediche, Chirurgiche e Odontoiatriche, University of Milan, Milan, Italy;* [4]*U.O. Malattie del Metabolismo Osseo e Diabete, IRCCS Istituto Auxologico Italiano, Milan, Italy;* [5]*Endocrine Unit, University Hospital of Pisa, Pisa, Italy;* [6]*SC Endocrinologia, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy;* [7]*Unità di Endocrinologia,*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Dipartimento di Patologia Umana dell'Età Adulta e dell'Infanzia, University of Messina, Messina, Italy; [8]Unità di Endocrinologia, Dipartimento di Specialità Mediche, Azienda Ospedaliero-Universitaria di Modena, Ospedale Civile di Baggiovara, Modena, Italy; [9]Endocrinologia, Diabetologia e Malattie del Metabolismo, Dipartimento di Scienze Mediche, Università di Torino, Turin, Italy; [10]Endocrinologia Oncologica, Dipartimento di Oncologia, Università di Torino, Turin, Italy; [11]Struttura Complessa di Endocrinologia e Diabetologia Territoriale, ASL Cuneo 1, Cuneo, Italy; [12]Endocrinologia, Diabetologia e Malattie del Metabolismo, Ospedale Santa Croce e Carle, Cuneo, Italy; [13]Dipartimento di scienze biomediche, Humanitas University, Rozzano, Italy; [14]Unità operativa di endocrinologia, diabetologia e andrologia medica, IRCCS Humanitas Research Hospital, Rozzano, Italy; [15]Dipartimento di Pediatria, Ospedale San Raffaele, Milan, Italy; [16]Ospedale San Raffaele, Day Hospital di Medicina Interna, Milano, Italy [17]Unità di Chirurgia Endocrina, Istituto Scientifico IRCCS San Raffaele, Milan, Italy; [18]Dipartimento di Scienze mediche e cardio-vascolari, Sapienza Università di Roma, Rome, Italy; [19]Unità di Endocrinologia e Diabetologia, ASST Papa Giovanni XXIII, Bergamo, Italy

Background: Primary hyperparathyroidism (PHPT) is uncommon in children and adolescents, but it frequently presents with significant end-organ involvement at diagnosis. In this setting, identifying a hereditary etiology is clinically relevant because it may anticipate multiglandular disease, recurrence, and the need for tailored surgical strategies and long-term surveillance. Pathogenic variants in *CDC73* (encoding parafibromin) underlie hyperparathyroidism–jaw tumour syndrome and are strongly linked to aggressive parathyroid disease, including atypical parathyroid tumours and parathyroid carcinoma. Consequently, defining the clinical, biochemical, renal, and histopathological correlates of *CDC73* variants in early-onset PHPT may refine risk stratification and inform follow-up intensity.

Methods: We performed a retrospective analysis of 49 patients diagnosed with PHPT at age ≤21 years. Genetic testing with NGS was available in 39 individuals. Carriers of pathogenic *CDC73* variants were compared with patients without detected mutations with respect to biochemical severity, renal involvement, and histopathology.

Results: Genetic testing was available in 39/49 patients; 11/39 (28%) carried a pathogenic variant in a PHPT-associated gene, including 7/39 (17.9%) with a pathogenic *CDC73* variant with a median age of 16 years (IQR 15.5-18). Among surgically treated patients (37/49), histopathology was available in 36/37 (97%). Overall, adenoma was the predominant finding (30/36, 83%), whereas atypical parathyroid tumour accounted for 4/36 (11%) and parathyroid carcinoma for 2/36 (6%) with patients with atypical parathyroid tumours were diagnosed at a younger age than those with adenoma (15.3 ± 1.0 vs 17.4 ± 2.9, $P = .048$). When histology was analysed by diagnostic category (adenoma vs atypical tumour vs carcinoma), a significant association emerged between genetic status and histological spectrum ($P = .0008$), reflecting a disproportionate representation of atypical tumours and carcinoma among *CDC73* carriers. Non-adenoma histology (atypical tumour/carcinoma) was documented in 6 patients, and 5/6 (83%) were *CDC73*-positive. In direct comparisons, *CDC73* carriers exhibited a more severe biochemical phenotype, with higher albumin-corrected serum calcium (13.7 ± 1.9 vs 11.6 ± 1.3 mg/dL, $P = .0017$), higher ionized calcium (1.9 ± 0.3 vs 1.6 ± 0.2 mmol/L, $P = .021$), and higher 24-hour urinary calcium excretion (813 ± 357 vs 392 ± 189 mg/24h, $P = .005$) than mutation-negative patients. Renal stone disease was also more frequent in *CDC73* carriers (Pearson $\chi^2 = 4.83$; $P = .028$; Fisher's exact $P = .041$).

Conclusions: In young patients with PHPT, pathogenic *CDC73* variants are associated with greater biochemical severity, increased renal stone burden, and a markedly higher prevalence of non-adenomatous parathyroid pathology. These findings support targeted genetic testing and structured, long-term multidisciplinary follow-up in *CDC73* carriers.

Abstract citation ID: lvag096.297

P97 - ECE_2376 - Real-life data about pregnancy and delivery in Italian women with X-linked hypophosphatemia: a survey-based multicenter study (the PPL-XLH study)

Silvia Carrara[1], Gaetano Arcidiacono[2], Marco Barale[3], Giampiero Baroncelli[4], Maria Luisa Brandi[5,6], Valentina Camozzi[7], Elena Castellano[8], Filomena Cetani[9], Pasquale Comberiati[10], Simone Della Valentina[11], Lucia Digitale Selvaggio[12], Natascia Di Iorgi[13,14], Cristina Eller Vainicher[15], Michela Ferrarese[7], Danilo Fintini[16], Nadia Foligno[17], Sandro Giannini[2], Laura Gianotti[18], Anna Grandone[19], Giorgia Grassi[15], Martina Lagana[20], Silvia Lai[21], Gemma Marcucci[22], Laura Masi[23], Stefano Mora[24,25], Francesca Paglia[26], Andrea Palermo[27], Daniela Pasquali[12], Adolfo Marco Perrotta[21], Francesca Pigliaru[28], Marco Pitea[24], Massimo Procopio[29], Vincenzo Rochira[26,30], Silverio Rotondi[21], Rosaria Maddalena Ruggeri[20], Elena Ruotolo[31], Noemi Sagone[29], Marco Onofrio Torres[2], Silvia Vai[1], Giuseppe Vezzoli[17], Marta Zampogna[15] and Sabrina Corbetta[1,32]

[1]Bone Metabolism Diseases and Diabetes Unit, IRCCS Istituto Auxologico Italiano, Milan, Italy; [2]Department of Medicine, University of Padova, Clinica Medica 1, Padua, Italy; [3]Division of Oncological Endocrinology, Department of Medical Sciences, University of Turin, Turin, Italy; [4]Division of Pediatrics, Department of Obstetrics, Gynecology and Pediatrics, University Hospital of Pisa, Pediatric and Adolescent Endocrinology, Pisa, Italy; [5]Donatello Bone Clinic, Villa Donatello Hospital, Florence, Italy; [6]F.I.R.M.O. Onlus Italian Foundation for the Research on Bone Diseases, Florence, Italy; [7]Endocrine Unit, University-Hospital of Padova, Padua, Italy; [8]Department of Endocrinology, Diabetes and Metabolism, Ospedale Santa Croce and Carle Hospital, Cuneo, Italy; [9]Endocrine Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [10]Department of Clinical and Experimental Medicine, Section of Paediatrics, University of Pisa, Pisa, Italy; [11]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [12]Department of Advanced Medical and Surgical Sciences, University of Campania Luigi Vanvitelli, Naples, Italy; [13]Department of Pediatrics, IRCCS Istituto Giannina Gaslini, Genoa, Italy; [14]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova, Genoa, Italy; [15]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [16]Endocrinology and Diabetology Unit, Pediatric University Department, IRCCS Bambino Gesù Children's Hospital, Rome, Italy; [17]Nephrology and Dialysis Unit,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

IRCCS San Raffaele Scientific Institute, Milan, Italy; [18]ASL Cuneo 1, Struttura Complessa di Endocrinologia e Diabetologia Territoriale, Cuneo, Italy; [19]Department of Woman, Child and General and Specialised Surgery, Centre of Paediatric Endocrinology, Naples, Italy; [20]Unità di Endocrinologia, Dipartimento di Patologia Umana dell'Adulto e dell'Età Evolutiva "Gaetano Barresi", University of Messina, Messina, Italy; [21]Nephrology Unit, Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy; [22]Bone Metabolic Diseases Unit, Department of Experimental and Clinical Biomedical Sciences, University Hospital of Florence, Florence, Italy; [23]Metabolic Bone Diseases Unit, University Hospital of Florence, Florence, Italy; [24]Department of Pediatrics, IRCCS Ospedale San Raffaele, Milan, Italy; [25]Laboratory of Pediatric Endocrinology, IRCCS Ospedale San Raffaele, Milan, Italy; [26]Endocrinology Unit, Department of Medical Specialties, Azienda Ospedaliero-Universitaria Policlinico di Modena, Ospedale Civile di Baggiovara, Modena, Italy; [27]Unit of Metabolic Bone and Thyroid Disorders, Fondazione Policlinico Campus Bio-medico, Rome, Italy; [28]Endocrinology Unit, AOU Cagliari, Cagliari, Italy; [29]Division of Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [30]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [31]Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [32]Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

X-linked hypophosphatemia (XLH) is the most common genetic phosphate disorder leading to hypophosphatemia and bone mineralization defects. Recent recommendations from international panels of experts have proposed management of women with XLH during pregnancy; the main items are: 1) preconception genetic counseling; 2) supplementation with phosphate/calcitriol aimed to normalize serum phosphate; 3) monitoring of mineral metabolism. However, evidence supporting the recommendations are limited. We aimed contributing through a survey-based study.

Sixty-three women with XLH (aged 43.1 ± 14.6 years) were enrolled on September-December 2025. Thirty-six women (57.1%) experienced a total of 58 pregnancies, delivering 46 newborns, while 12 (20.7%) ended in miscarriages, predominantly in the first trimester. Thirty-four (72.7%) pregnancies were managed by cesarean delivery. None experienced fractures/pseudofractures during pregnancy or delivery, except one femur fracture after miscarriage. Symptomatic kidney stones occurred in two pregnancies.

Considering the above three major statements, we found that: 1) 36% of pregnant women with XLH received preconception genetic counseling; 2) 7 women (19.4%) received phosphate/calcitriol supplementation during pregnancy; of them, 6 women were on conventional therapy at time of conception and were older than the untreated women (35.0 vs 28.9 years, $P = .0022$); 3) only 9 (25.0%) women were referred to a bone specialist during pregnancy and biochemically monitored; of them, 6 women received conventional treatment. Monitored women compared with not monitored women underwent a similar number of orthopaedic surgeries (3.1 vs 3.3), more often received preconception genetic counseling (88.9% vs 18.5%, $P = .0003$), had a lower number of spontaneous conceptions (1.17 vs 1.74, $P = .0679$), 3 women needed in vitro fertilization with 7 embryo transfers exiting in 3 newborns, were older at first conception (35.2 vs 30.1 years, $P = .0014$), 1 women experienced worsening of bone and joint pain (vs 9 unmonitored women), delivered a lower number of newborns (1.0 vs 1.5, $P = .0488$), did not differ in prevalence of miscarriages (33.3 vs 33.3%), in gestational weeks of deliveries (38.1 vs 38.0), in prevalence of cesarean sections (88.9% vs 75.0%). Monitored pregnant women had a lower prevalence of XLH affected newborns (44.4% vs 80.0%), with a lower prevalence of psychomotor development delay (11.1% vs 63.0%; $P = .0178$).

In conclusion, a gap between recommendations and the real-life data is evident, suggesting that women with XLH received inadequate attention during their fertile life and were referred to bone specialists when subfertility emerges. However, conventional therapy during pregnancy may prevent bone and joint pain worsening, while the effects on delivery and offspring are not clear.

Abstract citation ID: lvag096.298

P98 - ECE_2985 - Primary hyperparathyroidism in young women—a retrospective cohort study of outcome in surgically treated patients

Mathias Alstrup[1], Jacob Lilja-Fischer[1], Christine Holm Egebæk[1], Lars Rejnmark[2] and Lars Rolighed[1]
[1]Department of Otorhinolaryngology, Head- and Neck surgery, Aarhus University Hospital, Aarhus N, Denmark; [2]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus N, Denmark

Background: Primary hyperparathyroidism (PHPT) predominantly affects postmenopausal women but is occasionally also seen in young women.

Methods: We performed a retrospective cohort study of women aged 15-49 years who underwent parathyroidectomy (PTX) for PHPT at Aarhus University Hospital between 2015 and 2023. Clinical, genetic, surgical, biochemical, and reproductive data were obtained through manual review of electronic medical records.

Results: A total of 215 women were included, median age of 42.7 years. Genetic testing was performed in 81% and 7% were pathogenic (MEN1, MEN2, MEN4 or CDC73). Most patients had mild to moderate PHPT (PTH 13 pmol/L and Ca^{2+} 1.45 mmol/L). During PTX, mean PTH reduction was 85%. In sporadic PHPT, the majority had single gland disease (94%). Operations were safe with very few permanent complications (recurrent laryngeal nerve palsy in 1 patient, and hypoparathyroidism in 2 MEN1 patients). Temporary nerve palsy was seen after PTX in 3 patients and 2 patients had a re-operation due to hematoma. In sporadic PHPT ($N = 200$), cure rate was 95%. The remaining 11 patients had missed adenoma ($n = 1$) or multi-gland disease ($n = 10$) and were cured at another operation. Five women (2%) were cured with PTX during pregnancy, without maternal, fetal, or obstetric complications. Pregnancy patterns did not suggest an increased risk of infertility in PHPT.

Conclusions: PTX in young women with PHPT is safe and effective, with excellent surgical and biochemical outcomes. Genetic evaluation is important due to high prevalence of hereditary disease. Surgery during pregnancy appears safe when performed in specialized centers.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.299

P99 - ECE_3689 - "Surgical vs conservative management of primary hyperparathyroidism: renal and skeletal outcomes from a single-centre registry"

Anyat Ali[1], Elhassan Awadin[2], Ahmed Elabasy[1], Osman Abdalrazag[3] and Suresha Muniyappa[4]
[1]*Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, Northern Ireland;* [2]*Royal Bolton Hospital, Bolton, Northern Ireland;* [3]*Barnsley Hospital, Barnsley, United Kingdom;* [4]*Doncaster Royal Infirmary, Doncaster, Northern Ireland*

Background: Primary hyperparathyroidism (PHPT) may be managed with curative parathyroidectomy or conservative medical treatment with surveillance. This service evaluation assessed management patterns, biochemical outcomes, and end-organ complications among patients with PHPT recorded in the parathyroid registry at Doncaster and Bassetlaw Teaching Hospitals (DBTH), with particular focus on renal and skeletal outcomes.

Methods: A retrospective review of 175 patients recorded in the DBTH parathyroid registry was undertaken. Twenty-two patients (12.6%) underwent parathyroidectomy, while 153 (87.4%) were managed conservatively. Data collected included postoperative calcium outcomes, cinacalcet use, DXA scan, osteoporosis prevalence among those scanned, and rates of renal failure. Outcomes were compared descriptively between surgical and non-surgical groups as part of this service evaluation.

Results: Among surgically treated patients, 81.8% achieved postoperative normocalcaemia, while 18.2% had persistent or recurrent hypercalcaemia requiring ongoing medical management. Cinacalcet use was higher in the surgical group with persistent disease compared with the conservatively managed cohort (18.2% vs 9.8%). DXA scanning was performed in 59.1% of surgical patients and 58.2% of those managed conservatively. Among patients who underwent DXA scanning, osteoporosis was more prevalent in the surgically managed group (53.8%) compared with the conservatively managed group (43.8%), likely reflecting selection of patients with more advanced skeletal disease for surgery. Renal failure was less common in patients who underwent parathyroidectomy (9.1%) compared with those managed conservatively (17.6%). Most surgically managed patients had preserved renal function (90.9%), whereas renal impairment affected nearly one in five patients in the non-surgical cohort. Overall, conservative management accounted for the majority of PHPT care within the service. However, a substantial proportion of conservatively managed patients demonstrated renal impairment or osteoporosis, highlighting the cumulative burden of long term disease.

Conclusions: Parathyroidectomy was associated with favourable outcomes in patients with end-organ involvement, particularly lower rates of renal impairment compared with conservative management, supporting surgery in appropriately selected patients. We recommend that all patients who are fit for surgery and meet guideline criteria for parathyroidectomy should be referred for surgical assessment. Interpretation of skeletal outcomes is limited by incomplete availability of DXA scan data within the registry, as some assessments may have been performed outside the local service.

Implications: This audit supports current PHPT management practices at DBTH while identifying key quality improvement priorities, including optimisation of surgical outcomes, structured postoperative biochemical surveillance, and proactive renal risk assessment in conservatively managed patients. These findings inform patient counselling, support guideline concordant care and guide future service development.

Abstract citation ID: lvag096.300

P100 - ECE_3782 - Baseline eGFR predicts lower palopegteriparatide maintenance dose requirements in chronic hypoparathyroidism

Dimitra Lygerou[1,2], Ioannis Petrakis[1], Grigoria Betsi[3], Maria Sfakiotaki[3], Vasiliki Daraki[3], Ariadni Androvitsanea[1], Nicos Papadakis[1], Myrto Konidaki[1], Konstantinos Stylianou[1] and Paraskevi Xekouki[3]
[1]*Nephrology, University Hospital of Heraklion, Heraklion, Greece; ;* [3]*Endocrinology, University Hospital of Heraklion, Heraklion, Greece*

Background: In chronic hypoparathyroidism (HypoPT), conventional therapy with oral calcium and active vitamin D may contribute to hypercalciuria, adverse renal outcomes, and ectopic calcifications. Real-world determinants of palopegteriparatide (TransCon PTH; Yorvipath) maintenance dose requirements across baseline kidney function remain incompletely characterized.

Methods: Single-center observational cohort of adults with chronic HypoPT treated with palopegteriparatide. Baseline and last follow-up data were collected for palopegteriparatide dose, elemental calcium, alfacalcidol, serum phosphate, serum creatinine, and eGFR (CKD-EPI 2021). CKD was defined as baseline eGFR <60 mL/min/1.73 m^2. Data are presented as median (IQR). Between-group and paired comparisons used non-parametric tests. Associations between maintenance dose and baseline eGFR (continuous), disease duration, and ectopic calcifications were explored using Spearman correlation and robust multivariable linear regression.

Results: Twenty patients were analyzed (70% female), median age 67.0 (45.3-73.3) years; 80% had post-surgical HypoPT and disease duration was 16.5 (9.0-31.3) years. Median time on palopegteriparatide was 7.5 (3.0-13.0) months. Baseline CKD was present in 8/20 (40%); CKD patients were older (74.0 [72.3-79.5] vs 49.5 [34.3-66.5] years; $P = .0020$) and had longer disease duration (31.0 [15.0-37.0] vs 11.5 [3.8-19.5] years; $P = .0337$). At last follow-up, palopegteriparatide maintenance dose was lower in CKD vs non-CKD: 15.0 (12.0-22.5) vs 28.5 (24.0-42.0) μg ($P = .0114$). From baseline to last follow-up, conventional therapy decreased markedly (elemental calcium 3000 [1500-3125] to 0 [0-500] mg/day, $P = .00013$; alfacalcidol 1.75 [0.88-3.0] to 0.0 [0.0-0.06] μg/day, $P = .00018$), serum phosphate improved (5.3 [4.48-5.88] to 4.1 [3.48-4.35] mg/dL, $P = .00013$), and eGFR remained stable (71.5 [53.5-98.0] to 70.5 [55.8-89.0] mL/min/1.73 m^2; $P = .452$). Baseline eGFR correlated positively with maintenance dose (Spearman ρ=0.701, $P = .00058$) and remained an independent predictor after adjustment for disease duration ($\beta = .237$ μg per 1 mL/min/1.73 m^2; $P = .025$; VIF ~1.76). Ectopic calcifications (65%) were also associated with lower dose (18.0 [12.0-24.0] vs 33.0 [28.5-42.0] μg; $P = .0035$).

Conclusions: Lower baseline eGFR—modeled as a continuous measure or categorized as CKD—was associated with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

lower palopegteriparatide maintenance dose requirements in chronic HypoPT. Ectopic calcifications may further identify patients maintained on lower doses and warrant longitudinal confirmation. Conventional therapy was substantially reduced, phosphate homeostasis improved, and overall kidney function remained stable during Yorvipath treatment.

Abstract citation ID: lvag096.301

P102 - ECE_2592 - Effect of testosterone replacement therapy on fracture risk in men with hypogonadism: a systematic review and meta-analysis of randomized-controlled trials

Panagiotis Anagnostis[1,2], Efstathios Divaris[3], Maria Zidrou[1], Evanthia Kassi[4] and Symeon Tournis[5]
[1]3rd Department of Internal Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]Department of Endocrinology, Diabetes and Metabolism, 424 General Military Hospital, Thessaloniki, Greece; [4]Endocrinology Unit, 1st Department of Propaedeutic Internal Medicine, National and Kapodistrian University of Athens, Centre of Expertise in Rare Endocrine Diseases, C.E.R.E.D – Disorders of Calcium and Phosphate Metabolism, LAIKO General Hospital of Athens, Athens, Greece; [5]Laboratory for Research of the Musculoskeletal System "Th. Garofalidis", Medical School, National and Kapodistrian University of Athens, Athens, Greece

Objective: Testosterone replacement therapy (TRT) is the treatment of choice in men with hypogonadism. Although its beneficial effect on bone mineral density is well-established, the evidence regarding its impact on fracture risk remains inconclusive. The purpose of this study was to systematically review and meta-analyze the highest quality available evidence regarding the effect of TRT on fracture risk in hypogonadal men.

Study Design: A systematic literature search was conducted in PubMed, Scopus and Cochrane databases from inception through 30 September 2025. Only randomized-controlled trials were eligible for inclusion. Outcomes were summarized using odds ratio (OR) and mean difference (MD), respectively, with a 95% confidence interval (95% CI). The I2 index was used in order to quantify heterogeneity.

Results: Initial search yielded 1145 results after removal of duplicates, seven of which underwent full-text assessment. Finally, two studies were included in the qualitative and quantitative analysis ($n = 2711$). TRT was associated with increased risk of clinical fractures compared with placebo (OR 1.58, 95% CI 1.23-2.04, $P < .0001$, I2 = 0%). However, no difference between groups was observed when the analysis was restricted to major osteoporotic fractures (hip, spine, wrist, and arm) (OR 0.61, 95% CI 0.11-3.46, $P = .58$, I2 64%). This was also the case for vertebral (OR 0.87, 95% CI 0.34-2.26, $P = .80$, I2: 11%) and hip fractures (OR 0.99, 95% CI 0.33-2.93, $P = .98$, I2: 0%), when analyzed separately.

Conclusions: This is the first meta-analysis showing that TRT is associated with an increased incidence of predominantly non-major fractures, while the risk of major osteoporotic fractures, including hip and vertebral fractures, was not increased.

Abstract citation ID: lvag096.302

P103 - ECE_3282 - Is hypothyroidism associated with an increased risk of fractures in females with Ehlers–Danlos syndrome?

Jędrzej Jedliński[1,2], Ivan Rychlik[3], Aleksandra Żuk-Łapan[1,2], Jan Domański[1,2], Michalina Andrzejak[1,2], Bernadetta Kałuża[1,2] and Edward Franek[1,2,4]
[1]Department of Internal Medicine, Endocrinology, and Diabetology, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland; [2]Students Scientific Group of the Medical University of Warsaw at the Department of Internal Medicine, Endocrinology, and Diabetology, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland; [3]Department of Internal Medicine, Third Faculty of Medicine, Charles University, and Královské Vinohrady University Hospital, Prague, Czech Republic; [4]Department of Human Epigenetics, Polish Academy of Sciences, Mossakowski Medical Research Institute, Warsaw, Poland

Background: Ehlers–Danlos syndrome is a group of genetic conditions involving abnormal synthesis of connective tissue, particularly collagen, which manifests as musculoskeletal abnormalities including joint hypermobility and increased risk of fractures. Thyroid hormones play an important role in bone turnover, and their deficiency slows osteoblast and osteoclast activity. The aim of this study was to assess the risk of fractures in females with Ehlers–Danlos syndrome concomitant with hypothyroidism.

Material and Methods: We assessed thyroid hormone levels in 30 female patients with classical or hypermobile Ehlers–Danlos syndrome. The patients were divided into two groups: Group 1—patients with no history of fractures ($n = 17$) and Group 2—patients with a history of fractures ($n = 13$).

Results: The two groups did not differ in terms of the rates of hypothyroidism (7.69% vs 29.41%, $P = .16$), autoimmune thyroiditis (25.38% vs 23.53%, $P = .61$), or the levels of thyroid stimulating hormone (1.69 ± 0.77 vs 2.44 ± 1.64 [μIU/ml], $P = .21$), free triiodothyronine (3.54 ± 0.8 vs 3.26 ± 0.49 [pg/ml] $P = .52$), free thyroxine (1.33 ± 0.15 vs 1.35 ± 0.28 [ng/dl], $P = .63$), or thyroid peroxidase antibody levels (49.38 ± 139.92 vs 26.26 ± 31.05 [IU/ml], $P = .89$). Univariate logistic regression analysis showed no correlation between either hypothyroidism (OR 5 [0.506–49.44], $P = .17$) or autoimmune thyroiditis (OR 1.69 [0.26–11.07], $P = .58$) and the risk of fracture.

Conclusions: Female patients with Ehlers–Danlos syndrome showed no association between hypothyroidism or autoimmune thyroiditis and an increased risk of fractures.

Abstract citation ID: lvag096.303

P104 - ECE_3612 - Effect of antiresorptive therapy on post-parathyroidectomy bone mass gain in primary hyperparathyroidism: a pilot study

Nicolò Bisceglia[1,2], Anna Piazza[1,2], Sara Capra[1,2], Cristiana Cantone[1,2], Virginia Samaritani[1,2], Matteo Malagrinò[1,2], Giulia Vandi[1,2], Uberto Pagotto[1,2] and Guido Zavatta[1,2]
[1]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [2]Bologna, Italy

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: In primary hyperparathyroidism (PHPT), the impact of antiresorptives on bone mineral density gain (ΔBMD) after parathyroidectomy (PTx) remains controversial.

Materials and Methods: We retrospectively identified 112 patients with PHPT who underwent PTx in our Hospital from 9/2021 to 12/2024 (cases) and 64 PHPT patients treated conservatively (controls). We included 82 cases with densitometry (DXA) and blood tests performed just before and 12 months after PTx, and 17 controls with comparable assessments. All DXAs were performed with the same machine, allowing the estimation of Least Significant Change (LSC) for each skeletal district. According to pre-PTx antiresorptive exposure (bisphosphonates/denosumab), cases were classified as: naïve (never treated; $n = 32$), short-exposure (<6 months; $n = 23$), chronic-exposure (>6 months; $n = 27$).

Objectives: Primary: to evaluate whether antiresorptive therapy pre-PTx influences median annualized ΔBMD post-PTx, also analyzing the percentage of responders (patients with significant ΔBMD according to LSC in at least one skeletal site). Secondary: to investigate correlations between bone turnover markers (BTMs) and ΔBMD post-PTx.

Results: Cases were younger than controls (65 vs 78 years), with higher albumin-adjusted calcium (10.6 vs 10.4 mg/dL) and PTH levels (137 vs 102 pg/mL), and lower phosphate (2.8 vs 3.1 mg/dL) at baseline. Overall, PTx resulted in significant ΔBMD at spine (+5.3%) and femur (+2.9%), with stability at radius (−1.6%). Responders were 84.1%. Across subgroups, ΔBMD at 3 sites was comparable, with numerically greater gains in short-exposure at spine (ΔBMD = 4.1%; vs naïve = 1.6% and chronic = 2.2%) and femur (ΔBMD = 2.4%;vs naïve = 1.3% and chronic = 1.2%). All three surgical subgroups showed significantly greater ΔBMD compared with controls at spine (ΔBMD = −0.9%) and femur (ΔBMD = −0.3%). The number of responders was comparable, with a prevalence of short (91.3%) vs chronic-exposure (81.5%) and naïve (81.2%). However, femoral responders were significantly higher in short-exposure (90.9%;vs naïve = 56.2% and chronic = 51.9%). In all groups, a reduction in BTMs (ΔCTX,ΔBAP) was observed. ΔCTX was numerically greater in short (−75.9%) vs chronic-exposure (−70.7%) and naïve (−68.1%). In chronic-exposure higher ΔBMD at spine was associated with greater ΔCTX ($P = .017$; rho = −0.464). In the other subgroups no robust correlations were found.

Conclusions: Parathyroidectomy appears to significantly increase BMD and reduce BTMs regardless of antiresorptive exposure; however, short-term antiresorptive treatment pre-PTx could lead to greater BMD gains and higher proportion of patients achieving a significant skeletal response. This effect may be mediated by an early widening of post-PTx anabolic window, initiated before surgery because of antiresorptive therapy. Larger prospective studies are needed to define the optimal sequencing of PTx and antiresorptives to maximize post-surgical BMD recovery.

Abstract citation ID: lvag096.304

P105 - ECE_3425 - Pseudohyperparathyroidism of lactation successfully treated with carbergoline

Genevieve Tellier[1], Rhiannon Berkeley[1], Mei-Ju Hwang[1,2] and Anthony Wilton[1]

[1]Endocrinology, Ysbyty Gwynedd, Bangor, United Kingdom; [2]Breast Surgery, Ysbyty Gwynedd, Bangor, United Kingdom

Physiological changes in maternal calcium metabolism occur in normal lactation to facilitate sufficient supply of calcium for foetal skeletal formation. These changes have been described as a brain-breast-bone circuit and entail increased secretion of prolactin by the suckling reflex or milk expression. The increased prolactin suppresses hypothalamic gonadoptrophin releasing hormone secretion with a sequential decrease in gonadotrophins and oestradiol. The latter upregulates the receptor activator of the nuclear factor beta-ligand (RANKL) which downregulates osteoprotegerin with resultant stimulation of octeoclastic activation and bone resorption. Hyperprolactinaemia also stimulates release of 5-hydroxytryptophan which increases parathyroid hormone related protein (PTHrP) production by breast epithelial cells. Excess activity of these processes can result in hypercalcaemia with suppressed parathyroid hormone levels.

Case Report: A 19 year old 3-week postpartum primigravida patient presented to primary care with a 7-day history of abdominal pain and fatigue. Pregnancy had been asymptomatic and delivery uncomplicated. The finding of hypercalcaemia at adjusted calcium levels ranging from 2.79-2.90 mmol/L coincidental with parathyroid hormone level of 1.3 pmol/L led to secondary care referral.

A history of painful engorged breasts secondary to suckling had led her to milk expression with no symptomatic relief. Expert breast examination confirmed very engorged breasts with typical lactational changes. Investigations confirmed adjusted 3.01 mmol/L, parathyroid hormone 1.1 pmol/L, vitamin D 39 nmol/L, prolactin 6941 mU/L and alkaline phosphatase 176 U/L. Unfortunately PTHrP assay was not available. The finding of low parathyroid hormone level excluded primary hyperparathyroidism and other diagnoses for hypercalcaemia were also excluded.

Subsequent serial investigations recorded increases in adjusted calcium, prolactin and alkaline phosphatase following milk expression. Agreement to convert to breast milk substitute was obtained but ongoing severe breast discomfort and lactation led us to treat with a single dose of 0.5 mg of cabergoline which resulted in rapid resolution of symptoms and biochemical abnormalities.

Discussion: Initial reports of lactational hypercalcaemia were in patients with gigantomastia who were treated with bilateral mastectomies. Subsequent reports described the same phenomenon in women with normal size breasts practising milk expression. Treatments by means of cessation of breastfeeding, IV fluids, bisphosphonates, calcitonin and bromocriptine were of limited success. We believe that cabergoline should be considered as first-line therapy in lactational hypercalcaemia as in addition to its efficacy it excludes other causes of hypercalcaemia in this rare but troublesome condition. We also suggest describing the phenomenon as a breast-brain-hypothalamic-pituitary-bone circuit.

Abstract citation ID: lvag096.305

P106 - ECE_2294 - PTH washout and 99mTc-MIBI scintigraphy with SPECT/CT—complementary or interchangeable methods of presurgical localization for patients with primary hyperparathyroidism?

Maja Cieślewicz[1], Ewelina Szczepanek-Parulska[2,3], Paweł Komarnicki[2], Dorota Filipowicz[2], Agnieszka Witowska[2], Rafał Czepczyński[2], Ariadna Zybek-Kocik[2] and Marek Ruchala[2]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Poznań, Poland; [2]Department of Endocrinology, Metabolism and Internal Diseases, Poznan University of Medical Sciences, Poznań, Poland; [3]Departament of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznań, Poland

Background: Surgery is the only curative treatment for primary hyperparathyroidism (PHPT). Accurate preoperative localization of parathyroid lesion is essential to facilitate minimally invasive surgical approaches. Although 99mTc-MIBI scintigraphy with SPECT/CT (MIBI) remains the standard imaging modality, parathyroid hormone washout (PTHw) has emerged as a promising adjunct, particularly when radiation exposure is a concern.

Aim: The aim of this study was to assess the diagnostic performance and concordance of PTHw and MIBI in patients with PHPT and to compare different cutoff values for PTHw positivity.

Methods: This retrospective study included 54 patients who underwent surgery for PHPT. All patients had ultrasound-guided fine-needle aspiration with PTHw measurement and 99mTc-MIBI scintigraphy with SPECT/CT performed. PTHw was considered positive when the PTH concentration in the washout fluid exceeded the corresponding serum PTH level. An additional analysis was conducted using a PTH washout-to-serum PTH ratio (PTHw/PTHser) cutoff >3.

Results: The sensitivity of PTHw was 92.59% (95% CI, 82.45-97.08%), compared with 87.04% for MIBI (95% CI, 75.58%-93.58%). All patients had localization of lesion confirmed in at least one imaging technique. Concordant positive findings were observed in 79.63% of cases. In paired analyses, detection performance did not differ significantly between MIBI and PTHw (McNemar test, $P = .55$), with 11 discordant results, including 4 MIBI-positive and 7 PTHw-positive cases. When analysis was restricted to histopathologically confirmed parathyroid adenomas (excluding hyperplasia and other diagnoses), positive localization was observed in 37 of 41 cases with PTHw and in 36 of 41 cases with MIBI. Median ionized calcium levels were significantly higher in the PTHw-positive group compared with the PTHw-negative group (6.22 [IQR 6.03-6.68] vs 5.76 [IQR 5.68-5.85]; $P = .03$; $r = 0.75$). In MIBI-positive cases maximal lesion diameter was significantly larger than in MIBI-negative cases (12 mm[IQR 9.50-16.50] vs 9 mm[IQR 7-10.50]; $P = .02$; $r = 0.55$). Univariate logistic regression demonstrated a consistent trend toward higher MIBI detection with increasing lesion size (OR = 1.32; $P = .06$). Application of a PTHw/PTHser cutoff >3 reduced sensitivity to 79.63% (95% CI, 67.10%-88.23%).

Conclusions: PTHw and MIBI demonstrate comparable sensitivity for preoperative localization in PHPT but show limited concordance at the patient level, highlighting their complementary rather than interchangeable roles. Larger adenomas were more frequently detected by MIBI. A PTHw/PTHser cutoff >1 maximized sensitivity and appears preferable to a cutoff >3, although specificity could not be assessed owing to the study design. Larger prospective studies are warranted to validate these findings.

Abstract citation ID: lvag096.306

P107 - ECE_1433 - Pulse methylprednisolone therapy suppresses bone turnover without short-term loss of bone mineral density

Fatima Siddiqui[1,2], Lawrence Law[3], Amal Al-Aamri[4], Siok Bee Chionh[1,3], Pei Chia Eng[3,5] and Chin Meng Khoo[1,3]

[1]Department of Medicine, Yong Loo Lin School of Medicine, Singapore, Singapore; [2]Department of Medicine, National University Hospital, Singapore, Singapore; [3]Division of Endocrinology, Department of Medicine, National University Hospital, Singapore, Singapore; [4]Nizwa Hospital, Nizwa, Oman; [5]Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom

Introduction: Chronic glucocorticoid (GC) therapy is a leading cause of secondary osteoporosis, but the skeletal effects of intermittent high-dose intravenous pulse GC regimens are unclear. These regimens are widely used for treatment of autoimmune and inflammatory conditions and may reduce cumulative GC exposure. In this study, we evaluated the impact of pulse methylprednisolone (MP) on bone mineral density (BMD), bone turnover markers in adults without osteoporosis.

Methods: We conducted a systematic review and meta-analysis in accordance with PRISMA guidelines. Pubmed, EMBASE, Scopus and Google Scholar were searched to September 2025 for longitudinal, cohort, case-control or randomised studies in all adults receiving pulse MP with BMD and/or bone markers measured before and after pulse MP therapy. Outcomes included BMD, trabecular bone score (TBS), bone turnover markers, calcium, vitamin D and parathyroid hormone axis. Risk of bias was assessed using ROBINS-E. Pooled mean differences (MD) were estimated using random- or fixed-effects models; a 4% BMD change was prespecified as the least significant change.

Results: Nine studies with a total of 257 participants (73% women, mean age of 40 years old) were included. Pulse MP after a mean follow up of 5.3 months did not reduce BMD at the lumbar spine (MD 0.01 g/cm^2; 95% CI −0.02 to 0.03), femoral neck (MD −0.01 g/cm^2; 95% CI −0.03 to 0.01), or total hip (MD −0.03 g/cm^2; 95% CI −0.06 to 0.01) with all changes below the least significant change threshold. TBS was similarly unchanged (MD −0.02; 95% CI −0.10 to 0.07). In contrast, P1NP (MD −36.95 ng/mL; 95% CI −56.86 to −17.03) and CTX (MD −0.19 ng/dL; 95% CI −0.32 to −0.07) decreased, indicating suppression of both bone formation and resorption. Serum 25-hydroxyvitamin D increased modestly, while calcium and parathyroid hormone remained stable. Heterogeneity was low for BMD and higher for turnover markers; no major publication bias was detected.

Conclusions: In adults without osteoporosis, intravenous MP suppresses bone turnover without causing short-term BMD loss. IV MP may be less detrimental to bone health than chronic long-term GC regimens when clinically appropriate. Future studies comparing pulse GC and chronic GC regimens are needed to clarify long-term skeletal safety of pulse GC therapy.

Abstract citation ID: lvag096.307

P108 - ECE_1756 - Clinical outcomes after parathyroidectomy in elderly patients with primary hyperparathyroidism

Christine Holm Egebæk[1], Jacob Lilja-Fischer[1], Mathias Alstrup[1], Torben Harsløf[2] and Lars Rolighed[1]

[1]Department of Otorhinolaryngology – Head & Neck Surgery, Aarhus University Hospital, Aarhus N, Denmark; [2]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus N, Denmark

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Primary hyperparathyroidism (PHPT) is increasingly detected in older individuals and often associated with osteoporosis. Benefit from parathyroidectomy (PTX) in elderly patients is debated. We evaluated biochemical outcomes, bone mineral density (BMD) and survival after PTX in elderly patients.

Methods: Retrospective cohort study of patients aged ≥75 years undergoing PTX for PHPT between 2014 and 2019. Patients were grouped as <80 or ≥80 years. Biochemical outcomes and changes in BMD at the spine and hip were assessed pre- and postoperatively. We evaluated percent change (Δ% BMD) and adjusted Δ% BMD with linear regression and accounting for body mass index, creatinine, and anti-osteoporotic therapy.

Results: 171 patients (114 <80 and 57 ≥80 years) were included and 116 (68%) had osteoporosis. Cure rate was 95%, one had nerve palsy, and another had hypoparathyroidism after PTX. There was no disease or procedure related mortality. BMD improved by 3.3% in the spine but not in the hip (0.0%). The increase was higher in patients < 80 years ($P = .03$). The difference between age-groups disappeared when we adjusted for BMI, creatinine, and osteoporotic treatment. For patients in osteoporosis treatment, BMD improved significantly in spine and hip (4.8% and 1.6%) compared with patients without osteoporosis treatment (1.5% and 0.0%).

Conclusions: PTX in a selected group of elderly patients with PHPT is safe and biochemically effective with low complication rates. The positive BMD changes are mitigated by increasing age and decreasing kidney function. Further, simultaneous medical treatment seems to improve the BMD benefit from PTX.

Keywords parathyroidectomy, primary hyperparathyroidism, elderly, bone mineral density

Abstract citation ID: lvag096.308

P109 - ECE_2168 - Teriparatide treatment of osteoporosis in solid organ transplant recipients – a single-center experience

Talia Diker Cohen[1,2], Ilana Shraga-Slutzky[1,2], Keren Kaminer[1,2], Alexander Gorshtein[1,2], Idit Dotan[1,2] and Gloria Tsvetov[1,2]

[1]Rabin Medical Center, Beilinson Campus, Institute of Endocrinology, Diabetes and Metabolism, Petah Tikva, Israel; [2]Gray Faculty of Medicine and Health, Tel Aviv University, Tel Aviv, Israel

Background: Solid organ transplant (SOT) recipients are at high risk for osteoporosis and fragility fractures due to pre-existing organ dysfunction and chronic immunosuppressive therapy, particularly glucocorticoids. Evidence supporting the efficacy and safety of anabolic osteoporosis therapy in this population is limited, and fracture data are scarce.

Methods: We conducted a retrospective cohort study at a large transplant center, including adult kidney, lung, liver, and heart transplant recipients treated with teriparatide for post-transplant osteoporosis for ≥6 months. Bone mineral density (BMD), incident fractures, biochemical parameters, renal function, and adverse events were assessed during treatment and follow-up.

Results: Thirty-nine SOT recipients (33% men; mean age 61.3 ± 11.6 years) were included, with kidney ($n = 20$), lung ($n = 10$), and liver ($n = 9$) transplants. Ninety percent had prior fragility fractures, and 79% had multiple fractures. Median teriparatide duration was 22.3 months. Significant BMD increases were observed at the lumbar spine (+11 ± 15%, $P = .01$), femoral neck (+8 ± 14%, $P = .05$), and total hip (+11 ± 16%, $P = .05$). Six patients sustained fractures after teriparatide initiation; only two occurred during active treatment, while four occurred after discontinuation. Hypercalcemia occurred in one patient and led to treatment cessation. Estimated glomerular filtration rate declined modestly during the first six months of therapy but stabilized thereafter and did not differ from contemporaneous untreated transplant controls. No cases of graft rejection were observed.

Conclusions: In this large real-world cohort of SOT recipients with severe osteoporosis, teriparatide therapy was associated with significant improvements in BMD, low rates of treatment-limiting adverse events, and no apparent excess risk to graft function. These findings support the selective use of anabolic therapy in high-risk transplant recipients and highlight the need for prospective studies to define optimal patient selection and treatment sequencing.

Abstract citation ID: lvag096.309

P110 - ECE_3936 - Effect of parathyroidectomy on bone mineral density in patients with primary hyperparathyroidism

Ozge Sahin Kimyon[1], Simge Saydam[1], Zeynep Elüstü Belten[1], Selin Celik[1], Muge Yurdacan Sahin[2], Evin Bozkur[1], İlkay Çakir[1], Meral Mert[1], Sema Ciftci[1] and Hamide Piskinpasa[1]

[1]Department of Endocrinology and Metabolism, University of Health Sciences, Bakırkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Türkiye; [2]Department of General Surgery, University of Health Sciences, Bakırkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Türkiye

Background: Primary hyperparathyroidism (PHPT) is characterized by bone loss, predominantly affecting cortical bone. Parathyroidectomy (PTX) is the definitive treatment and is associated with subsequent skeletal recovery. The aim of this study was to evaluate trabecular and cortical bone mineral density (BMD) changes following PTX in patients with PHPT.

Methods: This retrospective cohort study included patients who underwent PTX for PHPT between 2019 and 2024. Patients with persistent or recurrent hyperparathyroidism after surgery were excluded. Patients with available preoperative and at least one-year postoperative dual-energy X-ray absorptiometry (DXA) measurements were included. BMD measurements of the lumbar spine, femoral neck, total hip, and distal radius were analyzed, and osteoporosis prevalence at each skeletal site was assessed. Preoperative and postoperative clinical, laboratory, and BMD parameters were compared.

Results: A total of 86 patients (76 females/10 males; mean age 55.3 ± 8 years) were included. At baseline, osteoporosis was present in 70.9% of patients, most commonly affecting the distal radius (51.2%), followed by the lumbar spine (22.1%). The mean interval between surgery and follow-up DXA was 31.9 ± 19.8 months. After PTX, osteoporosis persisted in 70.9% of patients who had osteoporosis at any skeletal site

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

preoperatively. Persistence rates were 21.1% at the lumbar spine, 75.0% at the femoral neck, 16.7% at the total hip, and 81.8% at the distal radius. A history of low-trauma fracture was present in five patients preoperatively and in one patient postoperatively. Comparison of preoperative and postoperative DXA parameters revealed statistically significant increases in lumbar spine BMD (0.940 ± 0.122 vs 0.994 ± 0.123 g/cm^2, $P <$ .001), femoral neck BMD (0.806 ± 0.098 vs 0.847 ± 0.110 g/cm^2, $P <$ .001), and total hip BMD (0.875 ± 0.148 vs 0.906 ± 0.116 g/cm^2, $P =$ .004). In contrast, no significant change in BMD was observed at the distal radius (0.665 ± 0.113 vs 0.673 ± 0.116 g/cm^2, $P =$ .390).

Conclusions: In patients with PHPT, parathyroidectomy results in significant increases in bone mineral density, particularly at trabecular-rich and mixed skeletal sites. In contrast, no significant BMD improvement was observed at the distal radius, a site rich in cortical bone. The limited recovery at the distal radius likely reflects the lower remodeling capacity and more stable nature of cortical bone compared with the dynamic remodeling of trabecular bone. However, further studies with larger sample sizes are needed to confirm these findings.

Abstract citation ID: lvag096.310

P112 - ECE_3242 - Specific cord serum microRNAs and sclerostin are associated with bone mineral density (BMD) assessed by REMS, in infants up to the first year of life: results from the REMS-bone study

Anna-Mariia Shulhai[1], Virginia Beretta[1], Letteria Anna Morabito[2], Domenico Corica[2], Giorgia Pepe[2], Federica Grassi[1], Tommaso Aversa[2], Francesca Bossi[1], Andrea Dall'asta[1], Malgorzata Wasniewska[2], Serafina Perrone[1] and Maria Street[1]

[1]Pediatric Clinic, Medicine and Surgery, University of Parma, Parma, Italy; [2]University of Messina, Messina, Italy

Background: The REMS-bone study-clinical trial(NCT06750523) aimed to evaluate bone status from intrauterine life and to investigate factors that may affect BMD in infancy. MicroRNAs(miRNAs) are key post-transcriptional regulators involved in bone formation, remodeling and mineralization. To date, there is no data on cord serum miRNAs and BMD. The aim of this study was to measure specific miRNA, known to be involved with bone metabolism, in cord serum and assess any possible relationships among these, bone metabolism markers and BMD in infants during the first year of life.

Methods: This was a prospective longitudinal cohort study including 88 full-term healthy AGA infants. Hsa-miR-199a-5p, hsa-miR-335-5p,hsa-miR-494-3p,hsa-miR-369-3p, hsa-miR-379-5p,hsa-miR-503-5p,hsa-miR-140-5p,hsa-let-7a-5p, and hsa-let-7c-5p were assayed in cord serum. Expression was established using qRT-PCR, normalized by hsa-miR-16-5p and analyzed using the $2-\Delta\Delta Ct$ method. Bone-related proteins,including osteocalcin, collagen type I(CrossLaps), sclerostin(SOST), Dickkopf-1(DKK-1), irisin, and HMGB1, were assayed by ELISA methods. BMD was assessed by Radiofrequency Echographic Multi Spectrometry(REMS), a non-invasive, radiation-free technology for bone quality assessment. This method was validated in newborns and infants alongside this study. BMD z-scores were calculated at 48 hours after birth, at 1,3,6 and 12 months of life. Associations between miRNA expression levels, markers of bone metabolism and BMD z-scores across time points were evaluated by correlation and multivariable linear regression analyses.

Results: miR-199a-5p, miR-335-5p, miR-494-3p, miR-369-3p, miR-379-5p, miR-503-5p and miR-140-5p were expressed in cord serum. Cord serum DKK-1 was 3.71 ± 1.63 ng/ml, CrossLaps $0.86 + 0.22$ ng/ml, SOST 222.05 ± 108.83pg/ml, osteocalcin 21.42 ± 4.71ng/ml, irisin 7.270 ± 7.30ug/ml and HMGB1 14.037 ± 18.32ng/ml. No differences were found between sexes. MiR-199a-5p and miR-369-3p were associated with irisin levels(r:−0.320, *P*:.044 and r:−0.387, *P*:.013, respectively) and might be irisin suppressors. MiR- 503-5p was associated with DKK-1 (r:−0.363, *P*:.013), suggesting a potentially protective role for bone health. MiR-140-5p was associated with BMD z-score at 1 month(r:0.333, *P*:.039) and at 12 months(r:0.552, *P*:.002), suggesting a potential role in later BMD. Pathway enrichment analysis showed that miR-140-5p was involved in TGF-beta,Jak-STAT,Wnt and mTOR signaling pathways and osteoclast differentiation. Among proteins, only sclerostin showed a negative association with BMD z-score at 6 months(r:-0.391, *P*:.030). This association was further supported by a multivariable regression model, which showed miR-140-5p and sclerostin as significant predictors of BMD z-scores at 12 months(F:5.536, *P*:.006).

Conclusions: Cord serum miRNAs were associated with bone metabolism markers and BMD during infancy. In particular, miR-140-5p was associated with BMD at 1 year of life. These findings support the hypothesis that miRNAs may act as mediators in the prenatal programming of postnatal bone development.

Abstract citation ID: lvag096.311

P113 - ECE_2153 - Severe PTH-independent hypercalcemia in secondary adrenal insufficiency during critical illness

Aakansha Sinha[1], Zaiem Zarkasi[1] and Aye Aye Thant[1,2]

[1]Diabetes and endocrinology, Wythenshawe hospital, Manchester, United Kingdom; [2]Diabetes and Endocrinology, Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, United Kingdom

Introduction: Hypercalcemia in critically ill patients is most often attributed to immobilization or malignancy, but less common endocrinological causes may be overlooked. Adrenal insufficiency (AI) is a recognized cause of parathyroid hormone (PTH)-independent hypercalcemia, reported in approximately 5%-6% of patients with primary AI, and less frequently in secondary AI, where severe hypercalcemia is rarely described. Azole antifungals, including fluconazole, can inhibit adrenal steroidogenic enzymes and precipitate adrenal insufficiency in susceptible individuals. We report a critically ill burn patient with severe refractory hypercalcemia, in whom recognition of relative adrenal insufficiency led to rapid biochemical resolution with glucocorticoid replacement.

Case Presentation: A 40-year-old previously healthy man was admitted following a 40% total body surface area burn. His hospital course was prolonged (107 days) and complicated by

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

extracorporeal membrane oxygenation (ECMO), bilateral pneumonia, sepsis, and a subarachnoid hemorrhage. On day 58 of admission, he developed severe hypercalcemia with an adjusted calcium of 3.93 mmol/L, rising to 4.20 mmol/L (normal range 2.20-2.60 mmol/l). Despite aggressive intravenous hydration and bisphosphonate therapy. PTH was suppressed at 0.7 pmol/L, consistent with PTH-independent hypercalcemia. Renal function was mildly deranged with EGFR of 58 mL/min/1.73 m^2 and creatinine of 132 µmol/L. Despite severe physiological stress, a morning cortisol level was inappropriately low at 242 nmol/L, suggesting relative AI. Intravenous hydrocortisone was commenced, resulting in rapid normalization of serum calcium within 48 hours to 2.32 mmol/l. Further evaluation revealed suppressed ACTH (<4 pg/mL), raising concern for secondary AI. Although prior subarachnoid hemorrhage suggested possible pituitary injury, pituitary MRI was unremarkable. CT TAP showed bilateral extensive consolidation but no malignancy. A temporal association was noted with concurrent fluconazole therapy for Candida parapsilosis, inhibit the steroidogenesis as a contributing factor. Hydrocortisone was subsequently transitioned to oral maintenance therapy. The patient will undergo outpatient endocrine follow-up for education, dynamic testing with a short Synacthen test, and anterior pituitary hormone assessment.

Conclusions: This case highlights severe hypercalcemia as an important metabolic red flag for adrenal insufficiency. In critically ill patients, particularly those with major burns or on ECMO, a "normal" or mid-range cortisol level may represent an inadequate stress response. Severe-refractory PTH-independent hypercalcemia should prompt assessment of the hypothalamic–pituitary–adrenal axis. Clinicians should remain vigilant for secondary AI in patients with intracranial pathology or exposure to azole antifungals, as early recognition and glucocorticoid replacement can be rapidly life-saving.

Abstract citation ID: lvag096.312

P114 - ECE_2811 - Impact of conventional treatment on chronic complications among subjects with hypoparathyroidism

Roman Králik[1], Martin Kuzma[1], Juraj Payer[1], Jana Lešková[2], Peter Vanuga[2] and Martin Straka[2]
[1]*5th Department of Internal Medicine, University hospital Bratislava, Bratislava, Slovakia;* [2]*Endocrinology, National endocrinology and diabetology department, n.o, Ľubochňa, Slovakia*

Background: Chronic hypoparathyroidism (hypoPT) is a rare disease associated to long-term disturbances in calcium-bone metabolism, renal burden and decreased quality of life. These complications arise from the disease itself and from its conventional treatment.

Aim of the Study: To assess the burden of chronic complications, mainly bone changes, aortic and renal calcifications, sarcopenia and quality of life among HypoPT patients on conventional treatment (vitamin D analogues and calcium supplementation).

Methods: A case-control study of hypoPT patients ($n = 38$, mean age 52.6yrs, females $n = 32$, males n6, mean hypoPT duration 168 months) regardless of ethiology (postsurgical $n = 29$, non-surgical $n = 9$) exclusively on conventional treatment with alfacalcidol and calcium compared to healthy controls across two tertiary centres in Slovakia. Measurement of serum calcium-phosphate metabolism, urea, creatinine, 25-hydroxyvitamin D, glomerular filtration rate (GFR), pro collagen type 1N peptide (P1NP), C-terminal telopeptide of type 1 collagen (CTX), 24-hour urine calcium and phosphate in both groups was performed. Chronic complications screening: renal ultrasound, aortic calcification screening on abdominal X ray, areal bone mineral density (aBMD at lumbar spine a proximal femur), trabecular bone score (TBS), 3Ddensitometry (3D-DXA), SF-36 questionnaire (QoL) and muscular ultrasound (for sarcopenia).

Results: HypoPT patients showed lower calcium, parathormone, CTX levels ($P < .001$) and greater phosphate levels ($P < .001$),aBMD measurements (all sites $P < .05$), cortical surface BMD, trabecular vBMD (total and neck), and cortical neck thickness than controls (all $P < .05$). Significantly lower physical health and emotional health SF-36 scores in the hypoPT group were observed. No association between QoL and disease duration was observed. A significant negative association of PTH levels with all aBMD measures ($P < .05$), cortical thickness and cortical surface BMD ($P = .008$) was observed. No differences in TBS, aortic calcifications, nephrolithiasis or sarcopenia measures were found.

Conclusions: Chronic hypoPT patients on conventional therapy (alfacalcidol and calcium) showed typical biochemical features of hypoparathyroidism—hypocalcemia, hyperphosphatemia, suppressed bone turnover. Compared with controls, hypoPT patients had higher aBMD at all sites and increased 3D-DXA metrics (higher trabecular and cortical vBMD and greater cortical thickness), changes that inversely correlated with PTH levels. There were no differences in TBS, aortic calcifications, nephrolithiasis or sarcopenia. QoL was impaired, especially physical and emotional domains – with greater physical role limitation linked to higher daily calcium dose, disease duration showed no association. Overall, conventional therapy increases bone density/structure measures but does not mitigate the clinical and perceived burden, indicating it cannot replicate PTH's physiological effects on bone and well-being.

Abstract citation ID: lvag096.313

P116 - ECE_1381 - Simulating hypoparathyroidism: a web-based tool for interactive and personalized therapeutic decision-making

Marta Gallach Martínez[1,2], Laura Rambla Aguilar[3], Isabel Huguet[3], Marina Jara Vidal[1], Luyi Zeng[3], César Gonzalvo Díaz[1], Inmaculada Moreno-Ruiz[3], Cristina Lamas[1], Cristina Sevillano-Collantes[3] and José Joaquín Alfaro Martínez[1]
[1]*Complejo Hospitalario Universitario de Albacete, Albacete, Spain;* [2]*Endocrinología y Nutrición, Complejo Hospitalario Universitario de Albacete, Albacete, Spain;* [3]*Hospital Universitario Infanta Leonor, Madrid, Spain*

Introduction: Hypoparathyroidism is a rare endocrine disorder characterized by parathyroid hormone (PTH) deficiency, leading to hypocalcemia and hyperphosphatemia. The most common etiology is postsurgical iatrogenesis. As no standardized treatment algorithms exist, its management requires individualized

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

therapeutic adjustments and it largely depends on the patient's biochemical response and clinical expertise. Due to the low prevalence of this condition, opportunities for systematic clinical exposure and experience acquisition are limited. To address this challenge, an online simulator has been developed to recreate clinical scenarios and predict biochemical responses to therapeutic modifications.

Methods and Materials: A mathematical model was developed using R and implemented as a web-based application through the Shiny framework, derived from expert knowledge in calcium-phosphate metabolism. Expected serum calcium responses to therapeutic modifications were estimated across predefined hypoparathyroidism scenarios and used to model calcium changes based on baseline levels and dose adjustments. Urinary calcium excretion was modeled as dependent on serum calcium levels, treatment regimen, and individual patient-specific factors. Each simulated patient was assigned a minimum urinary calcium excretion value corresponding to a serum calcium level of 7,5 mg/dL, from which calciuria increased proportionally with rising serum calcium. Symptoms, clinical signs, and electrocardiographic abnormalities were incorporated when hypo or hypercalcemia occurred. To enhance realism, a random variability component was incorporate, allowing results to fluctuate within ±5%. The simulator is available at www.morpho.org.es/SimuladorHipopara.

Results: The simulator includes 42 simulated patient cases with heterogeneous clinical characteristics. Serum calcium evolution depends on baseline calcium levels and the therapeutic regimen applied. Users can modify doses of calcium carbonate, calcitriol and thiazide diuretics. Following each therapeutic adjustment, updated serum calcium levels, urinary calcium excretion, and clinically coherent data reflecting a subsequent follow-up visit are generated. The simulator allows iterative decision-making, with the objective of maintaining biochemical and clinical parameters within appropriate target ranges while minimizing adverse outcomes.

Conclusions: This web-based simulator represents a valuable educational tool that facilitates structured training in the management of hypoparathyroidism. By allowing the safe exploration of multiple clinical scenarios and therapeutic strategies, it facilitates the understanding of the dynamic relationship between treatment adjustments and biochemical outcomes. The simulator promotes active learning and clinical reasoning in a controlled environment, potentially enhancing confidence and competence. This digital tool may complement traditional educational approaches and contribute to improving consistency and quality in clinical practice.

Abstract citation ID: lvag096.314

P118 - ECE_3489 - Cinacalcet use in primary hyperparathyroidism – a retrospective look at patient outcomes in a london hospital

Bara Taufik, Suhrab Sayfi and Ian Seetho
Department of Diabetes & Endocrinology, Northwick Park Hospital, London, United Kingdom

Introduction: Cinacalcet, a calcimimetic first approved for use in 2004, has become a mainstay of treatment in those awaiting or unable to undergo surgery for primary hyperparathyroidism. In this retrospective study, we aimed to map clinical outcomes in patients who had been prescribed cinacalcet for a suspected or confirmed diagnosis of primary hyperparathyroidism, between 1st October 2022 and 30th September 2024, and to compare our practice with NICE guideline *NG132*, published in 2019.

Methodology: All instances where cinacalcet was dispensed from a pharmacy within the trust were logged – biochemical, demographic and clinical data were then gathered. Any patients with chronic or end-stage renal disease were excluded.

Results: Eighty-four patients were identified—fifty-five female (65%) and twenty-nine male—with ages ranging from twenty-five to ninety (mean age sixty-seven). 37% ($n = 31$) were referred for parathyroidectomy (mean age fifty); 16% ($n = 14$) went on to have surgery (mean age 56). Two patients had recurrence of hypercalcaemia post-operatively, and were subsequently restarted on cinacalcet; the remainder were cured. Seventy-one of the eighty-four patients were prescribed cinacalcet after *NG132* was published—of these, 49% ($n = 35$) were prescribed cinacalcet in adherence with the guidelines; in those where cinacalcet was prescribed outwith the guidelines, all but one was prescribed cinacalcet while awaiting surgery.

Conclusions: Cinacalcet was prescribed in adherence with NICE guideline *NG132* in just under half of cases; the overwhelming majority of prescriptions outwith the guidelines were for use as bridging therapy while awaiting parathyroid surgery – this is consistent with evidence elsewhere within the literature, and should be a key consideration to take into account for future guidelines, given the well-documented use of cinacalcet peri-operatively. Surgical outcomes were very favourable, with 85% of patients cured following surgery.

Abstract citation ID: lvag096.315

P120 - ECE_1946 - Bone and dental complications in adult XLH patients—a single-centre cohort cross-sectional pilot study

Marko Stojanovic[1], Ana Djinic Krasavcevic[2], Iva Milinkovic[2], Jelena Bajic[1], Bojana Caric[3], Valentina Stankovic[3], Mirjana Doknic[1], Sandra Pekic Djurdjevic[1], Zvezdana Jemuovic[1], Ivana Cekic[1], Ivan Jevtic[1], Boris Kurcubic[1] and Marina Nikolic Djurovic[1]
[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Center of Serbia, Belgrade, Serbia; [2]Department of Periodontology and Oral Medicine, School of Dental Medicine, University of Belgrade, Belgrade, Serbia; [3]Department of Endocrinology-, Banja Luka, Bosnia—Herzegovina., University Clinical Center of Republika Srpska- Banja Luka- Faculty of Medicine-University of Banja Luka, Banja Luka, Bosnia and Herzegovina

Introduction: X-linked hypophosphatemia (XLH) is a rare genetic disease of autonomous FGF-23 over-secretion, hallmarked by hypophosphatemia and osteomalacia with progressive skeletal deformities and dental complications.

Aim: Assessing bone and dental complications in a cohort of adult XLH patients on conventional treatment through cross-sectional pilot study

Patients and Methods: We analysed 11 adult XLH patients (9 females), 37.3 ± 4.0 years old, treated with active vitamin D and phosphate supplementation. History of fragility fractures was assessed. BMD was analysed by DXA (Hologic Discovery QDR) at L1-L4 spine (LS), femoral neck (FN) and mid-distal radius (MDR)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and expressed as Z-score (Zsc). Serum osteocalcin (OC), and beta-cross-laps (BCL) were analysed as bone turnover markers, expressed as index denominated by the upper limit of normal age, gender and menopausal status reference values (ULN). Seven patients underwent comprehensive dental-periodontal examination including radiographic analysis.

Results: 6 patients (54.5%) had a history of fragility fractures (femur in 5, radius and tibia in 1 each). Average LS Zsc was +1.2 ± 0.4 (BMD 1.156 ± 0.055); average FN Zsc: −0.7 ± 0.4 (BMD 0.755 ± 0.051); average MDR Zsc: −1.3 ± 0.6 (BMD 0.617 ± 0.038). Serum OC-ULN was 0.68 ± 0.16 and BCL-ULN 1.63 ± 1.38). Majority of patients (4/7) lost 4-17 teeth due to periodontitis and infections. One was fully edentulous. All of dentate patients had severe periodontal inflammation, with bleeding on probing (BOP) of 57-85% and plaque index (PI) of 80%-92%. Advanced periodontal disease was established with periodontal probing depth (PPD) of 2.8-3.4 mm, and clinical attachment level (CAL) of 1.8-4.0 mm. Radiographic analyses revealed 1-14 endodontically treated teeth in all patients. One patient, otherwise asymptomatic, was diagnosed with apical periodontitis in two intact teeth. Enlarged pulp chambers were observed in five dentate patients, affecting 3-20 teeth. Only 2 patients (19 and 21 years old and timely diagnosed with XLH in early childhood) had no extracted teeth.

Conclusions: Prior fragility fractures were common in our pilot cohort of XLH patients on conventional treatment (54.5%) with femur as most affected site. BMD was decreased at mid-distal radius (Zsc: −1.3 ± 0.6). Bone formation and bone resorption were unbalanced (2.71 ± 0.79-fold) in favour of resorption. Advanced periodontal disease, including asymptomatic apical periodontitis in intact teeth was prevalent, with 4-17 teeth lost per patient (one being edentulous at the age of 45) due to periodontitis and infections, except in patients with timely diagnosis and follow-up from childhood. Comprehensive and multidisciplinary follow-up of bone and dental complications is mandated in XLH patients.

Abstract citation ID: lvag096.316

P121 - ECE_3185 - Knowledge, attitudes, and practices regarding medication-related osteonecrosis of the jaw among oral surgery specialists and endocrinologists: a cross-sectional study

Rutie Mamlok Sherf[1], Dror Cantrell[2], Amir Laviv[3], Nirit Tagger-Green[4] and Michael Joachim[5]
[1]*Shamir medical center, Endocrine and Diabetes Institute, Zerifin, Israel;* [2]*Shamir medical center, Internal Medicine C, Zerifin, Israel;* [3]*Department of Oral and Maxillofacial Surgery, Tel Aviv University, Tel Aviv, Israel;* [4]*Department of Periodontology and Oral Implantology, Tel Aviv University, Tel Aviv, Israel;* [5]*Shamir medical center, Oral and Maxillofacial Surgery Unit, Zerifin, Israel*

Background: Medication-related osteonecrosis of the jaw (MRONJ) is a rare but serious complication associated with antiresorptive and antiangiogenic agents used in osteoporosis management. Although the incidence among osteoporosis patients treated with oral bisphosphonates is very low (0.001%-0.01%), risk increases with prolonged therapy, particularly beyond four years, and following invasive dental procedures. However, discrepancies between international and national guidelines regardinng MRONJ have led to inconsistency in clinical practice and treatment approaches. Despite growing awareness, studies reveal significant knowledge and practice gaps among healthcare professionals globally.

Objective: This study aims to evaluate MRONJ-related knowledge, attitudes, and preventive practices among endocrinologists and oral surgery specialists, addressing the impact of divergent guidelines on clinical decision-making and interdisciplinary collaboration.

Methods: A cross-sectional survey (January-March 2025) among oral and maxillofacial surgeons, periodontists, and endocrinologists evaluated MRONJ knowledge, risk factor awareness, clinical management, and interprofessional communication, with data analyzed using descriptive statistics and chi-square tests ($P < .05$).

Results: 112 specialists completed the survey (52 endocrinologists, 60 oral surgery specialists; Both groups demonstrated excellent medication knowledge regarding bisphosphonates and denosumab, with correct response rates exceeding 90% and 94.6%, respectively, but exhibited low levels of romosuzumab recognition (8.9%). Oral surgery specialists reported significantly higher MRONJ case experience (86.7% vs 48.1%, $P < .001$) and self-rated knowledge scores (3.60 ± 0.93 vs 3.12 ± 0.89, $P = .005$). Oral surgery specialists showed higher recognition of MRONJ risk factors: specifically smoking (46.7% vs 21.2%, $P = .004$) and prior MRONJ (25.0% vs 3.8%, $P = .002$). Endocrinologists utilized bone markers more frequently (34.6% vs 13.3%, $P = .007$). Management approaches varied considerably, particularly regarding drug holidays and timing procedures between doses, with case-dependent decisions most common for bisphosphonates (35.9%) and timing-based approaches preferred for denosumab (46.4%). Oral surgery specialists reported a slightly higher frequancy of communication between specialists as compared to endocrinologists (2.9 ± 1.4 vs 2.5 ± 1.3, $P = .154$).

Conclusions: There are significant gaps in knowledge and therapeutic approaches between endocrinologists and oral surgery specialists regarding MRONJ. Enhanced interprofessional education and standardized protocols could optimize MRONJ prevention and management.

Abstract citation ID: lvag096.317

P123 - ECE_2918 - Epicardial adipose tissue-derived extracellular vesicles in heart failure impair β-cell function and survival

Federica Bistolfi[1], Cristina Grange[1], Francesca Pedrolli[1], Iacopo Gesmundo[1], Guglielmo Gallone[1], Antonino Loforte[2], Gaetano Maria De Ferrari[1], Mauro Rinaldi[2], Stefania Bruno[1], Maria Felice Brizzi[1], Giovanni Camussi[1] and Riccarda Granata[3]
[1]*Department of Medical Sciences, University of Turin, Turin, Italy;* [2]*Department of Surgical Sciences, University of Turin, Turin, Italy;* [3]*Department of Molecular Biotechnology and Health Sciences, University of Turin, Turin, Italy*

Epicardial adipose tissue (EAT) is a metabolically active fat depot adjacent to the myocardium that undergoes pathological remodeling in cardiovascular disease, adopting a pro-inflammatory and catabolic phenotype that contributes to cardiac dysfunction. One mechanism by which EAT may exert systemic effects is through the release of extracellular vesicles (EVs) that reflect its molecular

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and metabolic state and deliver bioactive signals to distant target organs. Pancreatic β-cells are highly vulnerable to inflammatory and metabolic stress, yet the effects of EAT-derived EVs (EPI-EVs) on β-cell function and survival in heart failure (HF) remain largely unexplored. Thus, we aimed to investigate the role of EPI-EVs on pancreatic β-cell function and survival in HF. EVs were isolated from EAT samples obtained from patients undergoing cardiac surgery and classified into four groups: control without HF, HF with preserved ejection fraction (HFpEF), HF with reduced ejection fraction (HFrEF), and advanced HFrEF. EPI-EVs, isolated by sequential ultracentrifugation, were characterized by nanosight, transmission electron microscopy, Western blotting and sensitive flow cytometry, confirming the presence of specific EV markers (CD9, CD63 and CD81), as well as adipose tissue specific genes, adiponectin and FABP4. To evaluate functional effects, rat insulinoma INS-1E β-cells were exposed to EPI-EVs (15×10^3/cell) for 24 hours. Cell viability was assessed by MTT assay, and gene expression by real-time PCR. EPI-EVs induced a progressive reduction in β-cell viability that was associated with the severity of cardiac disease. At the molecular level, EPI-EVs elicited a stress and inflammatory response, as indicated by increased mRNA expression of the endoplasmic reticulum stress marker *Chop* and the inflammatory cytokines *Il1b* and *Ifng*. In addition, EPI-EVs consistently downregulated the key β-cell transcription factor *Pdx1* across all HF groups, indicative of functional impairment and early loss of mature β-cell identity. These findings suggest a novel mechanism of heart-pancreas communication mediated by EPI-EVs, whereby cardiac disease associated alterations in EAT may contribute to β-cell stress and metabolic dysregulation in HF.

Abstract citation ID: lvag096.318

P127 - ECE_1305 - Dementia risk in type 1 and type 2 diabetes: a nationwide population-based comparison with the general population

Ji Eun Jun[1], Seohyun Kim[2], In-Kyung Jeong[1] and Jae Hyeon Kim[2]
[1]*Kyung Hee University Hospital at Gangdong, Seoul, South Korea;* [2]*Samsung Medical Center, Seoul, South Korea*

Objective: We aimed to compare the risk of all-cause dementia, Alzheimer's disease (AD), and vascular dementia (VaD) among individuals with diabetes and non-diabetic participants using a nationwide Korean cohort.

Methods: This population-based retrospective cohort study used data from the Korean National Health Insurance Service (2013-2024). A total of 1 322 651 adults aged ≥40 years without prior dementia were included. Participants were classified as non-diabetic, type 2 diabetes (T2DM) with oral hypoglycemic agents (OHA), T2DM with insulin, or type 1 diabetes (T1DM). Incident dementia was identified using ICD-10 codes and antidementia prescriptions. Multivariable Cox proportional hazards models adjusted for demographic, lifestyle, and clinical factors estimated adjusted hazard ratios (aHRs) for dementia.

Results: During follow-up, 4.3, 12.7, 17.9, and 21.1 dementia cases per 1000 person-years occurred in non-diabetic, T2DM with OHA, T2DM with insulin, and T1DM groups, respectively. Compared with non-diabetic participants, adjusted HRs for all-cause dementia were 1.29 (95% CI 1.26-1.32) for T2DM with OHA, 2.14 (2.00-2.28) for T2DM with insulin, and 2.35 (2.12-2.59) for T1DM. Similar gradients were observed for AD and VaD. Dementia risk was highest in individuals with T1DM and insulin-treated T2DM, with no significant difference between the two groups.

Conclusions: Patients with diabetes had a higher risk of dementia compared with non-diabetic individuals. Among diabetic subgroups, both T1DM and insulin-treated T2DM were associated with markedly elevated dementia risks. Proactive cognitive screening and stabilization of glycemic variability—potentially aided by continuous glucose monitoring—may help mitigate dementia risk in these high-risk groups.

Abstract citation ID: lvag096.319

P128 - ECE_3379 - Risk of trauma-related hospitalization in young adults with type 1 diabetes: a nationwide historical cohort study

Neriya Levran[1,2], Adi Vinograd[3], Sami Gendler[4], Irina Radomislensky[5], Noah Levek[1,6], Dana Weiner[7], Arnon Afek[8], Gilad Twig[9,10] and Orit Pinhas-Hamiel[10,11]
[1]*Pediatric Endocrine and Diabetes Center, Edmond and Lily Safra Children's Hospital, Ramt Gan, Israel;* [2]*Sheba Medical Center, Nutrition Unit, Ramt Gan, Israel;* [3]*Israel center of disease control, Ministry of Health, Ramt Gan, Israel;* [4]*Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel;* [5]*Tel Hashomer, Israel Defense Forces Medical Corps, Ramat Gan, Israel;* [6]*Maccabi Healthcare, Juvenile Diabetes Center, Raanana, Israel;* [7]*Sheba Medical Center, Nutrition Unit, Ramat Gan, Israel;* [8]*Sheba Medical Center, Ramt Gan, Israel;* [9]*Sheba Medical Center, Tel Hashomer, Division of Endocrinology, Diabetes and Metabolism, Ramt Gan, Israel;* [10]*Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel;* [11]*Pediatric Endocrine and Diabetes Center, Edmond and Lily Safra Children's Hospital, Ramat Gan, Israel*

Background: Type 1 diabetes is a lifelong condition characterized by glycemic instability and progressive microvascular complications that may substantially increase the risk of physical injury. Episodes of hypoglycemia and diabetes-related complications, including neuropathy and retinopathy, can impair cognition, sensation, balance, and vision, potentially increasing vulnerability to trauma. Prior limited data suggest an elevated risk of trauma and hospitalization among adults with type 1 diabetes; however, nationwide evidence assessing vulnerability to trauma among youth and young adults remains limited.

Objective: To quantify the risk of trauma-related hospitalization and severe injury in young adults diagnosed with type 1 diabetes during adolescence compared to a healthy control group.

Methods: This nationwide historical cohort study cross-referenced data from the Military Health Examinations Database (MHED) and the National Trauma Registry (INTR). The study population included individuals assessed before military recruitment between 2008 and 2020 at ages 16.5-18 years. The exposure group consisted of individuals with a type 1 diabetes diagnosis code. Analysis was conducted across two cohorts: the total population and a "Medically non-combat eligible" cohort to minimize bias from military service risks. Primary outcomes included hospitalization for injury and injury severity (ISS).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: In the total population analysis ($n = 868\,982$), 2898 individuals had type 1 diabetes. The rate of trauma-related hospitalization was 1.28% ($n = 37$) in the type 1 diabetes group compared to 1.91% ($n = 16\,561$) in the non-diabetic population ($P = .013$). When restricting the analysis to the medically non-combat eligible cohort ($n = 255\,461$) to ensure comparable risk exposure, the type 1 diabetes group showed no statistically significant difference in injury rates compared to the non-diabetic control group ($n = 3690$, 1.46%; $P = .411$). Gender-stratified analyses within the non-combat cohort further confirmed no significant risk elevation for either females (0.84%; $P = .483$) or males (1.58%; $P = .384$).

Conclusions: Individuals with type 1 diabetes were not at increased risk of serious injury related hospitalization. These findings suggest that adolescents and young adults with type 1 diabetes may effectively mitigate trauma risk, potentially through heightened self-awareness, education, and preventive behaviors.

Abstract citation ID: lvag096.320

P129 - ECE_2172 - SGLT2 inhibitors and cardiovascular effects in kidney transplant recipients with diabetes mellitus

Idit Dotan[1,2], Amir Polansky[1,2], Idan Bergman[2,3], Gida Ayada[2,3], Tanya Babich[2,4], Amit Akirov[1,2], Tali Steinmetz[2,5] and Talia Diker Cohen[1,2]

[1]Rabin Medical Center, Beilinson Campus, Institute of Endocrinology, Diabetes and Metabolism, Petah Tikva, Israel; [2]Gray Faculty of Medicine and Health, Tel Aviv University, Tel Aviv, Israel; [3]Rabin Medical Center, Beilinson Hospital, Internal Medicine C, Petah Tikva, Israel; [4]Hod Hasharon, Israel; [5]Rabin Medical Center, Beilinson Campus, Institute of Nephrology, Petah Tikva, Israel

Objectives: SGLT2 inhibitors (SGLT2i) reduce major adverse cardiovascular events and mortality in patients with type 2 diabetes mellitus (T2DM), but kidney transplant recipients (KTRs), a high-risk group, were excluded from major trials. We aimed to evaluate the cardiovascular effects of SGLT2i in KTRs with diabetes.

Methods: In this retrospective matched-cohort study at a large transplant center, KTRs with diabetes treated with SGLT2i were compared to matched controls receiving other antihyperglycemic agents. Major outcomes were: (1) a composite of acute coronary syndrome (ACS), stroke/transient ischemic attack (TIA), or all-cause mortality; and (2) a composite of heart failure hospitalizations or all-cause mortality.

Results: A total of 480 patients (240 per group; 20% women; median age 63-64 years) were followed for up to three years. The incidence of ACS, stroke/TIA, or death was 7.9 vs 13.6 events per 100 person-years in the SGLT2i and control groups, respectively (adjusted HR 0.64, 95% CI 0.42-0.97, $P = .039$). Heart failure hospitalizations or death occurred less frequently in SGLT2i users (5.7 vs 11.6 events per 100 person-years), though the difference was not statistically significant after adjustment (HR 0.82, 95% CI 0.50-1.32, $P = .410$).

Conclusions: SGLT2i use was associated with a lower risk of major cardiovascular events in KTRs with diabetes, consistent with benefits observed in non-transplant populations. Given the elevated cardiovascular risk in KTRs, these findings support further investigation of SGLT2i therapy in this population.

Abstract citation ID: lvag096.321

P130 - ECE_1089 - Euglycemic diabetic ketoacidosis revealing atezolizumab-induced type 1 diabetes in a patient with type 2 diabetes

Oğuzhan Kara[1], Seda Nur Yalçın[1], Nisa Babacanlar[1], Mustafa Can Senoymak[1], Mina Karakullukcu[2] and Arif Yonem[1]

[1]Endocrinology Clinic, Department of Endocrinology and Metabolism, Sultan 2. Abdulhamid Han Training and Research Hospital, Istanbul, Türkiye; [2]Department of Medical Oncology, Sultan 2. Abdulhamid Han Training and Research Hospital, Istanbul, Türkiye

Introduction: Although diabetic ketoacidosis (DKA) is typically associated with type 1 diabetes mellitus (T1DM), certain antidiabetic agents have been linked to atypical forms of DKA. In particular, SGLT2 inhibitors promote urinary glucose excretion and may precipitate ketosis despite near normal blood glucose levels, a condition known as euglycemic DKA. Immune checkpoint inhibitors (ICIs) enhance antitumor immune responses while potentially triggering autoimmune reactions against pancreatic β-cells. Consequently, new-onset type 1 diabetes may develop in patients previously diagnosed with type 2 diabetes mellitus (T2DM). In this case, a patient with T2DM receiving an SGLT2 inhibitor and treated with atezolizumab for small cell lung cancer (SCLC) presented with euglycemic DKA, which was subsequently attributed to atezolizumab-induced type 1 diabetes.

Case Presentation: A 52-year-old woman with a 4-year history of T2DM and a diagnosis of SCLC 3 months prior presented to the emergency department with polydipsia and increased appetite. On physical examination mildly decreased skin turgor was noted, while other systemic examinations revealed no significant abnormalities. Laboratory studies showed arterial blood gas pH: 7.06, HCO_3^-: 8 mmol/L, urine ketone 3+, and urine glucose 3+. Blood glucose was 196 mg/dL. These findings were consistent with euglycemic DKA. The patient had etoposide–carboplatin–atezolizumab chemotherapy initiated approximately two months ago for extensive stage SCLC, with a pre-treatment HbA1c level of 7.0%. During the treatment course, the patient was using metformin and empagliflozin, and the third dose of atezolizumab had been administered 10 days prior. The patient was managed with intravenous isotonic fluids, 5% dextrose, insulin infusion, and potassium replacement. Oral antidiabetic medications were discontinued. The patient resolved from DKA by hospital day 2, continuing with basal-bolus insulin therapy thereafter. Follow-up evaluation for ICI-associated T1DM revealed negative anti-insulin and islet cell antibodies, but anti-GAD antibody was positive at 182 IU/mL and C-peptide level was 0.22 ng/mL. The patient's HbA1c was 7.72%. Based on these findings a diagnosis of atezolizumab-induced new-onset T1DM was made. Basal-bolus insulin therapy was continued and the patient was discharged after achieving clinical stabilization.

Conclusions: This case highlights the potential for euglycemic DKA in patients with preexisting T2DM who are treated with SGLT2 inhibitors and concurrently receive ICIs. Clinicians should maintain a high index of suspicion for ICI-induced new-onset T1DM, even in patients previously diagnosed with T2DM, particularly when presenting with atypical DKA. Early recognition and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

prompt initiation of insulin therapy are crucial to prevent morbidity and ensure safe continuation of oncologic treatment.

Abstract citation ID: lvag096.322

P131 - ECE_1459 - Proportion of diabetes of the exocrine Pancreas among adult patients classified as type 2 diabetes mellitus and evaluation of gut-pancreatic hormones for its detection

Ankitesh Kumar[1,2], Sv Madhu[1], Nishant Raizada[1] and Shuchi Bhatt[3]
[1]Endocrinology, University College of Medical Sciences, New Delhi, India; [2]Endocrinology, Sitaram Bhartia Institute of Science and Research, New Delhi, India; [3]Radiology, University College of Medical Sciences, New Delhi, India

Introduction: Diabetes of the exocrine pancreas (DEP), or type 3c diabetes mellitus, is frequently misclassified as type 2 diabetes mellitus (T2DM) with significant clinical implications. It is characterised by altered gut-pancreatic hormone responses that may help differentiate DEP from T2DM.

Methodology: This cross-sectional observational study included 310 adults with apparent T2DM attending an endocrinology clinic. Patients with type 1 diabetes mellitus (anti GAD antibody positive), major comorbidities, prior pancreatitis, prior pancreatic or upper gastrointestinal surgery, pregnancy, or incretin-based therapy were excluded. All participants underwent clinical and biochemical evaluation with fecal elastase-1 testing; CT with pancreatic protocol was performed in those with fecal elastase-1 <200 µg/g to confirm DEP according to Ewald criteria. Pancreatic polypeptide (PP) response to a mixed meal was assessed in all participants, while mixed-meal testing for peptide-YY (PYY), ghrelin, and C-peptide was performed in a predefined subgroup. Statistical analyses included non-parametric tests, receiver operating characteristic analysis, and ANCOVA for age, sex, and BMI.

Results: DEP was diagnosed in 51 of 310 participants (16.45%), with 71% being asymptomatic for clinical features of exocrine insufficiency. Compared with T2DM, DEP patients had a lower BMI, worse glycaemic control, and a higher prevalence of diabetic neuropathy, while rates of retinopathy and nephropathy were similar. PP levels at baseline and 30 mins did not differ between DEP and T2DM (AUC <0.55). Hormonal analyses in a subgroup of 80 patients (40 DEP, 40 T2DM) showed significantly lower fasting and post-mixed meal C-peptide levels in DEP, with good diagnostic accuracy (AUC 0.76 and 0.69) and high sensitivity (95% and 92%) but modest specificity (50% and 47.5%) at 0 and 30 minutes, respectively. PYY response at 30 minutes and PYY fold rise (0-30 minutes) were also reduced in DEP ($P = .003$ and $P = .015$), with an AUC 0.69 and 0.66 respectively, with specificity of 87.5% for PYY (30 minutes) and sensitivity of 82.5% for fold rise. Ghrelin responses did not differ significantly between groups and showed no discriminatory value. Differences in PYY and C-peptide parameters remained significant after adjustment for age, sex, and BMI.

Discussion and Conclusions: DEP accounted for 16.45% of adults with apparent T2DM and was frequently clinically silent. PP lacked diagnostic utility. Whereas reduced c-peptide and impaired postprandial PYY responses characterised DEP in a subgroup, while ghrelin didn't differ. A diagnostic strategy combining fecal elastase-guided imaging with selective hormonal assessment may improve recognition and classification of DEP, with important implications for clinical management.

Abstract citation ID: lvag096.323

P132 - ECE_3255 - Disulfiram attenuates high-fat diet–induced metabolic dysfunction in a rat model of metabolic syndrome

Ondřej Šeda[1], Hana Malínská[2], Irena Marková[2], Martina Hüttl[2], Blanka Chylíková[1] and Lucie Šedová[1]
[1]First Faculty of Medicine, Charles University, Institute of Biology and Medical Genetics, Prague, Czech Republic; [2]Center for Experimental Medicine, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Disulfiram (DSF) is a traditional drug used in the treatment of alcohol dependence, but recently its effects on limiting tumor proliferation, inflammation, and various aspects of metabolic syndrome have been described. The aim of this study was to analyze the effect of DSF administration in a model of metabolic syndrome, the inbred PD strain of laboratory rats.

Methods: Adult male PD rats were fed for 7 weeks a standard diet (STD, $n = 7$), high-fat diet (HFD; ssniff E15186-347, $n = 9$), or HFD supplemented with DSF (0.25 g/kg; $n = 9$), followed by comprehensive metabolic phenotyping (oral glucose tolerance test, insulin, lipid profile, leptin, Fibroblast Growth Factor 21, and hepatic triacylglycerols (TAG) and cholesterol) and transcriptome profiling of liver and visceral adipose tissue (Affymetrix GeneChip Rat Gene 2.1 ST array; multiple comparison adjustment -FDR <0.05, fold change >20%).

Results: As expected, HFD induced marked metabolic deterioration, including increased body weight and adiposity, impaired glucose tolerance, elevated plasma and hepatic TAG, hyperinsulinemia and hyperleptinemia, and reduced HDL cholesterol. Co-administration of DSF with HFD normalized body weight, plasma TAG, total cholesterol, and fasting insulin; glucose tolerance, leptinemia, and hepatic TAG were significantly improved vs HFD but remained above STD levels. Transcriptomic analyses mirrored these physiological effects: HFD caused extensive gene-expression remodeling in both tissues (liver: 895 significantly altered transcripts; visceral adipose: 411), whereas DSF largely blunted the HFD-driven transcriptional changes. Consistent with partial normalization, the disulfiram-treated group displayed substantially fewer residual differences relative to STD (liver: 220 transcripts; adipose: 108) compared with HFD alone. There was a strong counteracting pattern of DSF actions in liver including genes related to lipid/cholesterol metabolism regulators *like Dhcr7, Fads1, Pcsk9, Acacb* and others.

Conclusions: DSF significantly mitigated the adverse metabolic effects of HFD and broadly reversed the accompanying tissue transcriptomic perturbations, supporting DSF as a candidate for repurposing to counteract diet-induced metabolic dysfunction.

Abstract citation ID: lvag096.324

P133 - ECE_1408 - Rhein antagonizes glucocorticoid receptor signaling to activate SIRT1-dependent thermogenesis in brown adipose tissue and ameliorate obesity

Hannah Hui
Hong Kong, Hong Kong

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Rhein, a natural anthraquinone derivative, has emerged as a promising therapeutic agent for combating obesity, while its detailed mode of action is unknown. In this study, we unravel that Rhein acts as an antagonist of glucocorticoid receptor (GR) and thereby enhances SIRT1 protein stability followed by brown adipose tissue (BAT) activation. Rhein-treated mice were resistant to diet-induced obesity, reduced adiposity and exhibited improved glucose tolerance, insulin sensitivity. Notably, Rhein augmented BAT thermogenic activity, and thereby enhanced the whole body energy expenditure of the mice. Mechanistically, Rhein enhances SIRT1 expression which in turn boosts mitochondrial biogenesis and thermogenic function in BAT. Adipocyte-selective ablation of SIRT1 almost completely abolished Rhein's anti-obesity and thermogenic effects, confirming SIRT1 as a critical mediator. Furthermore, we identified ARGLU1, a GR co-activator, as a direct Rhein-binding protein. Rhein antagonized GR/ARGLU1 signaling, thereby relieving GR-mediated suppression of JNK activity. Activated JNK subsequently phosphorylated and stabilized SIRT1 protein, establishing a novel Rhein-ARGLU1-GR-JNK-SIRT1 regulatory axis in BAT. Importantly, Rhein effectively counteracted corticosterone-induced obesity, SIRT1downregulation and BAT whitening in vivo. Our findings reveal Rhein as a potent BAT activator that ameliorates metabolic dysfunction through modulation of GR signaling, offering new therapeutic strategies for obesity and glucocorticoid-related endocrine disorders.

Funding: This work is supported by Health and Medical Research Fund (HMRF, 21220681).

Abstract citation ID: lvag096.325

P134 - ECE_3275 - Metabolic dysfunction-associated steatotic liver disease is associated with vascular dysfunction in type 1 diabetes

Jonathan Mertens[1], Hilde Heuten[2], Eveline Dirinck[2], Sven Francque[3] and Christophe De Block[1]
[1]*Endocrinology, diabetology and metabolism, Antwerp University Hospital, Edegem, Belgium;* [2]*Cardiology, Antwerp University Hospital, Edegem, Belgium;* [3]*Gastroenterology and hepatology, Antwerp University Hospital, Edegem, Belgium*

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is linked to atherosclerotic cardiovascular disease (ASCVD). Markers of arterial stiffness & subclinical atherosclerosis (carotid-femoral pulse wave velocity [cfPWV], carotid-intima media thickness [CIMT]) and endothelial dysfunction (flow-mediated dilation [FMD], nitroglycerine-induced dilation [NID]) might aid in ASCVD risk reclassification. This study examined the association between MASLD and markers of vascular dysfunction in type 1 diabetes (T1D).

Methods: We performed cross-sectional vascular assessments in non-smoking adults with T1D without ASCVD. MASLD was determined by ultrasound-assisted transient elastography. FIB-4 was calculated as an index for fibrosis. ASCVD risk was predicted using the validated Steno Type 1 Risk Engine. Subjects were included in a 2:1 control-to-case ratio and matched for age and diabetes duration.

Results: We examined 105 subjects, 30 had MASLD. Mean age was 51.7 ± 15.7 years, mean diabetes duration was 29.9 ± 14.3 years. Fifty percent were male, mean HbA1c was 55.1 ± 9.5 mmol/mol. MASLD was associated with lower NID (15.3 ± 6.3 vs 20.1 ± 7.5%, $P = .003$). NID and cfPWV were more often impaired in people with MASLD (53.3% vs 28.4%, $P = .018$, 56.7% vs 35.1%, $P = .043$, respectively). In adjusted multivariable logistic regression, MASLD was associated with increased cfPWV (OR 8.30, 95% CI 1.25-55.2, $P = .029$), as were age, sex and mean arterial pressure. cfPWV and CIMT strongly correlated with 5-year ASCVD risk (cfPWV $\rho = 0.76$, CIMT $\rho = 0.81$, $P < .001$), as did FIB-4 ($\rho = 0.74$, $P < .001$). CIMT (0.93), cfPWV (0.88) and FIB-4 (0.88) yielded the highest AUROC to identify significant ASCVD risk.

Conclusions: cfPWV is the most robust vascular marker associated with MASLD in people with T1D. cfPWV, CIMT and FIB-4 correlated strongly to incident 5-year ASCVD risk.

Abstract citation ID: lvag096.326

P135 - ECE_1009 - Deletion of FGFR1 in hypothalamic neurons alters energy homeostasis and negates the metabolic effects of α-klotho

Hu Huang[1,2]
[1]*Kinesiology, Physiology, East Carolina University, Greenville, United States;* [2]*Kinesiology, Physiology, East Carolina Dibetes and Obesity Institute, Greenville, United States*

Background: The global obesity epidemic highlights the need for novel therapeutic targets. While central administration of α-Klotho shows promise in ameliorating metabolic dysfunction in rodent models, the underlying molecular and cellular mechanisms remain poorly defined. Given that α-Klotho signals through fibroblast growth factor receptors (FGFRs), we hypothesized that FGFR1 in specific hypothalamic neuronal populations is critical for metabolic homeostasis.

Methods: To investigate the metabolic role of FGFR1 in the arcuate nucleus of adult mice, we employed an AAV-mediated CRISPR/Cas9 system, coupled with transgenic models, to achieve cell-type-specific deletion of FGFR1 in mature glutamatergic, GABAergic, and AgRP neurons.

Results: We found that selective deletion of FGFR1 in GABAergic neurons, but not in glutamatergic neurons, induced a profound disruption of energy balance, resulting in obesity characterized by excessive weight gain and increased adiposity. Targeted deletion of FGFR1 specifically within AgRP neurons recapitulated most of these phenotypes. Furthermore, FGFR1 deletion in AgRP neurons blocked α-Klotho signaling and abolished the ability of α-Klotho to modulate AgRP activity and eliminated its therapeutic benefits on glucose and energy metabolism.

Conclusions: Our findings establish FGFR1 signaling in arcuate nucleus GABAergic and AgRP neurons as an essential component of the pathway through which α-Klotho regulates systemic energy homeostasis, identifying it as a critical molecular target for anti-obesity therapeutics.

Conflicts of interest: The authors declare no conflicts of interest.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.327

P137 - ECE_2819 - Classification of diabetes subtypes in the All New Diabetics in Scania (ANDIS) study and comparison with Swedish National Diabetes Register (NDR) diagnoses

Shobitha Vollmer[1], Alice Maguolo[2], Axel Lindström[2], Sonia García-Calzón[3], Emma Ahlqvist[2], Katarina Fagher[1] and Charlotte Ling[2]

[1]Epigenetics and Diabetes Unit, Department of Clinical Sciences Malmö, Lund University, Skane University Hospital, Malmö, Sweden; [2]Lund, Sweden; [3]University of Navarra, Pamplona, Spain

Objective: Classifying diabetes in registry-based studies is challenging. Since 2008, adults with newly diagnosed diabetes have been registered in the All New Diabetes in Scania (ANDIS) study. Our aims are: 1) classify ANDIS individuals into diabetes subtypes using baseline and follow-up clinical data; 2) compare clinical characteristics across diabetes subtypes; 3) compare ANDIS diabetes subtypes with Swedish National Register (NDR)-reported diagnoses.

Methods: Baseline clinical data for 18 985 adults with newly diagnosed diabetes were included from ANDIS, with follow-up data, including ICD-10 codes for diagnoses and mortality, medication dispensations and laboratory results, obtained from NDR, the National Board of Health and Welfare, and regional healthcare databases. Using a new method adapted to registry-based data following ADA and EASD guidelines, individuals were classified to diabetes subtypes based on available clinical data, including autoantibodies, C-peptide levels and insulin treatment. These subtypes were compared with NDR-reported diabetes diagnoses.

Results: Individuals were classified as having type 1 diabetes (T1D, $n = 630$; 3.3%), type 2 diabetes (T2D, $n = 17\,475$; 92%), LADA ($n = 689$; 3.6%), type 3c ($n = 86$; 0.5%) or unspecified diabetes ($n = 105$; 0.5%). Individuals classified as T1D differed markedly from those with T2D regards to age, BMI, comorbidities and complications. LADA showed clinical characteristics largely overlapping with T2D, whereas type 3c individuals were often older, leaner, with more comorbidities and higher HbA1c. Only 87.4% of individuals had an NDR-reported diagnosis, of which 2957 had different diagnoses in NDR compared with our classification. Chi-squared test comparing our classification with NDR showed significant difference.

Discussion: Most individuals were classified as having T2D with the remaining classified into T1D, LADA, type 3c or unspecified, consistent with expected prevalences of these subtypes in literature. Baseline characteristics compared across subtypes highlighted clinical differences in diabetes onset and complications attributable to differing aetiologies. Comparison with NDR-reported diagnoses demonstrated substantial improvement with our classification as NDR does not distinguish between T1D and LADA or include type 3c. Most mismatched diagnoses were due to individuals classified as T2D in NDR but LADA in our cohort or unknown in NDR but T2D in ours, reflecting the management of preserved insulin secretion and the impact of missing data, overlapping diagnoses or fear of misclassification in clinical settings respectively.

Conclusions: We demonstrate that systematic classification following established guidelines and adapted to registry-based data can reliably distinguish diabetes subtypes in large cohorts and reveal heterogeneity that may be overlooked in registries, improving individualised analysis and research practices in diabetes precision medicine.

Abstract citation ID: lvag096.328

P138 - ECE_2898 - Robo4: a key endothelial link between atherosclerosis and MASLD?

Christina-Maria Flessa[1], Ioannis Kyrou[2], Maria-Eleni Chondrogianni[1,3], Narges Nasiri Ansari[1], George Agrogiannis[4], Maria Lianou[1], Antonios Chatzigeorgiou[5], Harpal S. Randeva[2] and Eva Kassi[1,3]

[1]Department of Biological Chemistry, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [2]University Hospitals Coventry and Warwickshire NHS Trust, Coventry, CV2 2DX, United Kingdom; [3]Endocrine Unit, 1st Department of Propaepeudic Internal Medicine, Laiko Hospital, National and Kapodistrian University of Athens, Athens, Greece; [4]First Department of Pathology, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [5]Department of Physiology, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Introduction: Endothelial dysfunction plays a critical role in all stages of atherogenesis. Metabolic dysfunction–associated steatotic liver disease (MASLD) is closely associated to increased cardiovascular risk. Robo4 is an endothelial-specific receptor that regulates cell migration, angiogenesis, and vascular integrity and is expressed in liver sinusoidal endothelial cells, positioning it as a possible molecular link between cardiovascular disease (CVD) and hepatic disease.

Aim: To investigate the role of Robo4 expression in the atherosclerosis process and in MASLD development.

Materials and Methods: Robo4(-/-) mice were crossed with ApoE(-/-) mice, an established model of atherosclerosis that develops MASLD following high-fat diet (HFD) feeding. Robo4(-/-), ApoE(-/-), and ApoE(-/-)/Robo4(-/-) mice were fed HFD for 15 weeks starting from their 6th week of age to accelerate atherosclerotic plaque formation and liver disease development. After sacrifice, aortas and livers were harvested for histomorphometric analysis of aortic root and liver sections. RNA was isolated from aortic and hepatic tissues and qPCR was performed to assess the expression of genes involved in inflammation, endothelial activation, extracellular matrix remodeling, lipid uptake and synthesis, and MASLD susceptibility, including MMP-2, MMP-9, TIMP-1, TIMP-2, IL-6, MCP-1, ICAM-1, VCAM-1, PNPLA3, TM6SF2 in liver and aorta, and CD36, ApoB, IL-1α, IL-1β, TNF-α, CCL-7, AGPAT-2, and GPAT-3 in liver.

Results: Histomorphometry of the aortic root showed atherosclerotic plaques in 100% of ApoE(-/-) mice, 66% of ApoE(-/-)/Robo4(-/-) mice, and none in Robo4(-/-) mice. Aortic MCP-1 mRNA was increased in ApoE(-/-)/Robo4(-/-) vs Robo4(-/-), while TIMP-1 and TIMP-1/MMP-2 were higher in ApoE(-/-) compared to Robo4(-/-) ($P < .05$). ApoE(-/-)/Robo4(-/-) aortas showed reduced VCAM-1 and TM6SF2 and increased PNPLA3 mRNA compared to ApoE(-/-), approaching significance ($p \leq 0.09$). Notably, liver histomorphometry revealed more severe MASLD in Robo4(-/-) mice, with significantly higher NAS scores than ApoE(-/-)/Robo4(-/-)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and ApoE(-/-) mice ($P = .03$ and $P = .002$, respectively). Hepatic TM6SF2 mRNA was increased in Robo4(-/-) mice compared to ApoE(-/-)/Robo4(-/-) ($P \leq .09$) and ApoE(-/-) mice ($P < .05$). Robo4(-/-) livers exhibited reduced MMP-9, CD-36, TIMP-1, TIMP-1/MMP-2, CCL-7, PNPLA3 levels vs ApoE(-/-)/Robo4(-/-) ($P < .05$), with AGPAT-2 and GPAT-3 also reduced, approaching significance ($P \leq 0.09$). Taken together, it appears that Robo4 loss mainly affects the lipoprotein and triglyceride handling during atherogenesis and MASLD progression.

Conclusions: Robo4 loss reduces atherosclerosis but paradoxically exacerbates MASLD, in an established ApoE(-/-) mouse model of atherosclerosis and MASLD, highlighting tissue-specific roles in cardiovascular–metabolic disease crosstalk. Further studies are needed to delineate the precise mechanisms mediating these effects.

Abstract citation ID: lvag096.329

P140 - ECE_2381 - Phoenixin—a novel modulator of proliferation and differentiation of rat brown preadipocytes

Joanna Fiedorowicz, Małgorzata Krążek, Tatiana Wojciechowicz and Marek Skrzypski
Department of Animal Physiology and Biochemistry, Poznań University of Life Sciences, Poznań, Poland

Phoenixin (PNX) is a neuropeptide derived from the SMIM20 protein that plays a significant role in reproduction and metabolism. Recent studies show that PNX is involved in white adipogenesis, but its role in brown adipogenesis remains unknown. This study examined SMIM20 and GPR173 (putative PNX receptor) expression during rat brown preadipocytes differentiation and in brown adipose tissue (BAT) from young (5-6 weeks) and adult (16-18 weeks) rats, as well as PNX effects on brown preadipocytes proliferation and differentiation.

Brown preadipocytes were isolated from intracapsular BAT of male Wistar rats (100-120 g). Gene expression was analyzed by real-time PCR and protein levels by Western blot. Cell proliferation was assessed using BrdU incorporation, lipid accumulation via Oil Red O staining, and intracellular cAMP levels by ELISA.

During brown preadipocytes differentiation, *Smim20* mRNA expression decreased while PNX protein levels increased. *Gpr173* mRNA was upregulated during differentiation, though this was not reflected at the protein level. In BAT, *Smim20* mRNA expression was higher in young vs adult rats, whereas PNX protein levels showed the opposite pattern. *Gpr173* mRNA expression was elevated in adults, while protein production remained unchanged. Furthermore, PNX increased brown preadipocytes proliferation after 24 hours (100 nmol/L) and 48 hours (10 and 100 nmol/L), accompanied by elevated intracellular cAMP levels and enhanced ERK1/2 phosphorylation, but not AKT. In addition, PNX did not induce preadipocytes proliferation in the presence of H89 (PKA inhibitor), U0126 (ERK1/2 inhibitor), ESI-09 (noncyclic nucleotide EPAC antagonist). These findings indicate that PNX promotes brown preadipocytes proliferation via PKA-, Epac-, and ERK1/2-dependent mechanisms. Furthermore, PNX (100 nmol/L) upregulated UCP1 expression at both the mRNA and protein levels in brown preadipocytes differentiated for 7 days. Among transcription factors modulating brown adipogenesis (*Pparγ, Pgc1a, Prdm16, Cebpα, Cebpβ*), only *Pparγ* mRNA expression was significantly increased by 100 nmol/L PNX treatment, with corresponding elevation in PPARγ protein levels during 7 days of differentiation of brown preadipocytes. Moreover, PNX (100 nmol/L) enhanced *Fgf21* mRNA expression, while 10 and 100 nmol/L PNX stimulated FGF21 protein production in brown preadipocytes differentiated for 7 days. PNX did not affect lipid accumulation. These results demonstrate that PNX enhances UCP1 and FGF21 production in rat brown adipocytes.

Overall, the results indicate that PNX may regulate energy homeostasis by modulating the proliferation and differentiation of brown preadipocytes in rats.

Funding: This study was financed by the National Science Centre, Poland (NCN) under project no. 2022/45/B/NZ5/03453.

Abstract citation ID: lvag096.330

P141 - ECE_3093 - Immune checkpoint inhibitor–associated diabetes mellitus in patients with cancer

Georgia Tsirou[1], Vasiliki Siampanopoulou[1], Petros Papalexis[2], Alexandros Lafioniatis[1], Varvava Chalmantzi[1], Despoina Tsopouzidou[1], Paschalia Bekiaridou[1], Dimitra Stefanou[3], Dimitrios Ziogas[3], Helen Gogas[3] and Anna Angelousi[1]
[1]Athens Medical School, National and Kapodistrian University of Athens, First Department of Medicine, Laikon General Hospital, Athens, Greece; [2]First Department of Medicine, Unit of Endocrinology, Laiko General Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [3]Laiko Hospital, First Department of Internal Medicine, Laikon General Hospital, Athens, Greece

Background: Immune checkpoint inhibitors (ICIs) are increasingly used as first-line therapy for melanoma and are associated with immune-related adverse events (irAEs), particularly involving the endocrine system. ICI-associated diabetes mellitus (ICI-DM) is an uncommon but potentially life-threatening complication, often presenting abruptly and requiring lifelong insulin therapy.

Objective: To evaluate the incidence, clinical characteristics, and associated endocrine phenotypes of ICI-DM in patients with melanoma treated with ICIs.

Methods: This retrospective study included adults (>18 years) with melanoma who received ICIs as first-line therapy between 2023 and 2026. Eligible patients were those who developed new-onset DM following initiation of immunotherapy or experienced deterioration of pre-existing diabetes requiring insulin therapy. The diagnosis of ICI-DM was further supported by the presence of pancreatic autoantibodies, diabetic ketoacidosis (DKA), and/or reduced or absent C-peptide levels.

Results: Among 853 patients treated with ICIs, 29 patients (15 males) with a median age of 72 years (range: 44-85) met the criteria for ICI-DM. These cases accounted for 10.9% (29/265) of all endocrine-related irAEs observed in the study population. Twenty-three patients (79.3%) received anti– Programmed Death-1 (PD-1)/ Programmed Death Ligand-1 PD-L1 monotherapy (PD-L1), while 4 patients (13.8%) were treated with a combination of anti–PD-1/PD-L1 and anti– Cytotoxic T-Lymphocyte-Associated protein 4 (CTLA-4) therapy. No cases of ICI-DM were observed in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

patients treated with anti–CTLA-4 alone. The median body mass index was 26.6 kg/m^2 (range: 18.6-36.9). Eighteen patients (62.1%) developed new-onset ICI-DM, while 11 patients (37.9%) had pre-existing diabetes progressing from oral antidiabetic agents to basal–bolus insulin therapy. Five patients (17%) had a medical history of hypothyroidism. Concomitant endocrine irAEs were observed in 19 patients (65.5%). Specifically, ir- hypothyroidism occurred in 8 patients (27.6%), ir-thyroiditis in 2 patients (6.9%), and ir- hypophysitis with corticotrope axis insufficiency in 9 patients (31.0%). Among patients with new-onset ICI-DM, 9 patients (31.0%) presented with DKA at diagnosis. Anti–glutamic acid decarboxylase antibodies were detected in 3 of 17 tested patients (17.6%), while reduced or undetectable C-peptide levels were documented in 7 of 23 patients (30.4%), indicating significant β-cell dysfunction.

Conclusions: ICI-DM occurred in the 3.3% of melanoma patients treated predominantly with PD-1/PD-L1 inhibitors and represented approximately the 11% of all endocrine irAEs. Most cases presented as new-onset insulin-dependent DM, and nearly one-third manifested with DKA, highlighting the need for early recognition and prompt management. The frequent coexistence of other endocrine irAEs suggests a broader autoimmune endocrine phenotype.

Abstract citation ID: lvag096.331

P142 - ECE_2889 - Diazoxide choline extended-release (DCCR) improves hyperphagia in both children and adults with Prader-Willi Syndrome

Evelien Gevers[1], Jennifer Miller[2], Lynne Bird[3], Heidi Shea[4], Ashley Shoemaker[5], Jennifer Abuzzahab[6], Parisa Salehi[7], Theresa Strong[8], Lisa Matesevac[8], Jessica Bohonowych[8], Jing Gong[9], Michael Huang[9] and Anish Bhatnagar[9]

[1]Centre for Endocrinology, Queen Mary University of London, Barts and The London Medical School, William Harvey Research Institute, London, United Kingdom; [2]University of Florida, Gainesville, United States; [3]Rady Children Hospital of San Diego, San Diego, California, United States; [4]Endocrine Associates of Dallas, Plano, United States; [5]Vanderbilt University, Nashville, United States; [6]Childrens Minnesota, St. Paul, United States; [7]Seattle Children's, Seattle, United States; [8]Foundation Prader Willi Research, Walnut, California, United States; [9]Soleno Therapeutics Inc., Redwood City, California, United States

Introduction: Prader-Willi syndrome (PWS) is a rare genetic condition characterized by hyperphagia, excess body fat accumulation, hypotonia, and behavioural/psychological complications. DCCR (diazoxide choline extended- release) is an oral, once-daily medication in development for the treatment of patients with PWS who have hyperphagia. To assess DCCR efficacy in improving hyperphagia, we compared data of both children and adults with PWS from a DCCR-treated cohort to a matched untreated historical cohort.

Methods: Pooled data from the multicentre, Phase 3 DCCR studies (C601/C602) were compared with patient-level data from untreated participants in the Paving the Way for Advances in the Treatments & Health (PATH) for PWS Natural History Study (NHS). The two cohorts (DCCR-treated/untreated) were matched for age, hyperphagia severity, and body weight. Hyperphagia was assessed using the Hyperphagia Questionnaire for Clinical Trials (HQ-CT), a 9-item scale (0-36), with higher scores representing more severe hyperphagia. Participants were included in the analysis if they had at least one HQ-CT assessment performed approximately 6 months post-baseline. Participants were classified as children (<18 years) or adults (≥18 years).

Results: A total of 123 participants from C601/C602 studies (DCCR-treated cohort) and 229 PATH participants (untreated cohort) were included. Children (<18 years) and adults, respectively, comprised 80.5% ($N = 99$) and 19.5% ($N = 24$) of participants in the C601/C602 cohort, and 56.3% ($N = 129$) and 43.7% ($N = 100$) in the PATH cohort. Mean (standard deviation) baseline HQ-CT total scores in children and adults, respectively, were 22.1 (6.7) and 19.4 (6.4) in the DCCR-treated cohort, and 18.5 (5.3) and 17.9 (4.6) in the untreated cohort.

DCCR-treated children and adults had significantly greater reductions in HQ-CT total scores, indicating an improvement in hyperphagia, compared with untreated historical controls at week 26, and this benefit was sustained through week 52 (Table 1).

Table 1 LS mean difference in reductions in HQ-CT total scores in DCCR-treated vs untreated controls.

	Week 26	Week 52
Children (<18 years)	−5.8 (95% CI: −7.8, −3.9) $P < .0001$	−6.4 (95% CI: −8.5, −4.3) $P < .0001$
Adults (≥18 years)	−6.3 (95% CI: −10.1, −2.5) $P = .0015$	−4.3 (95% CI: −8.0, −0.6; $P = .0236$

Conclusions: Results of our analysis demonstrate that DCCR administration significantly reduced hyperphagia in both children and adults with PWS. HQ-CT total score improvements at 26 weeks (first available time point) were sustained at least through 52 weeks. Findings demonstrate that DCCR has prolonged efficacy across different age groups and strengthen its role as an effective treatment for hyperphagia in people with PWS.

Abstract citation ID: lvag096.332

P143 - ECE_1310 - EDL6D an SHBG mimetic peptide: a new approach for treating the metabolic dysfunction-associated fatty Liver Disease

Anna Alvarez-Guaita[1], Beatriz Perez-Gonzalez[1], Maria Teresa Salcedo Allende[2], Lidia Fuertes Rioja[1], Lorena Ramos Perez[1], Cristina Hernandez[1], Rafael Simo Canonge[1] and David M Selva[1]

[1]Diabetes and Metabolism, Vall d'Hebron Research Institute, Barcelona, Spain; [2]Pathology, Hospital Vall d'Hebron, Barcelona, Spain

Metabolic dysfunction-associated fatty liver disease (MASLD) is linked to low plasma levels of sex hormone-binding globulin (SHBG). Previous studies showed that SHBG overexpression reduces liver fat accumulation by inhibiting lipogenesis. In the present work, we have developed an SHBG mimetic peptide (EDL6D) that could be used as a new treatment to prevent and treat MASLD development and arrest its progression to MASH. We have first tested the EDL6D effects in in vitro experiments using HepG2 cells treated daily with 30 mM fructose. We next have

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

studied the preventive and therapeutic effects of EDL6D using wild-type mice developing MASLD induced by high fat diet and 30% fructose in the drinking water over 8 and 20 weeks respectively. Our results clearly showed that the treatment with EDL6D was able to reduce liver fat accumulation and regress MASLD by reducing the mRNA expression and protein levels of key lipogenic enzymes (ACLY, ACC and FAS) as well as PPARγ. Moreover, EDL6D was able to prevent the development of mild fibrosis, which can be attributed to its capacity to downregulates the intrahepatic production of collagen 1A1 (Col1A1) and transforming growth factor beta 1 (TGF-β1). In summary, we have shown that EDL6D, an SHBG mimetic peptide reduces de novo and exerts an important anti-inflammatory effect preventing fibrosis development in MASLD mouse models. These results suggested that EDL6D could be used as a new treatment to prevent and treat MASLD development and arrest its progression to MASH.

Abstract citation ID: lvag096.333

P145 - ECE_1652 - Chemosensory dysfunction as identifier of metabolic–microbiome phenotype in patients with type 2 diabetes

Stylianos Kopanos[1], Sebastian Büscher[2], Julia Hassa[3], Timm Weber[4], Sarah Büyükdag[1], Tobias Purschke[1], Michael Wehmeier[5], Gabriele Anton[4], Tobias Busche[3], Annika Hoyer[2] and Joachim Feldkamp[1]

[1]Academic Department of General Internal Medicine, Endocrinology, Diabetes and Infectiology, Bielefeld University, Medical School and University Medical Center East Westphalia-Lippe, Bielefeld, Germany; [2]Medical School OWL, Bielefeld University, Biostatistics and Medical Biometry, Bielefeld, Germany; [3]Medical School East Westphalia-Lippe & Center for Biotechnology (CeBiTec), Bielefeld University, Bielefeld, Germany; [4]Medical School OWL, Bielefeld University, Biobank OWL (BOWL), Bielefeld, Germany; [5]Microbiology and Transfusion Medicine, University Medical Center OWL, Institute of Medical Laboratory Diagnostics, Bielefeld, Germany

Background: Type 2 diabetes mellitus (T2DM) is associated with multisystem metabolic dysfunction. Chemosensory impairment remains underrecognized despite its relevance for nutrition and metabolic control, while gut microbiome dysbiosis may mechanistically link metabolic disease and sensory dysfunction.

Methods: In this prospective clinical study, 146 adults (66 T2DM, 80 non-diabetic controls) underwent standardized assessment of taste and smell, neuropathy scoring (MNSI), and metabolic phenotyping. Stool samples from 146 participants were analysed using 16S rRNA gene sequencing. Group comparisons used non-parametric tests with false discovery rate correction. Multivariable regression models adjusted for age, sex, obesity, and COVID history were applied. Microbiome analyses included diversity, dispersion testing, and differential abundance analyses.

Results: Participants with T2DM demonstrated significantly lower taste (mean 8.21 vs 11.88; Δ −3.67, $P = .0087$) and smell scores (2.35 vs 3.98; Δ −1.64, $P = .009$) and higher neuropathy burden (MNSI 7.67 vs 1.98; Δ +5.68, $P = .0011$). Impaired taste and smell were more prevalent in T2DM (taste: $\chi^2 = 19.44$, $P < .001$; smell: $\chi^2 = 9.30$, $P = .0023$). After adjustment, diabetes independently predicted impaired smell (OR 2.74, 95% CI 1.14-6.58, $P = .024$) and impaired taste (OR 2.94, 95% CI 1.30-6.64, $P = .010$), while obesity independently contributed to impaired taste (OR 2.21, 95% CI 1.01-4.83, $P = .048$). Gut microbiome analysis revealed altered community structure with unequal dispersion ($F = 22.6$, $P < .0001$) and differential abundance, including depletion of Faecalibacterium, Anaerostipes, Agathobacter, and Blautia and enrichment of Enterobacteriaceae and *Escherichia–Shigella* (all $P < .01$).

Conclusions: Chemosensory dysfunction delineates a distinct metabolic–microbiome phenotype in T2DM, integrating glycaemic burden, neuropathy, and gut dysbiosis, supporting its potential role as a clinically relevant marker for metabolic disease severity.

Abstract citation ID: lvag096.334

P146 - ECE_2616 - Socioeconomic and psychobehavioural determinants of obstructive sleep apnea and risk of type 2 diabetes in Hispanic/Latino adults: a longitudinal analysis of the HCHS/SOL study

Manal Taimah[1], Paula Holland[1] and Guillermo Perez Algorta[2]

[1]Lancaster University, Lancaster, United Kingdom; [2]Division of Health Research, University of Lancaster, Lancaster, United Kingdom

Background: Type 2 diabetes mellitus (T2DM) and obstructive sleep apnea (OSA) are frequently comorbid conditions and represent major global public health challenges. OSA is characterised by recurrent episodes of partial or complete upper airway obstruction during sleep, and its coexistence with T2DM is associated with increased cardiovascular risk, mortality, and healthcare utilisation. Hispanic/Latino populations experience a disproportionate burden of both conditions. This study examined the association between OSA, socioeconomic, psychological, and behavioural factors, and incident T2DM in Hispanic/Latino adults.

Methods: Using a biopsychosocial framework, we conducted a longitudinal analysis of the Hispanic Community Health Study/Study of Latinos, including baseline (2008-2011) and follow-up (2014-2016) data from 3105 adults without T2DM or prediabetes at baseline. OSA was assessed using the apnea–hypopnea index derived from home sleep testing. Incident T2DM was identified through self-report and biomarker data (fasting glucose and HbA1c). Generalised estimating equation models examined the association between baseline OSA and incident T2DM, adjusting for age, sex, waist-to-hip ratio (WHR), employment status, depressive symptoms, and smoking. Effect modification by sex, age, and WHR was assessed.

Results: The mean age was 44.1 years (SD = 14), and 61.9% of participants were women. Participants with OSA were older, predominantly male, and more likely to be employed, with significantly higher prevalence of hypertension, dyslipidemia, and central obesity. OSA was associated with more frequent snoring and excessive daytime sleepiness, while depressive symptoms and behavioural factors showed limited differences. Over six years of follow-up, baseline OSA was associated with a nearly twofold higher risk of incident T2DM (OR = 1.99, 95% CI: 1.38-2.87). Elevated WHR independently predicted T2DM risk (OR = 1.88, 95% CI: 1.25-2.82). Associations were consistent across sex, age, and WHR subgroups (Figure 1).

Conclusions: These findings support integrated screening for OSA among individuals with metabolic risk and underscore the need for culturally tailored public health interventions to reduce

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

disparities. OSA was found to be an independent risk factor for T2DM, underscoring the importance of multidisciplinary, equity-focused prevention approaches. Future longitudinal research should examine bidirectional associations between OSA and T2DM and include diverse ethnic populations to enhance generalisability.

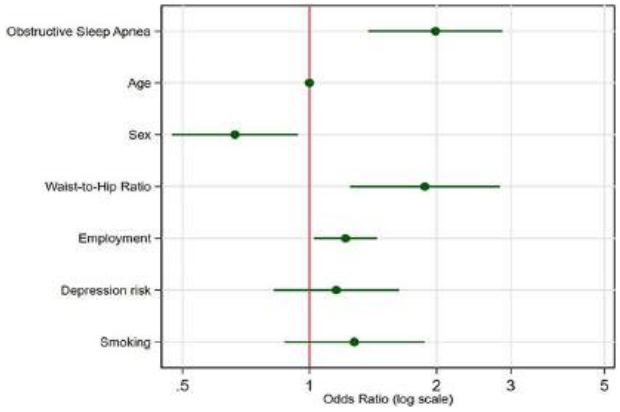


Figure 1 Adjusted associations between obstructive sleep apnea and Incident type 2 diabetes mellitus, fully adjusted generalised estimation equation model.

Abstract citation ID: lvag096.335

P147 - ECE_3952 - Extreme chronic hyponatraemia due to wheatgrass juice consumption followed by fatal osmotic demyelination syndrome upon discontinuation: a case report

Gergő Csitári[1] and Viktória Besir[1]
[1]*DBC-SZIEOK, Budapest, Hungary*

Hyponatraemia constitutes the most frequent electrolyte derangement encountered in clinical practice, encompassing hypovolaemic, hypervolaemic and euvolaemic aetiologies. Management of severe chronic hyponatraemia mandates precise correction rates, as overly rapid sodium repletion—even within guideline thresholds of ≤10 mmol/L per 24 hours—precipitates osmotic demyelination syndrome (ODS), characterised by central pontine and extrapontine myelinolysis with potentially irreversible neurological devastation.

We report the case of a 51-year-old female admitted for evaluation of extreme hyponatraemia (serum sodium 98 mmol/L) following prehospital trauma assessment. Relevant history comprised panic disorder, untreated anxiety-depression, suspected eating disorder and prior refusal of hospitalisation for severe metabolic acidosis (pH 7.02, 2015) and grand mal seizure (2019). Recurrent emergency presentations for headache, abdominal pain, diarrhoea, dizziness and gait instability culminated in admission after collapse.

Unremarkable head CT notwithstanding, emergency oxyologists—disregarding internal medicine consultation—administered 1500 mL 0.9% saline and 1 g intravenous sodium chloride bolus. Laboratory data from four months prior (117 mmol/L) confirmed chronicity. Within 12 hours, serum sodium increased 16 mmol/L, prompting free water intake and 5% dextrose infusion for deliberate relowering; extensive diuresis supervened despite intervention. Pharmacological agents and ethanol were excluded; on day 3, chronic exclusive consumption of 5 L daily wheatgrass juice—intended for weight loss and diuretic effects—was disclosed.

Neurological decline progressed from disorientation and dysthymia to mild ataxia. Day 9 witnessed pseudobulbar palsy, dysarthria and hemiplegia; repeat CT remained negative, but MRI confirmed pontine and basal ganglia demyelination diagnostic of ODS. Despite nasogastric feeding, quadriparesis advanced to locked-in syndrome and respiratory decompensation, culminating in death.

This case underscores the imperative of <8 mmol/L per 24-hour correction in high-risk chronic hyponatraemia, irrespective of initial acuity perception. Excessive wheatgrass juice—a purported "detoxification" agent lacking robust evidence—may induce profound water intoxication mimicking psychogenic polydipsia. Multidisciplinary vigilance for occult aetiologies, rigorous repletion limits and proactive relowering constitute essential prophylaxis against ODS, even when overcorrection appears contained.

Abstract citation ID: lvag096.336

P148 - ECE_2198 - Estrogen receptor beta activation orchestrates lipid remodeling and fatty acid oxidation to prevent lipotoxicity

Debora Rocha[1], Eloisa Vilas-Boas[2], Everton Vogt[1], Mariana de Carvalho[1], Maiara Queiroz[1], Camille Caldeira[1] and Alicia Kowaltowski[1]
[1]*Chemistry, Biochemistry, São Paulo, Brazil;* [2]*Faculty of Pharmaceutical Sciences, São Paulo, Brazil*

Non-selective hormone replacement with estradiol improves metabolic homeostasis during menopause. However, this treatment is not recommended for individuals with genetic predisposition to hormone-responsive cancers. In contrast, selective activation of estrogen receptor beta (ERβ) has shown promising results, promoting antitumor effects and modulating metabolic outcomes, although mechanisms in which these changes occur remain poorly understood. We investigated the effects of ERβ activation using diarylpropionitrile (DPN), a selective ERβ agonist, in both an in vivo post menopause model and in vitro models of metabolic overload. Female Wistar rats were submitted to ovariectomy (OVX) and later treated with DPN (1mg/kg, s.c.) for 15 days. ERβ agonist treatment recovered fasting glucose and lipid profiles, improved pancreatic islet morphology, and reduced retroperitoneal white adipose tissue. Serum ketone bodies and free fatty acid levels were also recovered to control levels, suggesting a modulation of liver lipid oxidation. Indeed, ERβ activation promoted expressive liver lipidome remodeling. To isolate the direct effects mechanistically, hepatocytes were submitted to nutrient overload and treated with DPN. In vitro, DPN also recovered ketone body secretion and promoted an increased dependence on complete fatty acid oxidation as well as decreased metabolic flexibility, as assessed by modulated extracellular flux analysis. In line with that, lipid species related to fatty acid metabolization were modulated by the treatment. Overall, these findings demonstrate the potential of ERβ as an alternative target for hormone replacement therapy, under conditions in which hepatic lipid remodeling to prevent lipotoxicity is desirable.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.337

P149 - ECE_2587 - Semaglutide and empagliflozin improve glycaemic control and body composition in type 1 diabetes (T1DM): results from the ENDIS trial

Maja Navodnik Preložnik and Aleksandra Šauperl
Departement of Angiology and Endocrinology, General Hospital Celje, Celje, Slovenia

Background: SGLT2 inhibitors and GLP-1RAs are not approved for the treatment of T1DM; however, accumulating evidence suggests potential benefits. In the ENDIS trial, we previously demonstrated improvements in endothelial function with empagliflozin and semaglutide. Here, we present prespecified subanalyses focusing on glycemic control, body weight, and body composition.

Methods: A total of 89 adults with T1DM, all users of continuous glucose monitoring systems (majority treated with insulin pump therapy), were randomized into three matched groups receiving empagliflozin ($n = 30$), semaglutide ($n = 30$), or standard care ($n = 29$). At baseline, participants were well controlled, with a mean HbA1c of 7.4%, mean body mass index (BMI) of 27 kg/m^2, time in range (TIR) of 62%-70%, and coefficient of variation (CV) of 33%-35%. Outcomes were assessed after 12 weeks of treatment.

Results: Both active treatments led to comparable improvements in glycaemic control. HbA1c was reduced by −0.4% (IQR 0.8) in the semaglutide group ($P = .016$) and by −0.1% (IQR 0.6) in the empagliflozin group ($P = .052$). Significant weight loss was observed with both agents, being more pronounced with empagliflozin (−8.0 kg, IQR 4.0; $P < .001$) compared with semaglutide (−4.2 kg, IQR 4.0; $P < .001$). Waist circumference decreased similarly in both groups (empagliflozin −3.5 cm, IQR 6.0; semaglutide −3.2 cm, IQR 6.0; both $P < .001$). Glycaemic variability was low at baseline due to the use of advanced technologies and was not significantly altered by either treatment (ΔCV −1.5% vs −1.2%; both $P > .1$). Total daily insulin dose was significantly reduced in both treatment groups (empagliflozin −2.7 IU, $P = .009$; semaglutide −6.0 IU, $P < .001$).

Both interventions resulted in a comparable reduction in fat mass. In the empagliflozin group, fat mass decreased from 19.5 kg to 17.6 kg (27.2% to 24.0%; $P = .004$), while in the semaglutide group it decreased from 19.8 kg to 15.8 kg (24.8% to 23.2%; $P = .001$). Lean body mass was modestly reduced in both groups. Semaglutide was associated with a slight increase in total and extracellular body water. Empagliflozin did not lead to clinically relevant increases in β-hydroxybutyrate; mild ketonaemia (≤1.1 mmol/L) occurred only during intercurrent illness.

Conclusions: n adults with T1DM, empagliflozin and semaglutide significantly improve glycaemic control, body weight, and waist circumference, primarily through reductions in fat mass, while lowering insulin requirements and without clinically relevant increases in ketone bodies.

Abstract citation ID: lvag096.338

P150 - ECE_1744 - Empagliflozin for the treatment of postprandial hypoglycaemia—a randomized placebo-controlled superiority study and meta-analysis

Matthias Hepprich[1,2], Deborah Zeiter[3], Justus Fischer[4,5], Stefanie Dobler[6], Monica La Vista[3], Lia Bally[7], David Herzig[8], Marco Cattaneo[5] and Marc Donath[2,9,10]
[1]Endocrinology and Nutrition Center, Endocrinology and Nutrition Center, Basel, Switzerland; [2]Medical Faculty,University of Basel, Basel, Switzerland; [3]Endocrinology and Diabetes, Kantonsspital Olten, Olten, Switzerland; [4]Internal Medicine, Kantonsspital Bruderholz, Binningen, Switzerland; [5]Clinical Trial Unit, University of Basel, Basel, Switzerland; [6]Internal Medicine, Spital Dornach, Dornach, Switzerland; [7]Inselspital Bern, Diabetes, Endocrinology, Nutritional Medicine and Metabolism UDEM, Bern, Switzerland; [8]Inselspital Bern, Bern, Switzerland; [9]Research Center, University Of Montreal/NPRI, University Hospital, Montréal, Canada; [10]Clinical Trial Unit, Baden Cantonal Hospital Heliport, Baden, Switzerland

Background: Postbariatric hypoglycaemia (PBH) significantly impairs quality of life and remains difficult to treat, with current therapies offering limited benefit. Although empagliflozin reduced hypoglycaemic episodes in an acute trial, its longer-term effects on hypoglycaemia and quality of life are unknown. We hypothesised that empagliflozin would reduce hypoglycaemic episodes and improve quality of life in individuals with PBH.

Methods: In this multicentre, randomized, double-blind, placebo-controlled trial, 40 adults (18-75 years) with frequent PBH were assigned to empagliflozin 10 mg daily or placebo for 28 days. Primary outcomes were changes in SF-36 mental and physical health scores and frequency of hypoglycaemic events measured by blinded continuous glucose monitoring (CGM). Secondary outcomes included patient-reported symptoms, metabolic measures, and safety. Analyses were performed in the full analysis set with per-protocol sensitivity analyses. A post-hoc random-effects meta-analysis combined these findings with prior studies.

Findings: Empagliflozin did not improve physical or mental quality-of-life scores compared with placebo. The number of CGM-detected hypoglycaemic episodes tended to be higher with empagliflozin ($P = .054$), supported by sensitivity analyses showing an increased risk (incidence rate ratio 1·86, 95% CI 1·07-3·23). Time spent in hypoglycaemia (<3·0 mmol/L) was significantly greater with empagliflozin (0·90% vs 0·40%). Despite this, participants reported fewer symptomatic episodes, with no differences in hypoglycaemia awareness or fear. Secondary metabolic and safety outcomes were similar between groups. Meta-analysis suggested reduced glycaemic variability but no reduction in hypoglycaemia exposure.

Interpretation: Empagliflozin did not improve quality of life or reduce hypoglycaemia in PBH and may increase unrecognized hypoglycaemic exposure, raising safety concerns.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.339

P151 - ECE_3297 - Inhibition of the androgen-activating enzyme AKR1C3 selectively decreases systemic and intra-adipose 11-oxygenated androgens in women

Lina Schiffer[1], Amarah Anthony[1], Laura Wittemans[2,3,4], Angela Taylor[5], Imken Oestlund[6], Antonio Miranda[1], Eka Melson[1,7], Tara McDonnell[8], Punith Kempegowda[5], Paul Smith[9], T Clark[5,9], Martin Wabitsch[10], Michael W. O'reilly[8], Michaele Peters[11], Andrea Wagenfeld[11], Jan-Peter Ingwersen[11], Jacky Snoep[6,12], William Scott[1,7], Jan Hilpert[11], Karl Storbeck[1,6] and Wiebke Arlt[1,7]

[1]MRC Laboratory of Medical Sciences, London, United Kingdom; [2]Big Data Institute at the Li Ka Shing Centre for Health Information and Discovery, University of Oxford, Oxford, United Kingdom; [3]Nuffield Department of Women's and Reproductive Health, Medical Sciences Division, University of Oxford, Oxford, United Kingdom; [4]Novo Nordisk Research Centre Oxford, Oxford, United Kingdom; [5]Department of Metabolism and Systems Sciences, University of Birmingham, Birmingham, United Kingdom; [6]Department of Biochemistry, Stellenbosch University, Stellenbosch, South Africa; [7]Institute of Clinical Sciences, Imperial College London, London, United Kingdom; [8]Royal College of Surgeons in Ireland, University of Medicine and Health Sciences, Dublin, Ireland; [9]Birmingham Women's Hospital, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom; [10]Division of Pediatric Endocrinology and Diabetes, University Hospital of Ulm, Ulm, Germany; [11]Research and Development, Pharmaceuticals, Bayer AG, Berlin, Germany; [12]Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

Androgen excess is a major diagnostic feature in polycystic ovary syndrome (PCOS), affecting 10-15% of women globally, and has been linked to the increased risk of metabolic disease in PCOS. Testosterone (T; classic androgen pathway) and 11-ketotestosterone (11KT; 11-oxygenated androgen pathway) are equipotent activators of the androgen receptor. Both circulate in similar concentration in premenopausal women whereas 11KT is predominant after menopause and in PCOS. *In vitro*, the enzyme aldo-keto reductase 1C3 (AKR1C3) activates precursors from classic and 11-oxygenated pathways to T and 11KT. Furthermore, AKR1C3 expression is upregulated by insulin, linking androgen excess and insulin resistance. Here, we investigated the contribution of AKR1C3 to female systemic and intra-adipose androgen production.

Using single-nucleus RNA-Seq (62 donors, 43 female), we established that, within adipose tissue, AKR1C3 primarily resides in adipocytes, with increased expression in women vs men and in obese vs lean individuals; androgen receptor expression mirrored this pattern. Using subcutaneous and visceral adipose tissue explants from women undergoing elective surgery ($n = 30$; BMI 20.8-56.8 kg/m^2, age range 32-74 years), we found that both subcutaneous and visceral adipose tissue preferentially activates 11-oxygenated androgens (8-10-fold higher 11KT over T). Pharmacological AKR1C3 inhibition selectively disrupted 11-oxygenated androgen activation in female adipose tissue explants, with only minor impact on T generation.

Treatment with an oral AKR1C3 inhibitor ($n = 9$) or placebo ($n = 12$) for 12 weeks in premenopausal women with normal circulating androgens resulted in selective inhibition of 11-oxygenated androgen activation, with only minor effects on circulating T. Similarly, in a single dose study in 16 postmenopausal women, a different, chemically unrelated AKR1C3 inhibitor yielded a significant decrease in circulating 11KT, with no discernible effects on T.

Next, we used a validated computational model that incorporates enzyme kinetic parameters obtained from *in vitro* experiments with multiple enzymes involved in androgen metabolism. We fitted the model to serum androgen concentrations measured by tandem mass spectrometry in 91 treatment-naïve women with PCOS (age 19-48 years) and 66 women without PCOS (age 22-48 years). Results showed a 2.6-fold increased systemic AKR1C3 activity in PCOS and predicted preferential effects of AKR1C3 inhibition on 11KT.

Taken together, we show that pharmacological targeting of AKR1C3 preferentially blocks 11-oxygenated androgen activation, both systemically and in adipose tissue. AKR1C3 inhibition provides a promising, novel strategy to alleviate 11KT excess in women and potentially also address related metabolic dysfunction. Future studies will quantify the impact of AKR1C3 inhibition in women with PCOS.

Abstract citation ID: lvag096.340

P152 - ECE_1208 - Metabolomic disparities between men and women with diabetes and obesity; differential predictors of tirzepatide response determined by obesity status

Ipsita Mishra[1] and Nirupama Chayani[2]

[1]IMS & SUM II, Phulnakhara, Soul Balance,Diabetes and Endocrine Centre of Excellence, Endocrinology,Diabetes and Metabolism, Cuttack, India; [2]DRIEMS, Mahaveer Lab, Microbiology, Cuttack, India

Background: Tirzepatide, a dual GIP/GLP-1 receptor agonist, demonstrates unprecedented efficacy for weight loss and glycemic control in type 2 diabetes (T2DM) and obesity. However, significant inter-individual variability in therapeutic response exists. We aimed to identify sex-specific metabolomic predictors of tirzepatide-induced weight loss response) in men and women with T2DM, stratified by obesity status(Class I: BMI 30-34.9 kg/m^2 vs Class II/III: BMI ≥35 kg/m^2).

Methods: A prospective cohort study of 220 adults (110 men, 110 women) with T2DM and obesity (mean BMI 37.1 ± 5.2 kg/m^2) initiating tirzepatide (10-15 mg weekly) were included. Baseline fasting serum samples were analyzed using untargeted high-resolution mass spectrometry (LC-MS/MS) and targeted quantification. Metabolomic data were analyzed using multivariate logistic regression and Random Forest models to identify baseline metabolites predictive of a "High Responder" status (≥15% TBWL) at 9 months. Models were developed separately for men and women and stratified by obesity class (Class I vs Class II/III).

Results: Overall, women were significantly more likely to be High Responders (62.7% vs 41.8% of men, $P = .003$).

In Men (Class II/III Obesity; BMI ≥35): High Responder status was negatively predicted by a cluster of branched-chain amino acids (BCAAs) and their catabolites. Specifically, elevated baseline valine, leucine,and 3-hydroxyisobutyrate were associated with non-response(OR: 0.72 per 1-SD increase, 95% CI: 0.59-0.88, $P = .001$).The predictive model for this group achieved an AUC-ROC of 0.81 (95% CI: 0.70-0.91).

In Men (Class I Obesity; BMI 30-34.9): The BCAA signature was not predictive ($P = .34$).Higher levels of specific long-chain

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

acylcarnitines (eg, C16:0, C18:1) were associated with non-response (OR: 0.79, 95% CI: 0.64-0.95, $P = .014$).

In Women (Class II/III Obesity; BMI ≥35). High baseline levels oflipid species i,e several lysophosphatidylcholines (LPCs) (eg, LPC 18:2, LPC 20:4) and dicarboxyl-acylcarnitines were positively associated with High Responder status (OR: 1.31 per 1-SD increase, 95% CI: 1.12-1.53, $P < .001$) with an AUC-ROC of 0.84 (95% CI: 0.74-0.93).

In Women (Class I Obesity; BMI 30-34.9): The predictive signature was less robust (AUC-ROC: 0.69), but trended towards an association with baseline bile acid profiles rather than lipids.

Conclusions: The metabolic pathways predicting tirzepatide response are fundamentally different between sexes and are further modified by obesity class.Men with high baseline BCAA signatures in the context of severe obesity are poor responders.Conversely, women with severe obesity and a favorable baseline lipid profile are likely to achieve significant weight loss. These findings highlight the potential for sex-stratified, metabolomics-based precision medicine to guide the use of incretin therapies.

Abstract citation ID: lvag096.341

P153 - ECE_2699 - MHC class II+ adipocyte in control of white adipose tissue browning

Yifan Zhao[1], Tuo Deng[2] and Hannah Hui[1]
[1]*Hong Kong, China;* [2]*Central South University, The Second Xiangya Hospital, Changsha, China*

Activation of beige adipocyte within white adipose tissue (WAT), a process called WAT browning, is emerging as a therapeutic approach to combat obesity and metabolic diseases. However, due to the incomplete understanding on the regulatory mechanism of beige adipocyte, efficient and safe strategy to enhance this process is currently lacking. We found that a subcluster of white adipocyte with MHCII antigen presenting activity (namely MHCII+ adipocyte) potentiates adipose inflammation and systemic insulin resistance in obesity via altering the immune cells in the visceral WAT. We found both the number and the activity of MHCII+ adipocytes are increased during WAT browning. Furthermore adipocyte-selective deletion of MHCII gene boosts WAT browning, suggesting MHCII+ adipocyte acts as a negative regulator of WAT browning. The mice with specific MHCII+ adipocyte depletion also exhibited impaired WAT browning, confirming the negative action of MHCII+ adipocyte on beige adipocyte activation. Meanwhile, we found a subcluster of adipose stem cell high in CD74 expression (CD74+ ASC) is present in iWAT. These CD74+ ASCs readily differentiate to MHCII+ adipocytes in vitro. Single cell RNA sequencing (scRNA-Seq) analysis showed that the adipose tissue precursor cells were significantly reduced in adipocyte-selective MHCII gene. In contrast the number of immune cells including T cells and myeloid cells was not significantly altered. These results suggest that MHCII+ adipocytes regulate beige adipocyte activation independent of its antigen presenting activity.

Acknowledgement: This work is supported by NSFC/RGC project (N_CUHK486/23).

Abstract citation ID: lvag096.342

P154 - ECE_2916 - Ghrelin gene-derived peptides induce browning and regulate thermogenesis in mouse and human adipocytes

Iacopo Gesmundo[1], Giuseppina Granato[1], Ramesh Kasarla[1], Federica Bistolfi[1], Francesca Pedrolli[1], Maria Alessandra Bocchiotti[2], Ahmed M. Mansour[3], Andrea Margara[4], Andrea Armani[5], Massimiliano Caprio[5], Mario Morino[6], Ezio Ghigo[1] and Riccarda Granata[7]
[1]*Department of Medical Sciences, University of Turin, Turin, Italy;* [2]*Department of Plastic Surgeon Gynecological and Obstetrician, City of Health and Science of Turin, Turin, Italy;* [3]*Faculty of Medicine, Alexandria University, Alexandria, Egypt;* [4]*Plastic Surgery Service, Humanitas Gradenigo Hospital, Turin, Italy;* [5]*Department for the Promotion of Human Sciences and Quality of Life, San Raffaele Roma Open University, Rome, Italy;* [6]*Department of Surgical Sciences, University of Turin, Turin, Italy;* [7]*Department of Molecular Biotechnology and Health Sciences, University of Turin, Turin, Italy*

Obesity arises from an imbalance between energy intake and expenditure. Whereas white adipose tissue (WAT) primarily functions as an energy storage depot, brown adipose tissue (BAT) dissipates energy as heat through the action of uncoupling protein 1 (UCP1). In addition, white adipocytes can undergo reversible transdifferentiation into thermogenic beige adipocytes through browning. Identifying novel factors that promote browning, and thermogenesis may therefore offer therapeutic strategies to combat obesity and its associated metabolic disorders. Ghrelin gene-derived peptides, acylated ghrelin (GHRL), des-acyl ghrelin (DAG), and obestatin (OBE), are key regulators of energy balance and lipid metabolism. However, their role in WAT browning and BAT thermogenesis has not been fully established. Here, we investigated the effects of GHRL, DAG, and OBE on the induction of browning and thermogenesis in differentiated 3T3-L1 mouse adipocytes and in human adipocytes obtained during bariatric surgery from obese, nondiabetic individuals. Human samples included abdominal subcutaneous and visceral adipose tissue fragments (hSAT and hVAT), as well as hSAT-derived mature adipocytes and preadipocytes. In 3T3-L1 adipocytes DAG and OBE, but not GHRL, significantly increased UCP1 mRNA and protein levels and upregulated the expression of brown and beige markers (*Pgc1a, Prdm16, Tmem26, Cd137,* and *Dio2*), as well as batokines (*Igf1, Il6, Adipoq, Ngf, Gdf15,* and *Fgf21*). In contrast, the adipogenic gene *C/ebp* was upregulated by GHRL but downregulated by DAG and OBE. Moreover, DAG and OBE increased intracellular cAMP levels and CREB phosphorylation, and enhanced isoproterenol-stimulated lipolysis, whereas GHRL had no effect. DAG and OBE also promoted GLUT4 translocation, increased glucose uptake, and activated the AMPK-SIRT1 pathway, as indicated by increased AMPK phosphorylation and elevated SIRT1 expression. Functionally, DAG and OBE stimulated thermogenesis, as evidenced by increased mitochondrial respiration and enhanced mitochondrial biogenesis. Finally, DAG and OBE, but not GHRL, upregulated brown/beige markers across all human samples and increased mitochondrial respiration in hSAT-derived beige adipocytes. Collectively, these findings indicate that DAG and OBE promote adipose tissue browning and thermogenesis,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

highlighting their potential therapeutic relevance in obesity and related metabolic disorders.

Abstract citation ID: lvag096.343

P156 - ECE_1204 - A4D—alarm for diabetes study: N-glycosylation of plasma proteins as a predictive biomarker for type 2 diabetes onset in at-risk individuals

Maja Baretić[1,2], Valerija Bralić Lang[2,3], Tamara Poljičanin[4], Domagoj Kifer[5], Olga Gornik Kljaić[5] and Martiana Džepina[6]
[1]*Internal Clinic, Department of Endocrinology and Diabetes, University Hospital Centre Zagreb, Zagreb, Croatia;* [2]*University of Zagreb, School of Medicine, Zagreb, Croatia;* [3]*Family medicine practice Valerija Bralić Lang, Zagreb, Croatia;* [4]*Zagreb County Health Centre, Zagreb, Croatia;* [5]*Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb, Croatia;* [6]*Medilab One Ltd, Zagreb, Croatia*

Background and Aims: The potential for early identification of individuals at risk for type 2 diabetes mellitus (T2DM) through biomarkers could shift from preventive to predictive medicine. Predictive healthcare strategies could direct resources toward individuals highly likely to develop T2DM soon. Biomarkers, such as N-glycans- oligosaccharide structures attached to plasma proteins, exhibit significant changes years before disease onset, making them promising predictive tools. This study investigates the association between plasma protein N-glycosylation patterns and the onset of T2DM within 24 months in individuals with initially normal glycated haemoglobin (HbA1c).

Materials and Methods: This prospective cohort study involved 1, 484 participants recruited from primary healthcare practices in Croatia. Inclusion criteria included ages 55-69 years, normal HbA1c levels, and a positive family history of diabetes in first-degree relatives. Individuals with known diabetes or those newly diagnosed during screening based on ADA criteria, those with autoimmune or malignant diseases, acute inflammatory processes, and those treated with corticosteroids or antipsychotic therapy were excluded. Plasma protein N- glycan profiles were analysed at baseline and after 12 months, while HbA1c levels were measured throughout the study period.

Results: Statistically significant differences in glycan profiles were observed between individuals who developed T2DM within 24 months ($n = 93$, 44% females, median age 61 [53-71] years, median BMI 30.46 [19.7-42.9] kg/m^2) and those without a diagnosis of T2DM ($n = 1392$, 64% females, median age 60 [47-75] years, median BMI 27.67 [18.-50.3] kg/m^2). Several glycan groups exhibited distinct alterations between groups, including GP 18, GP 20 (both disialylated biantennary glycans), GP 26 (disialylated triantennary glycans), GP 29 and GP 32 (both trisialylated triantennary glycans), and GP 36, GP 37, GP 38, and GP 39 (tri- and tetrasialylated tetraantennary glycans). Lower levels of GP 18, GP 29, GP 36, GP 37, GP 38, and GP 39, alongside higher levels of GP 20, GP 26, and GP 32, were associated with an increased predisposition to T2DM development within two years.

Conclusions: N-glycosylation profiling shows strong potential as a prognostic marker for the onset of T2DM, offering a novel approach for early risk stratification. These findings underscore the significance of glycosylation changes in disease progression and its potential role in monitoring lifestyle interventions, more frequent screening, and early introduction of pharmacotherapy. As T2DM can often be delayed or prevented through timely action, glycan-based risk assessment may enhance early preventive strategies for at-risk populations, alarming for diabetes.

Abstract citation ID: lvag096.344

P158 - ECE_2781 - Dapagliflozin alters the levels of leptin and TNF-α in patients with type 2 diabetes and metabolic dysfunction-associated fatty liver disease

Fedir Laniush, Myroslava Borovets and Alina Urbanovych
Endocrinology, State non-profit enterprise "Danylo Halytsky Lviv National Medical University", University Clinic State non-profit enterprise "Danylo Halytsky Lviv National Medical University", Lviv, Ukraine

Background: Metabolic dysfunction-associated fatty liver disease (MAFLD) affects one third of the adult population. It often coexists with type 2 diabetes (t2D) with a prevalence 70% among these patients. MAFLD is known to increase macro- and microvascular complications in T2D, such as cardiovascular events, chronic kidney disease, and retinopathy. Both MAFLD and T2D are linked with systemic changes in immune response and inflammation. Dapagliflozin has multiple beneficial effects on glycemia, renal function, and cardiovascular system. This study aimed to evaluate whether dapagliflozin improves liver function in MAFLD and alters proinflammatory cytokines levels.

Materials and Methods: : We conducted a study of 135 patients with T2D and MAFLD with no other medication taken previously but metformin. The average T2D duration was 2.04 ± 1.21 years; BMI 31.4 ± 4.3 kg/m^2; HbA1c level 8.35 ± 1.27%. We added dapagliflozin as the second medication for the next 6 months. The investigated parameters were ALT, AST, the De Ritis ratio, leptin, IL-2, IL-6, and TNF-α.

Results: After 6 months of metformin and dapagliflozin therapy, ALT level decreased from 43.11 ± 4.47 to 25.13 ± 3.19 U/L ($P < .05$); AST from 37.93 ± 3.30 to 25.13 ± 1.95 U/L ($P < .05$). The De Ritis ratio increased from 0.9 ± 0.05 to 1.06 ± 0.14 ($P < .05$). Leptin level declined from 26.09 ± 3.81 ng/ml to 15.45 ± 3.44 ($P < .05$); TNF-α level from 11.24 ± 0.96 to 3.87 ± 0.38 pg/mL ($P < .05$). IL-2 and IL-6 levels did not show a significant decrease after 6 months ($P > .05$).

Conclusions: Using dapagliflozin in T2D patients has multiple benefits including MAFLD improvement. It decreases the levels of transaminases as well as leptin and TNF-α which generally defines a reduction in systemic and local inflammation in liver. It prevents a liver from further dysfunction and fibrosis.

Abstract citation ID: lvag096.345

P159 - ECE_1751 - A Prothymosin-α biomarker signature predicts early fetal growth independent of maternal glycaemia

Maria Mirabelli[1], Marta Greco[1], Daniela Foti[2] and Antonio Brunetti[2]
[1]*Department of Health Sciences, Magna Græcia University, Catanzaro, Italy;* [2]*Department of Experimental and Clinical Medicine, Magna Græcia University, Catanzaro, Italy*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Gestational diabetes mellitus (GDM) is the most common endocrine complication of pregnancy and is associated with adverse neonatal outcomes. Alterations in fetal growth (FG) may occur early in gestation, often before the biochemical diagnosis of GDM. Maternal glycaemia alone does not fully explain FG variability, and fetal overgrowth can also occur in pregnancies without GDM, suggesting additional determinants. Maternal inflammation and placental angiogenic imbalance are potential contributors: pro-inflammatory cytokines such as IL-6 and TNF-α can influence maternal, placental and fetal insulin sensitivity, while angiogenic factors including VEGF and EGF regulate placental vascular development and nutrient transfer. Prothymosin-α (ProT-α), an immunomodulatory protein and emerging biomarker of obesity-related insulin resistance (IR) has not been well studied in GDM or FG. We therefore examined whether ProT-α, alongside inflammatory and angiogenic mediators, is associated with early FG trajectories independently of maternal glycaemia.

Methods: Forty-six women with singleton pregnancies underwent a 75-g OGTT at 24-28 weeks' gestation (WG). GDM was diagnosed according to IADPSG criteria (GDM $n = 8$; normal glucose tolerance $n = 38$). Plasma glucose and serum insulin were measured at fasting, 1h and 2h post-load. Circulating ProT-α, cytokines and angiogenic factors were assessed at the time of OGTT and, in a subset of very high-risk women, also at earlier screening. FG was evaluated using ultrasound-derived abdominal circumference and estimated fetal weight (EFW) percentiles at 20 WG and, when available, again at 24 WG, with near-perfect concordance between time points. Associations were explored using Spearman correlations and multivariable linear regression to identify independent predictors of FG.

Results: Women with GDM were older ($P = .020$) and tended to have higher pre-pregnancy BMI. As expected, glucose concentrations were significantly higher in GDM group at fasting, 1h and 2h (all $P < .01$). Compared with women with normal glucose tolerance, those with GDM exhibited lower circulating levels of IL-8 ($P = .034$), TNF-α ($P = .046$) and IL-1α ($P = .007$), alongside reduced ProT-α concentrations. In multivariable regression, 2h glucose ($\beta = .545$, $P = .010$), VEGF ($\beta = .380$, $P = .021$) and EGF ($\beta = .374$, $P = .047$) were independently associated with higher EFW percentiles, whereas IL-10 ($\beta = -.416$, $P = .030$) and ProT-α ($\beta = -.431$, $P = .022$) were independent negative predictors.

Conclusions: Early FG is better identified by an integrated glycaemic, immune, and angiogenic biomarker profile than by maternal glycaemia alone. The inverse association between ProT-α and EFW percentiles supports its potential as an immunometabolic biomarker for early FG risk, particularly in GDM and/or maternal IR pregnancies.

Abstract citation ID: lvag096.346

P161 - ECE_2089 - Glucose tolerance in a longitudinal perspective

Daniela Vejrazkova, Markéta Vaňková, Petra Lukasova, Martin Hill, Josef Vcelak and Bela Bendlova
Department of Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic

Background: Given the alarming increase in the incidence of type 2 diabetes mellitus (T2DM) worldwide and enormous societal burden of health complications associated with this metabolic disorder, such as dyslipidemia, hypertension, or central obesity, it is essential to focus on its prevention.

Aims: Our aim was to evaluate the long-term follow-up of 384 Czech adults who were not diabetic at study entry, but two-thirds of whom had an increased risk of developing T2DM due to family or personal history. We intended to determine anthropometric and biochemical markers that could serve as a suitable early predictors of deterioration in glucose metabolism.

Methods: 308 women and 76 men underwent detailed anthropometric and biochemical examinations including a 3-hour oral glucose tolerance test (OGTT) at the beginning and at the end of the monitoring. In both sexes, median of follow-up period was 10.2 years and median of age at study entry 38.4 years. During the baseline examination and re-examination, we ensured maximum adherence to a uniform protocol in terms of methodology.

Results: Based on the initial OGTT, prediabetes, ie, increased fasting glucose and/or impaired glucose tolerance in the 120th minute of the test was detected in 48 participants (13%) with no significant difference between the sexes. During the follow-up, the number of people with prediabetes/T2DM increased to 133 (35%), of which 98 (32%) were women and 35 (46%) were men. This was already a statistically significant difference ($P = .02$). A comparison of the group that remained healthy during monitoring with the group that developed prediabetes/T2DM pointed already during the baseline examination to higher blood pressure ($P = .001$), higher fat accumulation in the waist area ($P < .001$), less healthy lipid spectrum especially with regard to triglycerides ($P < .001$), higher liver GGT ($P < .001$) along with lower hepatic insulin extraction ($P = .01$) and also to lower IGF-1 levels ($P < .001$) in those whose metabolism deteriorated. These characteristics were already at the start of monitoring accompanied by higher fasting glycemia ($P < .001$) and insulinemia ($P < .001$) in the impaired group compared to the group that remained healthy, as well as by higher area under the curve of insulin measured during the 3-hour OGTT ($P < .001$), which is a manifestation of lower insulin sensitivity.

Conclusions: In addition to older age and male gender, we present other metabolic markers that can be considered predictive of (pre)diabetes and that warn of increased risk many years in advance.

Funding: AZV NU20-01-00308 and MZ ČR RVO EÚ00023761.

Abstract citation ID: lvag096.347

P162 - ECE_1279 - Real-world outcomes of hybrid closed-loop insulin therapy in children and young people with type 1 diabetes in a UK district general hospital

Manish Shah, Nazik Elamin and Gunjan Jain
Paediatrics, East & North Hertfordshire NHS Trust, Stevenage, United Kingdom

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: NHS England has expanded access to hybrid-closed-loop (HCL) insulin delivery systems for children and young-people (CYP) with type-1 diabetes mellitus (T1DM) through a five-year national implementation programme. Since January-2023, our district general hospital has adopted HCL therapy for CYP with T1DM. This study evaluates the real-world impact of HCL systems on glycaemic control, including HbA1c, time-in-range (TIR), and hypoglycaemia.

Method: CYP with T1DM initiated on HCL therapy between January-2023 and June-2024 were identified using electronic patient records. HbA1c values were obtained from clinical records, and continuous glucose monitoring (CGM) metrics were extracted from Glooko platform. Patients with incomplete datasets, insufficient CGM uploads, or lost follow-up were excluded. Paired pre- and post-HCL HbA1c measurements and early post-initiation CGM metrics were analysed.

Results: Of 120 CYP commenced on HCL therapy, 72 had complete data suitable for analysis. Median age at HCL initiation was 13.5 years (IQR 4-20), 53% were female, and median diabetes duration was 7 years (IQR 3-9). Omnipod-5 was the most commonly used system (75%). All participants used CGM and multiple daily injections prior. Mean HbA1c improved significantly from 72.34 ± 26.37 mmol/mol pre-HCL to 56.01 ± 8.41 mmol/mol at up to 18 months post-initiation (mean paired reduction 16.49 mmol/mol; 95% CI −22.88 to −10.10; $P < .001$). Early CGM outcomes were favourable. Mean 90-day time-in-range (3.9-10.0 mmol/L) was 65.55 ± 9.52%. Mean time below range (<3.9 mmol/L) was 1.53 ± 1.06%, and time in very-low range (<3.0 mmol/L) was 0.39 ± 0.60%.

Variable	Measure	Total
Age, year	Median, IQR	13.5 (4-20)
Gender, Male	n(%)	34 (47%)
Gender, Female	n(%)	38 (53%)
Diabetes Duration pre-HCL, Years	Median, IQR	7 (3-9)
Pre-HCL HbA1c, mmol/mol	Mean ± SD	72.34 ± 26.37
Post HCL Measures		
First 90-day Time-In-Range, TIR, % (3.9-10 mmol/L)	Mean ± SD	65.55 ± 9.52
First 90-day Time-Below-Range, TBR, %(<3.9 mol/L)	Mean ± SD	1.53 ± 1.06
First 90-day Time In Very Low-Range, %(<3 mol/L)	Mean ± SD	0.39 ± 0.60
Post-HCL Mean HbA1c (Paired), mmol/mol	Mean ± SD	56.01 ± 8.41
Pre-Post HbA1c difference, mmol/mol	Mean ± SD	16.49 ± 27.47

Conclusions: Hybrid closed-loop insulin delivery systems delivered substantial and clinically meaningful improvements in glycaemic control within a district general hospital setting, with achievement of recommended CGM targets and low exposure to hypoglycaemia. These real-world data demonstrate that HCL technologies can be implemented safely and effectively outside specialist tertiary centres. Our findings highlight the capability of DGH-based multidisciplinary teams to deliver high-quality, technology-enabled diabetes care, reinforcing the scalability and sustainability of HCL systems within national diabetes pathways. Continued longitudinal evaluation will clarify long-term outcomes and inform service planning.

Abstract citation ID: lvag096.348

P163 - ECE_3273 - Contemporary mortality rates in type 1 diabetes in the era of advanced therapeutic care: a large-scale healthcare registry study

Adi Vinograd[1], Shiraz Vered[2], Noah Levek[3], Neriya Levran[4], Liat Lev-Shalem[2], Gilad Twig[5,6] and Orit Pinhas-Hamiel[4,5]
[1]Ministry of Health, Israel center of disease control, Ramat-Gan, Israel; [2]Maccabi Healthcare, Tel Aviv-Yafo, Israel; [3]Juvenile Diabetes Center, Maccabi Healthcare, Raanana, Israel; [4]Pediatric Endocrine and Diabetes Center, Edmond and Lily Safra Children's Hospital, Ramat Gan, Israel; [5]Tel-Aviv, Israel; [6]Division of Endocrinology, Diabetes and Metabolism, Medical Center Dr. h Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel

Introduction: Technological advances enhancing glycemic control in type 1 diabetes have emerged over the past two decades, warranting an updated assessment of mortality in more recent cohorts.

Objective: To quantify all-cause mortality odds among individuals with type 1 diabetes compared with matches controls without diabetes and to assess temporal trends in mortality.

Methods: All individuals reported to the Type 1 Diabetes Registry of Maccabi Healthcare Services, between 2000 and 2022, and diagnosed before age 35 years, were included. Propensity score matching (1:4) was performed by sex and age to construct diabetes-free comparison cohort. Follow-up continued until 2023, death, or transfer to another provider, whichever occurred first. Logistic regression models were applied to estimate mortality odds.

Results: The study comprised 4299 individuals with type 1 diabetes and 17 196 matched controls (45.6% female; age 17.4 ± 9.1 years). During 204 102 person-years of follow-up, 112 deaths occurred, with incidence rates of 131.0 and 43.3 per 10^5 person-years among individuals with and without type 1 diabetes, respectively. Among decedents, age and BMI at death were comparable between groups. Type 1 diabetes was associated with higher mortality (OR of 3.90 (95% CI, 2.69-5.65) compared with matched controls, and this association remained consistent after adjustment. The association persisted when analyses were limited to individuals without pre-existing comorbidities or to those with a lean BMI. Females with type 1 diabetes exhibited higher mortality odds (aOR = 8.37; 95% CI, 3.18-22.04) than males (aOR = 2.49; 95% CI, 1.40-4.42), relative to matched controls. Individuals diagnosed earlier (2000-2010) had higher mortality odds than those diagnosed later (2011 and 2022), relative to period-matched controls.

Conclusions: Type 1 diabetes was associated with higher mortality odds, particularly among females. This association was attenuated among individuals diagnosed in more recent years.

Practical Implications: These findings highlight the importance of continued efforts and resources to improve overall diabetes management and glycemic control, which may contribute to

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

further reductions in mortality, particularly among females and individuals diagnosed in earlier calendar periods.

Abstract citation ID: lvag096.349

P165 - ECE_3802 - Beyond obesity: prevalence and correlates of underweight in 7-year-old children (WHO COSI 2008-2025)

Radka Taxová Braunerová, Markéta Vaňková, Tereza Svobodová, Tereza Metelcová and Josef Vcelak
Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic

Background: Childhood obesity represents a major global public health concern; however, underweight and thinness also pose significant risks to growth, development, health, and well-being. Many countries face a double burden of malnutrition, characterized by the coexistence of overweight and underweight within the pediatric population, yet data on childhood underweight in Europe remain limited. This study, part of the WHO Childhood Obesity Surveillance Initiative (COSI), aimed to evaluate factors associated with underweight in 7-year-old children.

Methods: We analyzed 11 307 Czech children aged 6.5-7.9 years from the COSI project (2008-2025). Anthropometric measurements included waist circumference, height, weight, and BMI. Underweight was defined as BMI-for -age standard deviation (SD) <−1, indicating children below the WHO reference range for normal weight. Children's guardians completed questionnaires on dietary habits, physical activity, family characteristics, and school environment. Data were analyzed using Chi-square tests (NCSS 2019) and multivariate regression with the O2PLS method (SIMCA).

Results: Overall, 18% of children were underweight, with no significant differences between boys and girls. An increasing trend in underweight prevalence was observed between 2008 and 2025, more pronounced in boys, although not statistically significant. Compared with normal-weight and overweight peers, underweight children consumed more fruits, vegetables, and high-fat milk, but also more chips. They participated less frequently in organized sports while reporting lower screen time. Mothers of underweight children had higher educational levels.

Conclusions: Underweight affects nearly one-fifth of 7-year-old czech children, highlighting that undernutrition remains a relevant public health issue alongside obesity. The coexistence of healthier dietary patterns with higher consumption of energy-dense foods, along with lower physical activity but reduced screen time, highlights the complexity of factors related to underweight. Higher maternal educational level among underweight children suggests that socioeconomic determinants should be considered when addressing undernutrition in childhood. Continued surveillance and targeted interventions are needed to address both undernutrition and overweight in children.

Funding: Supported by the Ministry of Health of the Czech Republic in cooperation with the Czech Health Research Council under project No. AZV NU23-09-00252 and project MH-CZ-DRO (EU00023761).

Abstract citation ID: lvag096.350

P166 - ECE_1502 - Insulin autoimmune syndrome—something to always keep in mind!

Angelos Theocharis[1], Sofia Chatzi[1], Angeliki Angelidou[1], Kanella Kantreva[1], Maria Gabriella Stathi[1], Elisavet Kontou[2], Alexandra Tsirogianni[2], Marinella Tzanela[1] and Georgia Ntali[1]
[1]Department of Endocrinology "D.Ikkos"—Diabetes Center, Endo-ERN, Nosokomeio Evangelismos, Athina, Greece; [2]Department of Immunology and Histocompatibility, Nosokomeio Evangelismos, Athina, Greece

Background: Insulin autoimmune syndrome (IAS), or Hirata's disease, is a rare hypoglycemic disorder characterized by spontaneous hypoglycemia without evidence of exogenous insulin administration, a high serum concentration of total immunoreactive insulin, and the presence of insulin autoantibodies in high titer. The majority of cases occur in the Asian population, and treatment is generally successful with watchful waiting or steroids.

Case Report: A 70-year-old female was admitted to the emergency room due to expressive aphasia. A capillary blood glucose of 35 mg/dL (confirmed later in laboratory) was detected so iv glucose solution was initiated resulting in clinical improvement and establishment of Whipple's Triad. The patient reported episodes of sweating, tremors, and palpitations that occasionally awakened her during the previous two weeks. She was a non-diabetic and had no history of exposure to insulin, insulin secretagogues or any drug known to precipitate hypoglycaemia. She had history of breast cancer but was disease-free. However, she reported a viral infection a month before the appearance of the symptoms and the occasional use of a supplement containing a-lipoic acid. After her admission endogenous hyperinsulinemic hypoglycemia was established as high insulin levels were measured in two occasions (episode 1: Glucose 45 mg/dl, Insulin 64,1 μU/ml, C-peptide 8,92 ng/ml—episode 2: Glucose 35 mg/dl, Insulin 61,3 μU/ml, C-peptide 13,3 ng/ml). Insulin autoantibodies (IAA) were markedly elevated: 65,2 U/ml (reference range 0,1-0,3 U/ml) (measured with radioimmunoassay methodology). A confirmatory test with chemiluminescence assay demonstrated again high levels of IAA >175IU/ml (<20). Findings in imaging with abdominal CT, MRI and 68Ga-DOTATATE PET/CT were unremarkable. Oral methylprednisolone 32 mg was initiated with subsequent resolution of the hypoglycemia. A continuous glucose monitoring (CGM) was placed to allow her to predict and respond to an imminent drop of blood glucose values and the patient was discharged. The dosage of methylprednisolone was gradually lowered. 6 months after the initial diagnosis IAA were still elevated 50,1 U/ml (reference range 0,1-0,3 U/ml). At the most recent follow-up the patient was asymptomatic under 4 mg of methyloprednisolone.

Conclusions: Insulin autoimmune syndrome, although rare, should always be considered as a diagnosis in a patient with hypoglycemia and endogenous hyperinsulinemia. Differential diagnoses of IAS include insulinoma and exogenous intake of insulin and sulphonylureas. Most cases of IAS are self-limiting, with gradual decrease of antibody titre and resolution of symptoms after removal of the trigerring factor.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.351

P167 - ECE_1564 - Glycemic control in type 2 diabetes patients in the context of humanitarian crisis in Ukraine: rescue therapy

Yeva Ilkiv[1,2], Viktoriia Yerokhovych[1], Oksana Sulaieva[3], Iuliia Komisarenko[1], Vitalii Gurianov[1], Ilona Rudnieva[1] and Nazarii Kobyliak[1,3]
[1]*Bogomolets National Medical University, Kyiv, Ukraine;* [2]*D. F. Chebotarev Institute of Gerontology of the National Academy of the Medical Sciences of Ukraine, Kyiv, Ukraine;* [3]*Medical Laboratory CSD, Kyiv, Ukraine*

Background/Introduction: Ukraine's situation is potentially the biggest migration crisis in Europe. As humanitarian crises become more widespread, chronic diseases such as type 2 diabetes mellitus (T2DM) are becoming increasingly important. Limited access to healthcare facilities, interrupted supply of hypoglycemic medications and economic hardship are just some of the many challenges faced by patients with T2DM. Therefore, it is necessary to develop strategies to improve glycemic control in humanitarian crises in order to provide effective and high-quality care to patients.

Purpose: to assess the effectiveness of different groups of antidiabetic drugs (ADD) under the conditions of a humanitarian crisis caused by war.

Methods: A total of 582 people with T2DM from all regions of Ukraine participated in the study. According to the hypoglycemic drugs taken by patients during martial law, the following treatment regimens were identified: 1—metformin, 2—sulfonylurea drugs, 3—metformin with sulfonylurea derivatives, 4—metformin with iDPP-4, 5—metformin with iSGLT-2, 6—triple combination of drugs. To assess the risk of elevated glycated hemoglobin (HbA1c) and the effectiveness of therapy with hypoglycemic drugs, patients were divided into two groups: group I—individuals without experience of military operations, occupation, forced resettlement ($n = 391$), group II—responders with experience ($n = 191$). For defining prognostic factors impacting T2D progression, logistic regression analysis and machine learning algorithms were applied.

Results: In group I, almost the same effect of all regimens was noted, which is close to 50% ($P = .740$); in group II the most effective was the variant with triple combination with sulfonylurea derivatives ($P = .012$). Univariate analysis for group II showed that the combination of metformin with sulfonylurea ($P = .04$) and the triple combination ($P = .001$) were more effective. Multivariate analysis show that the best results in terms of reducing HbA1c were obtained in respondents who took a triple combination ($P = .007$). The area under the curve was AUC 0.768 (95% CI 00.698—0.838).

Conclusions: sulfonylurea drugs demonstrated a significant positive effect for the control of diabetes in emergency situations, and their availability allows less well-off patients to purchase them and use during martial law and occupation.

Abstract citation ID: lvag096.352

P168 - ECE_1580 - Regulation of hypothalamic ketone metabolism and neuroinflammation by empagliflozin under metabolic stress

Joo Yeon Kim, Ji Hyun Bae, Min Jin Lee, Ah Reum Khang, Yang Ho Kang, Dong Hee Kim and Dongwon Yi
Yangsan, South Korea

Background and Aims: Sodium–glucose cotransporter 2 (SGLT2) inhibitors are widely used antidiabetic agents that improve systemic glucose homeostasis and induce weight loss primarily through enhanced urinary glucose excretion. Beyond their peripheral metabolic effects, emerging evidence suggests that SGLT2 inhibitors may also modulate central metabolic regulation in the brain. The hypothalamus is a key integrative center for energy balance and undergoes metabolic and inflammatory remodeling in response to chronic nutritional excess, such as high-fat diet (HFD)–induced obesity. In this context, astrocytes play a pivotal role by exhibiting metabolic reprogramming, including increased ketone body production, which can influence neuronal activity and neuroinflammatory responses. However, the effects of SGLT2 inhibition on hypothalamic ketone metabolism and neuroinflammation under metabolic stress remain poorly understood. The study investigates whether empagliflozin (EMPA), a selective SGLT2 inhibitor, modulates hypothalamic ketone metabolism and neuroinflammatory responses in an HFD-induced metabolic stress condition.

Materials and Methods: Mice fed a HFD were treated with EMPA, and hypothalamic expression of genes related to ketone body synthesis and inflammation was analyzed. Complementary in vitro experiments were performed using lipid-overloaded astrocytes treated with EMPA to assess inflammatory activation and metabolic alterations. Astrocyte–neuron co-culture and conditioned media experiments were conducted to evaluate the indirect effects of EMPA-treated astrocytes on neuronal viability under lipotoxic conditions.

Results: EMPA significantly attenuated HFD-induced upregulation of ketogenesis-related genes in the hypothalamus and reduced markers of glial inflammation. In vitro, EMPA suppressed inflammatory responses and improved metabolic homeostasis in lipid-overloaded astrocytes. Importantly, neurons exposed to conditioned media from EMPA-treated astrocytes exhibited enhanced survival under lipotoxic stress, indicating astrocyte-mediated neuroprotective effects.

Conclusions: EMPA modulates hypothalamic metabolic adaptation to nutritional excess by limiting maladaptive astrocytic ketone production and reducing inflammatory signaling. This central metabolic remodeling may contribute to neuronal protection and improved energy homeostasis, suggesting a previously underappreciated brain-centered mechanism underlying the actions of SGLT2 inhibition. These findings support further investigation into brain–periphery crosstalk in obesity and metabolic disease.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.353

P169 - ECE_2756 - Central-peripheral circadian misalignment: increased corticosterone levels in the inactive phase disrupt adipose BMAL1 and promote lipid accumulation in the obese rat model

Mariarosaria Negri[1,2], Feliciana Amatrudo[2], Nunzia Magnacca[1], Maria Anna Marciano[3], Cristina De Angelis[1], Chiara Simeoli[1], Erminio M. Crescenzo[1], Annamaria Colao[1,4], Raffaella Crescenzo[3], Rosario Pivonello[1,4] and Claudia Pivonello[5]

[1]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione—Università Federico II di Napoli, Naples, Italy; [2]Dipartimento di Psicologia e Scienze della Salute, Università Telematica Pegaso, Naples, Italy; [3]Department of Biology, Federico II University, Naples, Italy; [4]UNESCO Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy; [5]Dipartimento di Sanità Pubblica, Università degli Studi di Napoli Federico II, Naples, Italy

Circadian clocks regulate metabolic homeostasis by hierarchically synchronizing central and peripheral oscillators. Although obesity is associated with circadian dysfunction, the contribution of endocrine zeitgebers to central and peripheral clocks remains understood. The current study examined the effects of high-fructose/high-fat (Western) diet (WD) on circadian BMAL1 expression in rat hypothalamus and visceral adipose tissue (VAT), concomitantly with in vitro assessment of lipid accumulation. To induce obesity, sixty-day-old male Wistar rats were fed a four-week WD and compared with control rats fed a standard diet (SD). Serum, hypothalamus, and VAT samples were collected during early inactive (ZT3–5) and early active (ZT10–12) phases. BMAL1 and appetite-regulating neuropeptides hypothalamic, as well as BMAL1 and lipid-related markers VAT expression, were monitored by WB. Serum corticosterone, leptin and tryglicerides were measured by ELISA at both timepoints. Differentiated white adipocytes were subjected to Bmal1-knockdown to evaluate the role of Bmal1 on lipid accumulation and leptin production. Compared to SD, WD induced obesity with significantly increased body weight ($P = .01$) despite reduced food intake ($P = .001$). At both ZT3–5 and ZT10–12, hypothalamic BMAL1 expression was increased in obese rats (+68.7% and +65%, respectively) and was associated with higher POMC ($P = .007$) and reduced NPY protein expression (−21.30% and −71.25%, respectively), consistent with reduced food intake. In contrast, at ZT3–5, VAT BMAL1 expression was significantly reduced in obese rats ($P = .01$) and was associated with a significant increase in leptin protein expression ($P = .01$). At ZT10–12, VAT BMAL1 expression remained similarly low in both groups, whereas leptin expression was slightly increased in obese animals (+22.86%). These findings indicate that WD-induced alterations of adipose BMAL1 are observed during the inactive phase. At ZT3–5, corticosterone ($P = .03$), leptin ($P = .01$) and tryglicerides ($P = .01$) were significantly increased in obese rats, whereas at ZT10–12 no significant differences were observed between obese and control animals. Notably, corticosterone levels at ZT3–5 were inversely and significantly correlated with VAT BMAL1 expression ($P = .008$), indicating that higher circulating corticosterone was associated with lower VAT BMAL1 specifically during inactive phase. Consistently, Bmal1-knockdown (−64%) in adipocytes increased lipid accumulation ($P = .0002$) and leptin expression ($P = .02$). These findings demonstrate that abnormal glucocorticoid secretion during the inactive phase is associated with adipose BMAL1 rhythmicity disruption, promoting lipid accumulation and contributing to central-peripheral circadian misalignment in WD-induced obesity.

Abstract citation ID: lvag096.354

P170 - ECE_3407 - Hybrid closed-loop insulin systems improve hypoglycemia and insulin sensitivity with favorable effects on FIB-4 in poorly controlled type 1 diabetes

Maria Apostolopoulou[1,2], Dimitra Pappa[2], Stefanos Tamouridis[2] and Alexandra Bargiota[1,2]

[1]Larissa, Greece; [2]Department of Endocrinology and Metabolic Diseases, University Hospital of Larissa, Larissa, Greece

Background and Aims: Obesity and insulin resistance represent a rising burden in individuals with type 1 diabetes (T1D) and are associated with metabolic dysfunction–associated fatty liver disease (MAFLD). Hybrid closed-loop systems (HCLS) lead to better glycemic control and reduced insulin requirements compared to multiple daily injections (MDI) and open-loop systems. The aim of the present analysis is to compare glycemia, body weight, total daily dose (TDD) and indices related to MAFLD and liver fibrosis in patients initially on MDI or open-loop systems and after initiation of HCLS.

Methods: We studied individuals with T1D previously on MDI and open-loop systems at baseline (tA) and 6 months (tB) after hybrid-closed loop CSII initiation (Medronic 780 G, Medrum), who visited our outpatient clinic. Continuous glucose monitoring (CGM) metrics- time in range (TIR), time above range (TAR), time below range (TBR) and time below 54 mg/dl (TBR <54), HbA1c, BMI and TDD were analyzed.

Results: A total of 53 patients were included. At tA: 36/53 on MDI, 17/53 on open-loop systems with a mean age: 43.3 ± 15.8 years, BMI: 27.3 ± 6.3 kg/m^2, HbA1c 7.8 ± 1.3%, and diabetes duration 20 ± 12 years, without known history of liver disease. At tB they had lower TBR <54 (B: 0.15 ± 0.04 vs A: 0.45 ± 0.1%, $P = .02$) and a trend towards reduced TBR (B: 0.9 ± 0.7 vs A: 1.9 ± 0.2%, $P = .07$). TDD was lower after 6 months (B: 53.5 vs A: 50.5 IU, $P = .02$), consistent with improved insulin sensitivity. TIR, HbA1c and BMI remained unchanged. In 8 patients with available liver enzyme tests at both tA and tB, FIB-4 score showed a significant reduction (B: 0.90 ± 0.48 vs A: 0.91 ± 0.51, $P = .03$), while hepatic steatosis index remained unchanged.

Conclusions: HCLS initiation led to better glucose metabolism, lower TBR <54 and lower TDD at 6 months. Preliminary findings suggest beneficial effects on markers of liver fibrosis, which warrant further investigation and longer-term follow-up.

Abstract citation ID: lvag096.355

P172 - ECE_3990 - JUV-161 reverses skeletal muscle myopathy and functional decline in a translational model of myotonic dystrophy type 1

Ashil Koranne, Hee Ju Kim, Ritwik Datta, Vengadeshprabhu Karuppagounder, Han Song, Thach Mai, Zhihua Li, Banmeet Anand, Colin Hislop, Priya Handa, Hanadie Yousef and Jeremy O'connell

Juvena Therapeutics.Inc, Redwood City, United States

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Myotonic dystrophy type 1 (DM1) is a multisystemic neuromuscular disorder caused by toxic CUG repeat expansions in the 3′ untranslated region (UTR) of the DMPK gene, leading to progressive skeletal muscle weakness, myopathy, and functional decline. Despite substantial unmet clinical need, therapeutic development for DM1 has been limited by the lack of preclinical models that faithfully recapitulate the systemic pathology and functional impairments observed in patients.

At Juvena Therapeutics, we have developed a biologics-based drug discovery platform focused on identifying stem-cell secreted proteins capable of restoring tissue health. This platform led to the identification of JUV-161, a novel secreted protein engineered to enhance muscle regeneration and functional repair. To enable translational evaluation of JUV-161 in DM1, we developed the panCUG960/+ mouse model, a murine system that integrates key genotypic, phenotypic, and functional hallmarks of human DM1 within a single animal. The panCUG960/+ mouse harbors an expanded CUG repeat in the 3′ UTR of the DMPK gene, resulting in accumulation of nuclear RNA foci and widespread splicing abnormalities. These molecular defects drive canonical DM1-associated histopathologic changes accompanied by progressive functional deficits closely mirroring the clinical trajectory in patients with DM1.

Using this translationally relevant model, we evaluated the therapeutic efficacy of JUV-161. PanCUG960/+ mice received daily subcutaneous administration of JUV-161 at a dose of 12 mg/kg for 21 days. Treatment with JUV-161 significantly improved gastrocnemius muscle mass (180 mg vs 160 mg in vehicle, $P <$ .01) and tibialis anterior muscle cross-sectional area (1.92E3 μm^2 vs 1.82E3 μm^2, $P <$ .01) in male mice. Furthermore, treated animals demonstrated significant improvement in both specific forelimb grip strength (28.5 mN/g vs 23.2 mN/g in vehicle; $P <$ .01) and all-limb grip strength (66.4 mN/g vs 56.1 mN/g in vehicle; $P <$ .001). In contrast, vehicle-treated mice showed a steady decline in grip strength over the 3-week treatment period, indicating meaningful restoration of functional capacity with JUV-161. JUV-161 treatment also significantly lowered non-fasting blood glucose levels relative to baseline compared with vehicle treatment (−8.74% vs −0.04% in vehicle, $P <$ .05).

In conclusion, JUV-161 reverses both structural and functional manifestations of skeletal muscle myopathy in a robust and disease-relevant model of DM1. These findings support JUV-161 as a promising therapeutic candidate for treating DM1 and related muscle-wasting conditions.

Abstract citation ID: lvag096.356

P173 - ECE_3329 - Beyond steatosis grade: hepatic parenchymal heterogeneity on ultrasound as a marker of metabolic deterioration

Merve Şenay Özçalık, Deniz Türküm Atikcan, Ece Gül Köse Hamidi, Ozlem Turhan Iyidir, Asli Nar and Neslihan Başçıl Tütüncü
Endocrinology and Metabolism, Baskent University, Ankara, Türkiye

Background: Metabolic dysfunction–associated steatotic liver disease (MASLD) is increasingly recognized as a multisystem disorder closely linked to cardiometabolic morbidity. Ultrasonography (US) is widely used for the detection and grading of hepatic steatosis; however, the clinical relevance of hepatic fat distribution patterns beyond steatosis severity remains insufficiently defined. We hypothesized that ultrasonographic hepatic parenchymal heterogeneity reflects more advanced metabolic impairment. This study aimed to evaluate the association between hepatic steatosis distribution patterns and metabolic abnormalities in diabetic and non-diabetic individuals.

Methods: A total of 527 adults who underwent upper abdominal ultrasonography in 2025 were retrospectively analyzed. Hepatic steatosis was graded from stage 0 to 3, and parenchymal distribution was classified as homogeneous or heterogeneous. Anthropometric measurements and biochemical parameters obtained at the time of imaging were assessed, including body mass index (BMI), waist circumference, fasting plasma glucose, HbA1c, liver enzymes, lipid profile, and spot urine albumin-to-creatinine ratio. Participants were categorized as diabetic, prediabetic, or non-diabetic based on glycemic status.

Results: The mean age of the cohort was 55.4 ± 16.8 years; 33.8% were diabetic, 16.1% prediabetic, and 50.1% non-diabetic. Hepatic steatosis was absent in 36.2% of patients, while 26.4%, 29.0%, and 8.3% had stage 1, 2, and 3 steatosis, respectively. A heterogeneous parenchymal pattern was identified in 22.4% of cases. The prevalence of heterogeneous steatosis was significantly higher among diabetic patients and increased progressively with worsening glycemic status ($P = .003$). Steatosis severity was also strongly associated with parenchymal heterogeneity ($P < .001$). Patients with heterogeneous hepatic parenchyma exhibited significantly higher BMI, waist circumference, fasting glucose, ALT, and triglyceride levels, along with lower HDL cholesterol concentrations (all $P < .01$), compared with those showing a homogeneous pattern.

Conclusions: This study shows that heterogeneous hepatic parenchymal patterns on routine ultrasonography are linked to adverse metabolic features in both diabetic and non-diabetic individuals, underscoring the importance of steatosis distribution beyond severity alone.

Abstract citation ID: lvag096.357

P174 - ECE_1521 - Associations of skeletal muscle mass and muscle strength with arterial stiffness in patients with type 2 diabetes mellitus

Naoki Koike[1,2], Yuji Doi[1], Ryosuke Kemmotsu[1], Moe Kusushita[1], Yasuna Sakai[1], Tomonori Okita[1], Hiroyuki Sho[1], Ryoko Inui[1], Yoko Irie[1], Yukiko Tabuchi[1], Tunehiko Yamamoto[3] and Tetsuyuki Yasuda[1]
[1]Osaka, Japan; [2]Osaka International Medical & Science Center(Osaka Keisatsu Hospital), Osaka, Japan; [3]Hyogo, Japan

Background: Arterial stiffness is a major determinant of cardiovascular disease in patients with type 2 diabetes mellitus (T2DM). Brachial–ankle pulse wave velocity (baPWV) is a widely used, noninvasive measure of arterial stiffness and a strong predictor of cardiovascular events. Sarcopenia-related traits, including reduced skeletal muscle mass and muscle strength, are highly prevalent in T2DM; however, their vascular relevance remains incompletely understood. In particular, evidence linking skeletal muscle characteristics to baPWV as an intermediate vascular

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

phenotype in T2DM is limited. We therefore examined the associations of skeletal muscle mass index (SMI) and handgrip strength with baPWV in patients with T2DM.

Methods: This single-center, retrospective cross-sectional study included consecutive patients with T2DM admitted to our hospital between 2021 and 2024. Skeletal muscle mass was assessed by bioelectrical impedance analysis, and SMI was calculated as appendicular skeletal muscle mass divided by height squared. Muscle strength was evaluated using handgrip strength. Arterial stiffness was assessed using baPWV. Multivariable linear regression analyses were performed with baPWV as the dependent variable. To avoid multicollinearity, SMI and handgrip strength were entered into separate models adjusted for age, sex, mean arterial pressure, diabetes duration, smoking status, history of cardiovascular disease, glycated hemoglobin, estimated glomerular filtration rate, and body mass index.

Results: A total of 281 patients were analyzed (mean age 64.1 ± 15.1 years; 68.4% men). In univariate analyses, both SMI and handgrip strength were significantly and inversely correlated with baPWV. These associations remained significant after multivariable adjustment for established cardiovascular risk factors. Higher SMI was independently associated with lower baPWV ($\beta = -115.1$ cm/s per 1 kg/m^2, $P = .003$). Likewise, greater handgrip strength was independently associated with lower baPWV ($\beta = -12.2$ cm/s per 1 kg, $P < .001$).

Conclusions: Both SMI and handgrip strength were independently associated with arterial stiffness in patients with T2DM. Consistent with observations in the general population, these findings suggest arterial stiffness as a potential vascular link between skeletal muscle health and cardiovascular risk in T2DM. Future large-scale prospective studies are warranted to confirm these associations and clarify their clinical implications.

Abstract citation ID: lvag096.358

P176 - ECE_3752 - Evaluation of ChatGPT-5 utility in managing diabetes-related comorbidities

Özge Baş Aksu, Fatma Tuğçe Şah Ünal and Rifat Emral
Department of Endocrinology and Metabolism, Ankara University Faculty of Medicine, Ankara, Türkiye

Objective: With the increasing prevalence of AI-generated healthcare content, evaluating its reliability and quality is critical. This study assessed the readability, content quality, and reliability of ChatGPT-5 responses to clinical case scenarios for diabetes comorbidity management.

Methods: Five major diabetes comorbidities—dyslipidemia, obesity, metabolic dysfunction-associated steatotic liver disease [MASLD], hypertension, and nephropathy—were represented by clinical cases. Five questions were evaluated for each case, assessing risk assessment, treatment goals, treatment recommendations, second-line strategies, and follow-up plans. Three independent endocrinologists assessed ChatGPT-5 responses using the Modified DISCERN (mDISCERN) for reliability and the Diabetes Comorbidity Management Scale (DCMS) for content quality. Reliability was categorized as poor (0-2, 0%-40%), moderate (3, 60%), or strong (4-5, 80%-100%). Content quality was classified as low (0-11, <50%), moderate (12-17, 52%-74%), or high (18-23, 78%-100%). Readability was measured using the Flesch-Kincaid Grade Level (FKGL), Gunning Fog Index, and Flesch Reading Ease (FRE) tests. Inter-rater agreement was determined by the intraclass correlation coefficient (ICC).

Results: ChatGPT-5 achieved moderate reliability (mDISCERN: 3.2 ± 0.4; 64%) and high content quality (DCMS: 19.1 ± 1.7; 83%). Inter-rater agreement was excellent for DCMS (ICC = 0.89; 95% CI: 0.68-0.98; $P < .001$) and moderate for mDISCERN (ICC = 0.57; $P = .019$). The highest performance was observed in nephropathy (87%) and obesity (88%) cases, while MASLD cases demonstrated the lowest performance (75%). Among evaluated domains, risk assessment (96%) and treatment goals (90%) received the highest scores, whereas treatment recommendations (70%) and second-line strategies (73%) received the lowest. Readability analysis indicated that responses required education above the high-school level (FKGL: 11.3; FRE: 27.5).

Conclusions: ChatGPT-5 demonstrates high performance, particularly in risk assessment and goal-setting for diabetes comorbidity management, but shows limitations in specific treatment recommendations and in complex cases. Clinicians may use it as a supportive tool to confirm risk assessments and establish treatment goals; however, expert judgment remains essential for detailed treatment planning and complex clinical scenarios.

Abstract citation ID: lvag096.359

P177 - ECE_1410 - Glucagon-like peptide-1 receptor agonists vs sodium–glucose cotransporter-2 inhibitors and risk of incident asthma in patients with diabetes: a real-world cohort

Wan-Ting Huang[1], Yi-Tzu Wu[2], Wei Chuan Chang[1], Ching-Hui Loh[3,4] and Huei-Kai Huang[1,3,5]
[1]Center for Clinical Epidemiology and Biostatistics, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan; [2]Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan; [3]School of Medicine, Tzu Chi University, Hualien, Taiwan; [4]Center for Aging and Health, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan; [5]Hualien, Taiwan

Background: Diabetes mellitus is characterized by metabolic dysregulation and systemic low-grade inflammation and is associated with an increased risk of asthma. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have potential pulmonary and immunomodulatory effects, but existing evidence regarding their association with asthma remains inconsistent and has largely focused on patients with pre-existing asthma. The risk of incident asthma associated with GLP-1 RA use in patients with diabetes therefore remains unclear.

Objectives: To investigate the association between GLP-1 RAs and the risk of incident asthma in patients with diabetes mellitus, using sodium–glucose cotransporter-2 inhibitors (SGLT2is) as an active comparator.

Methods: Using the TriNetX U.S. Collaborative Network (2015-2024), we conducted a real-world cohort study of adults with diabetes initiating GLP-1 RAs or SGLT2is under a new-user, active-comparator design within a target trial emulation framework. Patients with prior exposure to either drug class, concomitant use, or pre-existing asthma or chronic pulmonary diseases

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

were excluded. Cohorts were balanced using propensity score matching on demographics, comorbidities, medication history, and laboratory data. For each GLP-1 RA agent, a separate matched cohort was constructed and analyzed. Cox proportional hazards models were applied to estimate the risk of incident asthma.

Results: After propensity score matching, 204 650 patients were included in each cohort. Overall, GLP-1 RA use was associated with a higher risk of incident asthma compared with SGLT2i use (hazard ratio [HR], 1.18; 95% confidence interval [CI], 1.14-1.22). Age- and sex-stratified analyses showed consistent trends toward a higher asthma risk among GLP-1 RA users across strata. In analyses of individual GLP-1 RAs, significantly increased risks of incident asthma were observed for exenatide (HR, 1.28; 95% CI, 1.09-1.50), liraglutide (HR, 1.25; 95% CI, 1.16-1.35), and dulaglutide (HR, 1.08; 95% CI, 1.03-1.14). In contrast, tirzepatide was associated with a significantly lower risk of incident asthma compared with SGLT2is (HR, 0.57; 95% CI, 0.51-0.65).

Conclusions: GLP-1 RA use was associated with an overall increased risk of incident asthma compared with SGLT2is; however, the association varied across individual GLP-1 RA agents, with several agents showing increased risks and tirzepatide demonstrating a lower risk. These findings highlight clinically relevant heterogeneity within the GLP-1 RA class regarding asthma risk and suggest a potential safety signal that warrants further investigation.

Abstract citation ID: lvag096.360

P178 - ECE_1547 - Sustained glycaemic benefits of a single intermittently scanned continuous glucose monitoring use in non-insulin-treated patients with type 2 diabetes: a randomised study

Ohk-Hyun Ryu
Endocrinology and Metabolism, Internal Medidine, Hallym University, College of Medicine, Chuncheon, South Korea

Background: Intermittently scanned continuous glucose monitoring (isCGM) has been shown to improve glycaemic control and promote behavioural change in people with diabetes. However, most evidence derives from insulin-treated populations or repeated CGM use. The potential for a single, short-term isCGM exposure combined with structured education to induce sustained glycaemic and behavioural benefits in non-insulin-treated patients with type 2 diabetes remains unclear.

Objectives: To evaluate the effects of a single 2-week isCGM use with structured education on glycaemic control, diabetes self-care, and treatment satisfaction, to assess the additional impact of short message service (SMS)-based feedback, and to identify factors associated with short-term glycaemic improvement.

Methods: Patients with type 2 diabetes managed with oral antidiabetic drugs or lifestyle modification (HbA1c 7.0%-8.9%) were enrolled. All participants wore an isCGM device (FreeStyle Libre) for two weeks and received standardised education on CGM interpretation and lifestyle-based glucose management. Participants were randomly assigned to a CGM-only group or a CGM plus SMS-feedback group.

HbA1c was measured at baseline, 10-12 weeks, and 24 weeks. Diabetes self-care behaviours and diabetes treatment satisfaction (DTSQ total score) were assessed at baseline and at 10-12 weeks only. Multivariable linear and logistic regression analyses were performed to identify determinants of HbA1c improvement at 10-12 weeks.

Results: Sixty-two participants completed the study (31 per group). Baseline characteristics were comparable between groups. At 10-12 weeks, HbA1c decreased significantly from baseline in the overall cohort; however, no significant difference was observed between the CGM-only and CGM + SMS groups ($-0.38\% \pm 0.63\%$ vs $-0.41\% \pm 0.70\%$, $P = .833$). Improvements in diabetes self-care domains and DTSQ scores were observed in both groups without between-group differences.

In multivariable analysis, higher scan frequency was independently associated with greater HbA1c reduction at 10-12 weeks ($\beta \approx -.26\%$ per scan-frequency category increase, $P = .021$), whereas intervention assignment was not. At 24 weeks, HbA1c remained significantly lower than baseline in the overall cohort, with no difference between groups.

Conclusions: A single short-term use of isCGM combined with structured education resulted in clinically meaningful and sustained reductions in HbA1c over 24 weeks in non-insulin-treated patients with type 2 diabetes. SMS-based feedback did not provide additional benefit beyond CGM use alone. Frequent glucose scanning emerged as a key determinant of short-term glycaemic improvement, highlighting the central role of patient engagement in CGM-based diabetes management.

Abstract citation ID: lvag096.361

P179 - ECE_2834 - Secondary prevention of type 1 diabetes using oral vitamin D receptor agonists: fifteen-year outcomes from the PRECAL study

Dimitrios Papadimitriou[1], Eleni Dermitzaki[1], Rodis Paparodis[2], Ioanna Grivea[1] and George Mastorakos[3]
[1]*Pediatric Endocrinology, Pediatrics, University of Thessaly, Larisa, Greece;* [2]*Hellenic Endocrine Network, Athens, Greece;* [3]*Endocrinology, Aretaieion University Hospital, Athens, Greece*

Background: Type 1 diabetes (T1D) affects approximately 1 in 300 individuals, with a steadily increasing incidence, particularly in early childhood. Population-based screening for T1D-associated autoantibodies (T1Abs) at key ages has demonstrated high sensitivity, yet an effective, scalable strategy for secondary prevention remains unavailable. Vitamin D has immunomodulatory properties, and early-life supplementation has been associated with a markedly reduced risk of T1D. In the absence of widely available antigen-specific immunotherapies, vitamin D receptor agonists represent a potential intervention to modify disease progression following seroconversion https://pubmed.ncbi.nlm.nih.gov/39834215/.

Methods: Following an initial pilot trial of T1Ab negativization under oral calcitriol https://pubmed.ncbi.nlm.nih.gov/23302101/, the PRECAL study (ISRCTN17354692) was initiated as a prospective, interventional, non-randomized clinical trial https://pubmed.ncbi.nlm.nih.gov/37238410/. We now report 15-year outcomes in 103 children (age 0.65-16.37 years) identified as being at high risk for T1D. Ninety-seven were T1Ab-positive, while six were T1Ab-negative but carried high-risk HLA-DQ/DR genotypes. At enrollment, 9 children had impaired glucose tolerance, 4 met criteria for pre-T1D, and 10 had newly

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

diagnosed T1D. Participants received oral calcitriol (0.05 μg/kg/day) or paricalcitol (0.15 μg/kg/day). Autoantibodies, glycemic indices, C-peptide, calcium–phosphate metabolism, vitamin D metabolites, and renal imaging (when indicated) were monitored every 3-6 months.

Results: Eighty-one participants had evaluable follow-up data. Fifty-four children achieved complete negativization of T1Abs within a median of 0.56 years (range 0.32-1.9). All HLA-positive/T1Ab-negative participants remained diabetes-free during follow-up. Among children with pre-T1D, two progressed to overt T1D, while the remainder either negativized T1Abs or remained progression-free. Of those presenting with new-onset T1D, six experienced partial or complete remission lasting up to two years, and one remains in remission after 2.9 years despite persistent autoantibody positivity. Relapse of autoantibodies occurred in seven children and resolved after treatment re-initiation. Transient hypercalciuria or hypercalcemia occurred in ten cases, including one reversible nephrocalcinosis, managed with dose adjustment or discontinuation.

Conclusions: Oral calcitriol and paricalcitol were effective in inducing T1Ab negativization and delaying or preventing progression to clinical T1D in a substantial proportion of high-risk children, with acceptable safety. These findings support vitamin D receptor agonists as promising candidates for secondary prevention of T1D, particularly when initiated soon after seroconversion.

Abstract citation ID: lvag096.362

P180 - ECE_3664 - Disease burden and long-term outcomes in a monocentric cohort of adults with glycogen storage diseases

Luis Baena Ariza, Elena Dios, Silvia Torres Degayon, Rosa Benitez Avila, Alfonso Soto and Eva Venegas Moreno
Clinical Management Unit of Endocrinology and Nutrition, Virgen del Rocio University Hospital, Sevilla, Spain

Study Objective: Cross-sectional descriptive study on the characteristics of a cohort of patients with glycogen storage diseases under active follow-up at the Adult Metabolic Disorders Unit of Virgen del Rocio University Hospital (HUVR).

Material and Methods: Demographic (age, sex) and anthropometric (weight, body mass index [BMI]) data were collected. Variables recorded included specific glycogenosis type, associated comorbidities (cardiac, hepatic, renal, muscular, metabolic), degree of metabolic control, and current treatment (diet, oral nutritional supplements, cornstarch).

Results: We included 10 patients: 4 females, mean age 35 ± 4 years, median age at diagnosis 3 years (range 1-30). BMI was 26 ± 5.9 kg/m^2: 6 normal weight, none overweight, and 4 with grade I obesity.

The identified glycogenoses were: 4 type IIIa (AGL gene), 2 type IXb (PHKB gene), 1 type IXa (PHKA2 gene), 1 type Ib (SLC37A4 gene), 1 type II (Pompe disease, GAA gene), and 1 type V (McArdle disease, PYGM gene).

The most frequent comorbidity was hypertrophic cardiomyopathy, present in 3/4 type IIIa patients, followed by Crohn's-like inflammatory bowel disease in 2 patients (one type Ib and one type IXb). Only one patient (type V) had renal involvement.

Muscular involvement was observed in 8 patients (excluding the type Ib and one type IXa), with persistent elevation of muscle enzymes in 5 of them (all 4 type IIIa and the type V). Three patients had hepatic fibrosis and 2 had hepatic steatosis.

Laboratory analysis showed a mean LDL-c of 120 ± 34 mg/dL and mean triglycerides of 131 ± 57 mg/dL. Lactate levels remained <2 mmol/L in all patients. During follow-up, there was one death (one type IIIa patient).

Hypoglycemia was present in 7 out of 10 patients, all effectively prevented with daily cornstarch intake.

All patients followed a fractionated diet, and 6 additionally required protein supplements to meet daily protein intake targets.

Conclusions: Our cohort showed a higher prevalence of glycogenosis type III than reported in the literature (4/10), confirming its characteristic muscular and cardiac involvement. Compared to other metabolic disorder cohorts at our center, the degree of obesity was lower, despite a high proportion of hypoglycemia.

The lipid profile was acceptably within target and untreated, compared to literature descriptions. The age at diagnosis was heterogeneous, though most cases were concentrated in early childhood.

Abstract citation ID: lvag096.363

P182 - ECE_3446 - Roflumilast effectiveness in Greek COPD patients with obesity: a subgroup analysis of the ARGO real-life study

Konstantinos Porpodis[1], Stavros Tryfon[2], Efthymia Papadopoulou[2], Nikolaos Angelis[3], Vasiliki Paraskeva[4], Maria Bertoli[4], Polyanthi Papanastasiou[4], Alexandros Gkinis[4] and Konstantinos Kostikas[5]
[1]*Pulmonary Department, George Papanikolaou Hospital, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece;* [2]*Pulmonary Department (NHS), George Papanikolaou General Hospital of Thessaloniki, Thessaloniki, Greece;* [3]*Private Pulmonary Site, Thessaloniki, Greece;* [4]*Medical Department, ELPEN Pharmaceutical Co. Inc., Athens, Greece;* [5]*Respiratory Medicine Department, University of Ioannina, Ioannina, Greece*

Background: Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease frequently coexisting with obesity, which may adversely affect symptoms, severity and disease management. The relationship between body weight and COPD is non-linear, with increased mortality risk observed at both extremes of body mass index (BMI). This subgroup analysis of the ARGO study aimed to evaluate roflumilast effectiveness on dyspnea, health-related quality of life (HRQoL) and lung function in patients with severe COPD and obesity in a real-world setting.

Methods: ARGO was a multicenter, non-interventional, observational study conducted in Greece (NCT05426915). Among 750 patients with severe COPD, 299 obese patients were stratified according to World Health Organization (WHO) obesity classes (Class I-III). Patients were evaluated at baseline (V_0) and after 3 (V_1), 6 (V_2), and 12 (V_3) months of treatment with roflumilast. Dyspnea was assessed using the modified Medical Research Council (mMRC) scale, HRQoL using the validated Greek version of the Clinical COPD Questionnaire (CCQ) and lung function by Forced Expiratory Volume in 1 second (FEV_1) % predicted.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: Across all obesity classes, dyspnea severity demonstrated a notable shift from higher (mMRC grades 4-3) to lower (grades 2-1) levels during follow-up. The same trend was observed in the total study population. HRQoL improved significantly in all obesity subgroups, exceeding the minimal clinically important difference (MCID > 0.4) at 3, 6 and 12 months of follow-up ($P < .001$). Mean CCQ scores progressively decreased from baseline to 12 months in Obesity Class I (3.40 ± 1.05 to 2.14 ± 1.08), Class II (3.62 ± 0.96 to 2.45 ± 0.97), and Class III (4.28 ± 1.04 to 2.45 ± 1.13). Lung function also showed clinically meaningful improvement, with FEV_1 increase (MCID≥0.1L) at 6 and 12 months across all obesity classes. Similar improvements in CCQ ($\Delta V_0–V_3 = -1.24$, $P < .001$) and FEV_1% predicted ($\Delta V_0–V_3 = +5.7$, $P < .001$) were observed in the total study population.

Conclusions: The ARGO study showed that treatment with roflumilast contributes to the reduction of dyspnea severity and leads to a clinically significant improvement in HRQoL and lung function both in obese patients with severe COPD, irrespective of obesity class, and in the total study population.

Abstract citation ID: lvag096.364

P185 - ECE_1552 - Preserved arginine-stimulated glucagon secretion despite profound β-cell failure in immune checkpoint inhibitor–induced type 1 diabetes: a case series

Ryosuke Kemmotsu[1,2], Yuji Doi[3], Naoki Koike[3], Moe Kusushita[3], Yasuna Sakai[3], Hiroyuki Sho[3], Tomonori Okita[3], Ryoko Inui[3], Yukiko Tabuchi[3], Masahiro Hatazaki[1] and Tetsuyuki Yasuda[3]

[1]Department of Diabetes and Endocrinology, Osaka Acute and General Medical Center, Osaka Prefectural Hospital Organization, Osaka City, Japan; [2]Department of Diabetes, Endocrinology and Metabolism, Osaka International Medical & Science Center(Osaka Keisatsu Hospital), Osaka, Japan; [3]Osaka International Medical & Science Center(Osaka Keisatsu Hospital), Osaka, Japan

Background: Immune checkpoint inhibitor–induced type 1 diabetes (ICI-T1D) is characterized by abrupt and near-complete β-cell failure and represents a rare immune-related adverse event. Pathological studies suggest relative preservation of pancreatic α-cells in ICI-T1D, yet human functional data on α-cell responsiveness remain limited. We evaluated arginine-stimulated glucagon secretion (ASGS) in patients with ICI-T1D.

Methods: Five consecutive patients who developed insulin-dependent diabetes after immune checkpoint inhibitor therapy underwent an intravenous arginine stimulation test (30 g) under fasting conditions while continuing basal insulin therapy. Plasma glucose, C-peptide, and glucagon (sandwich ELISA) were measured at 0, 15, 30, 60, 90, and 120 minutes. Peak glucagon, peak-to-baseline increment (Δglucagon), and incremental area under the curve from 0 to 120 minutes ($iAUC_{0–120}$) were calculated. Six tests were performed, including repeat testing five months apart in one patient.

Results: The cohort included four men and one woman aged 61-76 years treated with PD-1/PD-L1 inhibitors with or without CTLA-4 blockade for solid malignancies. Most patients presented with diabetic ketoacidosis or severe hyperglycemia. Testing was performed early after onset (10-17 days in three patients) and in long-standing ICI-T1D (approximately 6 years in two patients). Baseline plasma glucose ranged from 107 to 194 mg/dL. C-peptide was undetectable (<0.01 ng/mL) in four of six tests and minimally detectable in the remaining two. In contrast, glucagon increased in all tests from baseline levels of 5.9-71.7 pg/mL to peaks of 95.6-202 pg/mL at 15-30 minutes. Δglucagon ranged from 89.7 to 168.0 pg/mL, and median $iAUC_{0–120}$ was 5453 pg/mL·min (range 4556-7665). In the longitudinally assessed patient, peak glucagon responses were similar at both time points.

Conclusions: In this case series of ICI-T1D, arginine-stimulated glucagon secretion was consistently observed despite profound β-cell failure, suggesting relative preservation of α-cell responsiveness to non-glycemic stimulation. These functional findings align with pathological observations of α-cell preservation in ICI-T1D. Larger longitudinal and comparative studies, including assessment under hypoglycemic conditions, are warranted to clarify determinants, temporal dynamics, and clinical relevance of α-cell function in ICI-T1D.

Abstract citation ID: lvag096.365

P186 - ECE_1909 - Discordance between glycated haemoglobin (Hba1c) and glucose management indicator (Gmi) in type 1 diabetes mellitus—a comphrehensive analysis of multiple factors

Kaushiki Kirty[1], Kamal Abouglila[2] and Srikanth Mada[1]

[1]Endocrine and Diabetes, University hospital of North Durham, Durham, United Kingdom; [2]Durham, United Kingdom

Introduction: With the management of type 1 DM becoming more technology-centric, especially since the emergence of the COVID-19 pandemic, it is important for clinicians to be aware of the practical issues in the interpretation of data from continuous glucose monitoring systems (CGM). Glucose management indicator (GMI) is a measure of mean glucose from CGM and is increasingly being used as a substitute for Glycated haemoglobin (HbA_{1C}).

Background: Several studies have shown varying rates of concordance between HbA_{1C} and GMI. One of the first and very high-impact studies, which shows minimal discordance, has looked at a future where CGM metrics might be the major glucose management tool. On the other hand are studies, that show significantly higher rates of discordance, recommending caution in substituting accepted markers such as HbA_{1C} with CGM metrics. In these uncertain times, it is important that clinicians have confidence that parameters derived from CGM are an acceptable surrogate for standard biomarkers such as HbA_{1C}.

Materials and Methods: We carried out a retrospective, consecutive study of 66 patients of type 1 DM to assess the concordance rates between HbA_{1C} and GMI to assess if HbA_{1C} is a robust marker to predict glycaemic control in a real-world setting of patients using Freestyle LIBRE and to analyse factors that are associated with the significant discordance levels seen between the measurements.We analysed the data downloaded from the online LIBRE systems as well as the medical records stored on the CDDFT trust database. The patients were analysed in a sequential manner as they appeared on the LIBRE database. The HbA_{1C} and GMI were calculated in mmol/mol. The formula for calculating GMI was as follows: GMI = 12.71 + 4.70587x (mean glucose in mmol/L/) (1)

Results and Conclusions: Out of 66 patients, 28 were women and 38 were men. Clinically significant discordance (a difference of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

5.5 mmol/mol being equal to a discordance of 0.5% and 11 mmol/mol being a discordance of 1%) was found in 33.33% of the patient population (22 patients out of 66). Linear regression performed using an online tool showed that there is no significant discordance between HbA_{1C} and GMI in our patient population. Prediction interval plot had R-squared (R^2) equal to 0.7435, showing that 74.3% of the variability of GMI is explained by HbA_{1C}. Correlation (R) was found to be 0.8623. This showed that there is a very strong direct relationship between HbA_{1C} and GMI.

Abstract citation ID: lvag096.366

P188 - ECE_1049 - Clinical and ultrasound markers in familial partial lipodystrophy type 1: contribution to the phenotypic definition of Köbberling syndrome

Everardo J. Díaz-López[1,2], Antia Fernández-Pombo[1,2], Teresa Prado-Moraña[1,2], Ana I. Castro[1], Silvia Cobelo-Gómez[2], Sofía Sánchez-Iglesias[2] and David Araújo-Vilar[1,2]

[1]*Division of Endocrinology and Nutrition, University Clinical Hospital of Santiago de Compostela, Santiago de Compostela, Spain;* [2]*Unidade de Enfermedades Tiroideas e Metabólicas (UETeM)-Molecular Pathology Group, Department of Psychiatry, Radiology, Public Health, Nursing and Medicine, Center for Research in Molecular Medicine and Chronic Diseases (CIMUS), Santiago de Compostela, Spain*

Introduction: Familial Partial Lipodystrophy Type 1 (FPLD1), also known as Köbberling syndrome, is an underrecognized polygenic disorder characterized by selective loss of subcutaneous fat in the limbs, accompanied by redistribution of fat to the trunk. Clear diagnostic criteria to differentiate FPLD1 from common obesity remain lacking.

Methods: We studied 70 women divided into three groups: FPLD1 ($n = 46$), Mendelian lipodystrophies ($n = 9$), and common obesity ($n = 15$). All participants underwent biochemical testing, anthropometric measurements, handgrip dynamometry, and musculoskeletal ultrasound. In patients with suspected FPLD1, a next-generation sequencing (NGS) panel was performed to exclude pathogenic variants in genes associated with FPLD.

Results: Women with FPLD1 were older on average (61.7 ± 10.4 years) than those with other lipodystrophies (54.8 ± 10.2 years) or common obesity (52.5 ± 10.8 years; $P = .008$) and exhibited a later onset of body fat redistribution (26.7 ± 14.7 vs 14.1 ± 8.2 and 21.6 ± 15.1 years; $P = .044$). Menstrual activity was less frequent in the FPLD1 group (23.9%) compared to women with obesity (66.7%; $P = .010$). Renal disease was observed exclusively in FPLD1 (23.9%; $P = .033$), whereas hepatic steatosis was present in 65.2% of FPLD1, 100% of Mendelian lipodystrophies, and 20% of obesity cases ($P < .001$).

The waist-to-height ratio was higher in FPLD1 (0.695 ± 0.077) than in common obesity (0.751 ± 0.097; BMI-adjusted $P < .001$). Handgrip strength was lower in FPLD1 (22.2 ± 5.6 kg) compared to obesity (25.4 ± 6.6 kg; $P < .001$). The adiponectin-to-leptin ratio showed intermediate values in FPLD1 (1.28 ± 2.52) relative to other lipodystrophies (3.12 ± 2.32) and obesity (0.58 ± 0.70; BMI-adjusted $P = .007$).

Ultrasound revealed that total abdominal subcutaneous adipose tissue (SAT) was significantly lower in FPLD1 than in obesity (33.5 ± 9.6 mm; BMI-adjusted $P = .007$), and this difference persisted 2 cm above the measurement site. Femoral SAT was also greater in FPLD1 compared to Mendelian lipodystrophies, but markedly reduced compared to women with obesity (8.1 ± 5.2 mm vs 3.55 ± 2.51 and 20.75 ± 9.28 mm, respectively; $P < .001$ BMI-adjusted).. The upper abdominal/femoral SAT ratio demonstrated excellent discriminatory performance for FPLD1 (cutoff ≥ 0.62; sensitivity 97%, specificity 91.7%, AUC 0.83, 95% CI 0.70-0.95) and correlated positively with HOMA-IR ($r = 0.307$; $P = .025$).

Conclusions: FPLD1 defines a distinct adipose–metabolic phenotype, characterized by an increased waist-to-height ratio, reduced femoral fat, and partial preservation of abdominal subcutaneous tissue. The upper abdominal/femoral SAT ratio demonstrated strong discriminatory value, supporting its potential as a simple, noninvasive diagnostic tool for this syndrome.

Abstract citation ID: lvag096.367

P191 - ECE_2909 - Maternal obesity interacts with stress-coping phenotypes to program offspring metabolic health

Naama Netsach Pe'er, Adam Merai, Louis Avitan, Michaella Ben-Shachar, Albert Pinhasov and Tovit Rosenzweig

Department of Molecular Biology, and The Adelson School of Medicine, Ariel University, Ariel, Israel

Maternal obesity is an increasing global health concern with long-term consequences for both maternal well-being and offspring health. This study investigated the effects of high-fat diet (HFD)-induced maternal obesity on maternal behavior, oxytocin secretion, and offspring metabolic and behavioral outcomes, using a mouse model of stress resilience (dominant; Dom) and stress vulnerability (submissive; Sub).

Female Dom and Sub mice were maintained on either a standard diet (STD) or HFD before and during pregnancy. Maternal behavior was assessed during pre- and postnatal periods, serum oxytocin levels were measured on gestational day (GD) 19, and delivery outcomes were recorded. Offspring were examined at early postnatal stages for epigenetic alterations and in adulthood for metabolic parameters and behavioral traits, including anxiety-like behavior and sociability.

Maternal HFD exposure differentially affects maternal behavior depending on stress-coping phenotype. In Dom dams, HFD impaired maternal behavior, whereas in Sub dams, it paradoxically improved maternal care. Serum oxytocin levels were consistently higher in Dom dams compared with Sub dams, regardless of diet. Maternal HFD was associated with increased rates of stillbirths and delivery complications in both Dom and Sub mice.

Metabolic assessments revealed pronounced sex- and phenotype-specific effects. Glucose tolerance tests (GTT) demonstrated significant interactions between maternal diet, offspring diet, sex, and stress phenotype. In female offspring, impaired glucose tolerance was primarily driven by offspring HFD, with maternal HFD exerting only a minor effect, limited to Dom females. In contrast, male offspring exhibited a strong susceptibility to maternal HFD. Sub male offspring displayed the most severe glucose intolerance, with additive detrimental effects of maternal and offspring HFD exposure. Area-under-the-curve (AUC) analysis confirmed that maternal HFD did not affect

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

glucose homeostasis in females, while markedly exacerbating glucose intolerance in Sub males. Notably, glucose tolerance in Dom males remained largely unaffected, even following combined prenatal and postnatal HFD exposure.

Alterations in serum insulin and leptin levels, as well as hepatic steatosis, mirrored glucose intolerance patterns, with the most severe metabolic phenotype observed in Sub male offspring exposed to HFD both prenatally and during adulthood.

These findings demonstrate that maternal obesity programs offspring's metabolic health in a sex-specific and stress-phenotype-dependent manner. Stress vulnerability emerges as a critical modifier of susceptibility to HFD-induced metabolic dysfunction, highlighting the importance of behavioral and psychosocial factors in developmental metabolic programming.

Abstract citation ID: lvag096.368

P192 - ECE_1332 - Early changes in serum calcitonin during tirzepatide therapy in adults with obesity

Nicholas Angelopoulos[1], George Simeakis[2], Ioannis Androulakis[1], Andreas Rizoulis[1], Rodis Paparodis[1,3,4], Anastasios Boniakos[1], Dimitra Zianni[1], Valentina Petkova[1], Paraskevi Mentzelopoulou[1] and Sarantis Livadas[1]

[1]Hellenic Endocrine Network, Athens, Greece; [2]Endocrine Department, 401 General Military Hospital of Athens, Thyroid Cancer Outpatient's Clinic, Athens, Greece; [3]Loyola University Medical Center, Maywood, United States; [4]Edward Hines Jr VA Hospital, Hines, United States

Background: Glucagon-like peptide-1 (GLP-1) receptor agonists have been associated with calcitonin elevation and C-cell hyperplasia in rodent models, raising concerns regarding thyroid safety. Human data, particularly for the dual GIP/GLP-1 receptor agonist tirzepatide, remain limited. This study aimed to evaluate the temporal pattern of serum calcitonin changes during tirzepatide therapy in adults with obesity and no known thyroid disease.

Methods: In this prospective observational study, 76 adults with obesity (mean age 48.7 ± 10.8 years; 73.7% female; mean BMI 40.6 ± 8.2 kg/m^2) initiated tirzepatide for weight loss. Serum calcitonin was measured at baseline, 3 months, and 6 months using electrochemiluminescence immunoassay. Non-parametric paired analyses and linear mixed-effects models were applied due to skewed distributions. Secondary analyses assessed whether early calcitonin changes predicted subsequent elevations above predefined clinical thresholds (≥12 pg/mL). Weight loss outcomes were recorded to confirm treatment effectiveness.

Results: Median serum calcitonin increased modestly from 2.05 pg/mL (IQR 1.00-3.60) at baseline to 2.12 pg/mL (IQR 1.10-4.00) at 3 months and remained stable at 2.25 pg/mL (IQR 1.23-3.70) at 6 months (overall time effect, $P < .001$). The increase occurred early, with no further significant rise between 3 and 6 months ($P = .43$). Among participants with baseline calcitonin <12 pg/mL, two developed transient elevations above this threshold during early follow-up; no additional cases emerged at 6 months. Early change in calcitonin (baseline to 3 months) strongly correlated with 6-month change ($\rho = 0.73$, $P < .001$) and demonstrated excellent discriminatory ability for identifying individuals exceeding thresholds (AUC = 0.991). Tirzepatide therapy resulted in clinically meaningful weight loss (median −15.0% at 6 months).

Conclusions: Tirzepatide therapy is associated with an early, modest increase in serum calcitonin that does not progress with continued treatment over 6 months. Calcitonin elevations were infrequent, non-cumulative, and largely predictable from early changes. These findings support baseline and early follow-up calcitonin assessment, while suggesting that prolonged routine monitoring may not be necessary in patients without additional thyroid risk factors.

Abstract citation ID: lvag096.369

P194 - ECE_1680 - Ultrastructural and molecular effects of pioglitazone on cardiac steatosis and endoplasmic reticulum stress in a high-fat diet–induced rat model

Sezim Talaibekova[1], Ersen Karakilic[1], Metehan Uzun[2], Oya Evirgen[3], Neslihan Kaya Terzi[4], Damla Aykora[2], Havva Cinpolat[5], Hayri Bostan[6], Büşra Tunç Topuz[1] and Emre Sedar Saygılı[1]

[1]Endocrinology and Metabolism, Çanakkale Onsekiz Mart University Faculty of Medicine, Canakkale, Türkiye; [2]Physiology, Çanakkale Onsekiz Mart University Faculty of Medicine, Canakkale, Türkiye; [3]Histology and Embryology, Ankara University Faculty of Medicine, Ankara, Türkiye; [4]Medical Pathology, Çanakkale Onsekiz Mart University Faculty of Medicine, Canakkale, Türkiye; [5]Medical Biochemistry, Çanakkale Onsekiz Mart University Faculty of Medicine, Canakkale, Türkiye; [6]Endocrinology and Metabolism, Canakkale Mehmet Akif Ersoy State Hospital, Canakkale, Türkiye

Background: While lipotoxicity in organs such as the liver, skeletal muscle, and pancreas has been well described, myocardial steatosis remains less well characterized. This study aimed to investigate cardiac steatosis in a high-fat diet (HFD)-fed rat model and to evaluate the effects of pioglitazone, a PPAR-γ agonist, on myocardial lipid accumulation, endoplasmic reticulum (ER) stress, and ultrastructural changes.

Methods: A total of 32 male Wistar rats were fed either a normal chow diet (NCD) or a HFD for 17 weeks and treated with pioglitazone during the final 4 weeks. Cardiac tissue was evaluated using histopathological analysis, Oil Red O staining, transmission electron microscopy (TEM), and quantitative real-time PCR to assess myocardial lipid accumulation, ultrastructural alterations, ER stress, and apoptosis-related gene expression. Circulating NT-proBNP levels were measured as a marker of cardiac stress.

Results: Epididymal white adipose tissue mass was significantly greater in HFD-fed rats compared with NCD-fed rats (5.13 ± 1.59 g vs 3.26 ± 0.94 g, $P < .001$), reflecting the impact of a HFD on adipose tissue expansion. In TEM analysis, HFD feeding resulted in significant myocardial lipid accumulation, accompanied by marked ultrastructural alterations, including mitochondrial crista disruption, ER dilation, increased intercellular space, and inflammatory cell infiltration. Pioglitazone treatment attenuated ER stress signaling, reduced intracellular lipid droplet accumulation, decreased inflammatory cell presence and partially preserved mitochondrial and ER morphology. These changes were associated with a significant reduction in circulating NT-proBNP levels, particularly in HFD–fed rats. Pioglitazone markedly decreased NT-proBNP concentrations

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(1769 ± 312 pg/mL vs 851 ± 116 pg/mL, $P < .001$) in HFD-fed rats, whereas untreated HFD-fed rats showed no significant change over time ($P = .084$). Additionally, PCR analysis showed that HFD-fed rats treated with pioglitazone, the HFD-associated induction of unfolded protein response (UPR)/ER stress markers was significantly attenuated, with reduced expression of CHOP, ATF4, PERK, XBP1, sXBP1 and eIF2α compared with untreated HFD rats, indicating attenuation of ER stress activation.

Conclusions: Pioglitazone partially mitigates diet-induced myocardial steatosis by reducing cardiomyocyte lipid accumulation, attenuating ER stress, and preserving ultrastructural integrity. These findings may support a cardioprotective role of PPAR-γ activation through modulation of myocardial lipotoxicity.

Abstract citation ID: lvag096.370

P195 - ECE_2145 - NADH oxidase–mimetic nanozymes restore hepatic NAD+ homeostasis and ameliorate experimental MASH

Gregori Casals[1,2,3], Muling Zeng[4], Eudald Casals[5], Jie Tang[6], María Rodríguez[6], Manuel Maclas[1,7], María Rodríguez-García[1], Wladimiro Jiménez[1,2,7], Manuel Morales-Ruiz[1,2,7] and Guillermo Fernández-Varo[1,2]

[1]Department of Biochemistry and Molecular Genetics, Hospital Clínic of Barcelona, FRCB-IDIBAPS, Barcelona, Spain; [2]CIBEREHD, Madrid, Spain; [3]Department of Fundamental and Clinical Nursing, Faculty of Nursing, University of Barcelona, L'Hospitalet de Llobregat, Spain; [4]Institut de Ciència de Materials de Barcelona, ICMAB (CSIC), Bellaterra, Spain; [5]Premium Research SL, Guadalajara, Spain; [6]School of Biotechnology and Health Sciences, Wuyi University, Jiangmen, China; [7]Department of Biomedicine, University of Barcelona., Barcelona, Spain

Background: Metabolic dysfunction–associated steatotic liver disease (MASLD) is characterized by significant alterations in hepatic redox homeostasis, including a marked depletion of nicotinamide adenine dinucleotide (NAD^+). Reduced NAD^+ availability compromises mitochondrial function, lipid handling, and cellular stress responses, thereby facilitating the transition from simple steatosis to steatohepatitis (MASH) and accelerating disease progression. Therefore, restoring hepatic NAD^+ levels emerges as a major and promising therapeutic challenge. This study aimed to identify inorganic nanozymes with long-lasting NADH oxidase–like activity capable of restoring NAD^+ availability, and to evaluate their therapeutic relevance in MASLD.

Methods: We first screened inorganic nanozymes for NADH oxidase–like activity by monitoring UV–Vis spectral changes associated with NADH consumption. The panel included gold, cerium oxide, and iron oxide nanozymes. Absorbance decreases at 340 nm, and concomitant increases at 260 nm were used to quantify NADH oxidation activity. Gold nanozymes (AuNZs) were subsequently incorporated into a mesoporous silica ($mSiO_2$) framework to improve colloidal stability and biocompatibility. MASH was induced in 16 Wistar rats by a methionine- and choline-deficient diet for 3 weeks. Animals were randomly administered intravenously (iv) with AuNZs@$mSiO_2$ (0.25 mg/kg; $n = 8$) or vehicle ($mSiO_2$; $n = 8$) at weeks 1 and 2. Tissue biodistribution of nanozymes was assessed by mass spectrometry and their therapeutic efficacy was then evaluated through liver histology, serum biochemistry, hepatic gene expression profiling by PCR Array and RT-PCR, and targeted assessment of liver metabolism.

Results: Among all nanozymes tested, only AuNZs catalyzed the oxidation of NADH to NAD^+. This activity was strongly size-dependent, with 4 nm AuNZs displaying markedly higher catalytic rates than 10 nm particles. The NADH oxidase-like activity remained stable under physiological pH and ionic strength, and no NADPH oxidase activity was detected, confirming strict substrate specificity for NADH. After intravenous administration to rats with MASH, nanozymes accumulated efficiently in the liver, restored the mitochondrial hepatic NADH/NAD^+ redox balance, significantly reduced hepatic steatosis by 15% ($P < .001$) and serum alanine aminotransferase (ALT) levels by 40% ($P < .01$), and improved the expression of genes involved in metabolic pathways related to oxidative phosphorylation, lipid metabolism and transport, inflammatory response, and adipokine signaling.

Conclusions: Nanozymes with NADH-oxidizing activity can restore hepatic NAD^+ redox balance and represent a promising therapeutic approach for MASLD.

Abstract citation ID: lvag096.371

P196 - ECE_3434 - Sustained remission of severe insulin autoimmune syndrome following rituximab therapy: a two-year follow-up case report

Nektaria Papadopoulou-Marketou, Eirini Biliou, Anna Angelousi, Evanthia Kassi and Gregory Kaltsas

Endocrinology Unit, 1st Department of Propaedeutic Internal Medicine, National And Kapodistrian University Of Athens, ENETS–EURACAN Centre of Excellence for Neuroendocrine Tumors, Laiko General Hospital, Athens, Greece

Background: Insulin Autoimmune Syndrome (IAS), or Hirata disease, is a rare but important cause of endogenous hyperinsulinemic hypoglycemia. It is characterized by the triad of spontaneous hypoglycemia, inappropriately elevated insulin and C-peptide levels, and the presence of insulin autoantibodies (IAA), in the absence of exogenous insulin use. While many cases are self-limiting, severe or steroid-refractory presentations may necessitate immunosuppressive treatment.

Case Series: Case 1: A 28-year-old woman presented with recurrent episodes of loss of consciousness and adrenergic/neuroglycopenic symptoms. Point-of-care glucose was 30 mg/dL. Biochemistry revealed insulin >3000 μU/mL and C-peptide 7.1 ng/mL. Imaging (MRI, EUS, Ga-68 DOTATATE PET/CT) was negative for insulinoma. Strongly positive insulin autoantibodies (>175 U/mL) confirmed IAS. Initial treatment with high-dose diazoxide and steroids was poorly tolerated. Rituximab (2 × 1 g one week apart) led to rapid and sustained remission: insulin declined to 958 μU/mL at 1 month and 110 μU/mL at 28 months. CD19/CD20+ cells were fully depleted by 3 months. The patient remained asymptomatic with dietary management and discontinued all medications. Genetic testing revealed HLA-DRB1*0406 and a heterozygous MAPK8IP1 variant.

Case 2: A 79-year-old man was hospitalized with recurrent hypoglycemia and documented Whipple's triad. Fasting glucose was 38 mg/dL, with C-peptide 33.27 ng/mL and insulin >1000 μU/mL. Imaging (MRI, octreoscan) and selective arterial calcium injection (SACI) testing showed no pancreatic lesion or

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

lateralization. IAA were positive (2.6 U/mL; ref <1.1), confirming IAS. He had a history of polymyalgia rheumatica. Diazoxide was initially prescribed but stopped due to edema and GI intolerance. Prednisolone (40 mg) improved hypoglycemia but caused disabling myopathy. Rituximab was administered with complete resolution of hypoglycemia and disappearance of IAA at 1-year post-treatment.

Conclusions: These cases illustrate the diagnostic challenges of IAS and the limitations of standard therapy. Rituximab achieved sustained remission in both patients with steroid-refractory IAS, irrespective of age or autoimmune background. B-cell depletion may represent a valuable treatment option in selected severe cases. Long-term follow-up with biochemical monitoring is essential to assess durability of response.

Abstract citation ID: lvag096.372

P197 - ECE_1137 - The levels of advanced glycation end-products and glutathione in the plasma in patients with type 2 diabetes mellitus and different stages of cardiovascular autonomic neuropathy

Olha Monashnenko[1,2] and Borys Mankovsky[3]
[1]Center of Cardiology and Cardiac Surgery of the Ministry of Health of Ukraine, Kyiv, Ukraine; [2]Kyiv, Ukraine; [3]D.F. Chebotarev Institute of Gerontology of the National Academy of the Medical Sciences of Ukraine, Kyiv, Ukraine

Background and Aims: Cardiovascular autonomic neuropathy (CAN) is a progressive complication of type 2 diabetes mellitus (T2DM), associated with oxidative stress and accumulation of advanced glycation end-products (AGEs). This study aimed to evaluate AGEs and glutathione (GSH) levels in T2DM patients with different stages of CAN: no CAN, early CAN, and established CAN.

Materials and Methods: We examined 79 subjects divided for three groups. The first group included 16 patients with T2DM without CAN (age—63.2 ± 10.9 years, BMI—32.7 ± 6.2, mean diabetes duration—6.7 ± 4.2 years, HbA1c—7.6% ± 1.6%, (data are presented as mean ± SD). The second group included 22 patients with T2DM with early CAN (1 abnormal autonomic test) (age 60,7 ± 12.6 years, BMI —30.8 ± 4.7, mean diabetes duration—6.8 ± 4.6 years, HbA1c -7.5% ± 1.8%). The third group included 41 patients with T2DM and established CAN (2 and more abnormal autonomic tests) (age —63.5 ± 9.3 years, BMI—31.3 ± 4.7, mean diabetes duration—7.7 ± 4.9 years HbA1c—7.3% ± 1.7 %). AGEs and GSH levels in the plasma were measured using standardized laboratory methods of fluorometry and spectrophotometry. CAN was diagnosed by standard battery of tests. Statistical analysis was performed using unpaired Student's t-test (with Welch's correction for unequal variances).

Results: We found a trend towards decreased GSH levels in patients with established CAN group compared to the early CAN group and to the no CAN group (1077.24 ± 104.11 μg/mLto 1109.51 ± 141.74 and to 1136.27 ± 98.83 respectively, $P = .09$). The highest AGEs levels were observed in the **early CAN group** (90.76 ± 19.8), though intergroup differences were not statistically significant ($P > .05$ for all comparisons). The **established CAN group** showed levels comparable to the **no CAN group** (85.64 ± 16.76 vs 84.0 ± 11.12).

Conclusions: Early CAN is associated with **elevated AGEs levels**, which may serve as a marker of initial metabolic dysregulation. **CAN progression** correlates with a **declining GSH trend**, supporting the role of oxidative stress in its pathogenesis. Further studies with **larger cohorts** and additional biomarkers are needed to validate these findings and explore clinical implications.

Abstract citation ID: lvag096.373

P200 - ECE_1716 - Longitudinal clinical and metabolic profile of male patients with LMNA-related lipodystrophy syndromes

Dupuis Hippolyte, Quitterie Blois and Marie Christine Vantyghem
Endocrinology, Daibetology, Oncoendocrinology and Metabolism, Lille University Hospital, Lille, France

Introduction: Laminopathies are rare disorders caused by variants in the *LMNA* gene. They display clinical heterogeneity, ranging from frequent forms of partial lipodystrophy (FPLD2) with diabetes to rarer cardiac or muscular forms. A female predominance is observed in FPLD2 due to a phenotype easier to identify with severe metabolic complications. Diagnosis in male subjects is more challenging, and the disease course has been poorly studied.

Aims: To describe the clinical and metabolic follow-up of male subjects carrying a pathogenic *LMNA* variant and to compare carriers of the *R482-LMNA* mutation associated with FPLD2, with carriers of other *LMNA* variants.

Methods: This retrospective, single-center cohort included 33 *LMNA*-mutated men (median age at V1 42(28-51); BMI 25(23-28)) who were followed for a mean duration of 8 years in a referral centre. Clinical, biological and anthropometric (assessed with metabolic MRI & DEXA) data were compared between the first (V1) & the last visit (V2), and between the *R482-LMNA* carriers ($n = 10$) and those carrying other variants (*non-R482* group, $n = 23$).

Results: During the follow-up, in the treated whole group, a significant decrease in triglyceride, alanine aminotransferase, leptin, intra- and total abdominal fat was observed, along with a trend toward improvement in insulin-resistance parameters and femoral Z-score. At V1, *R482* carriers exhibited more metabolic complications (higher blood pressure, HbA1c, liver steatosis, intra/total abdominal fat ratio, & lower leptin levels) than *non-R482* patients, who presented with cardiac complications (implantable cardiac device (ICD), heart failure) in 40% of cases vs 0% in the *R482* group. Longitudinal analysis nevertheless revealed a substantial incidence of diabetes in the *non-R482* group and a significant increase in ICD in the *R482* group.

Conclusions: This study confirms the phenotypic diversity of laminopathies in men and highlights the need for repeated cardiometabolic evaluation and diabetes screening regardless of the pathogenic variant.

Keywords laminopathies, lipodystrophy, insulin-resistance, cardiomyopathy, leptin

Abstract citation ID: lvag096.374

P201 - ECE_1877 - Growth hormone–treated small-for-gestational-age offspring maintain glucose homeostasis on a balanced diet, but not after high-fat feeding

Obin Kwon[1], Hanbin Kim[1], Yoojin Lee[1] and Jaehyun Kim[2]
[1]Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, South Korea; [2]Department of Pediatrics,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Seoul National University Bundang Hospital, Seongnam, South Korea

Background: Individuals born small-for-gestational-age (SGA) often achieve catch-up growth, yet rapid or excessive catch-up and calorie-focused nutritional support have been linked to higher lifetime risks of obesity and type 2 diabetes. Recombinant human growth hormone (GH) is a standard therapy for those who fail to catch up, but its long-term metabolic safety remains uncertain because GH can counterregulate insulin action while potentially supporting beta-cell function; however, long-term adult metabolic outcomes remain incompletely defined. We examined how early-life GH treatment and subsequent dietary exposure shape adult growth and energy/glucose homeostasis.

Methods: Pregnant C57BL/6 mice were fed either normal chow or a protein-restricted diet (PRD; 9 kcal% protein) during pregnancy and lactation. SGA pups from PRD dams were treated with recombinant human GH or vehicle via subcutaneous injection from postnatal weeks 3-8. Growth and adiposity were traced until adulthood, while energy expenditure was assessed by indirect calorimetry. Glucose metabolism was evaluated by glucose and insulin tolerance tests, complemented by *ex vivo* assessment of glucose-stimulated insulin secretion and islet insulin content. In a separate cohort, mice were switched to a high-fat diet (HFD; 60 kcal% fat) from 8 weeks of age.

Results: Offspring from protein-restricted dams demonstrated reduced body length, a key feature of SGA, which GH treatment rescued. Under normal chow, GH did not alter adult fat mass or energy expenditure. GH also did not impair glucose homeostasis; glucose tolerance was even improved with increased islet insulin content and enhanced secretory capacity. By contrast, exposure to an HFD after completion of GH treatment attenuated GH-mediated recovery of body length in adulthood and increased visceral adiposity in GH-treated offspring born SGA. Glucose tolerance showed a trend toward impairment in female but not in male mice after post-treatment exposure to HFD.

Conclusions: These findings support the metabolic safety of GH therapy in SGA and highlight the importance of dietary management in clinical applications.

Funding: This study was supported by the National Research Foundation of Korea (NRF) grants funded by the Korea government (MSIT) (2020R1A4A3078962, RS-2024-00406845, and RS-2025-00515235), by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI) funded by the Ministry of Health & Welfare, Republic of Korea (RS-2024-00404132), and by grant No. 16-2018-010 from the SNUBH research fund.

Abstract citation ID: lvag096.375

P203 - ECE_2857 - Diagnostic predictors of endogenous hyperinsulinemic hypoglycaemia

Christina Romberg[1,2], Matthias Hepprich[2,3], Sandrine A. Urwyler[1,2], Julie Celine Refardt[2,4] and Emanuel Christ[1,2]
[1]Basel 4056, Switzerland; [2]Department of Clinical Research, University Hospital Basel, Basel, Switzerland; [3]Department of Endocrinology, Diabetes and Metabolism, Sankt Clara Hospital, Basel 4058, Switzerland; [4]Department of Internal Medicine, Section of Endocrinology, Erasmus Medical Centre, Rotterdam 3015, The Netherlands

Background/objective: The gold standard for diagnosing endogenous hyperinsulinemic hypoglycaemia (EHH) is the prolonged fasting test. While neuroglycopenic symptoms are crucial for the evaluation of the fasting test, the respective relevance of measuring insulin, C-peptide, proinsulin and beta-hydroxybutyrate remains unclear. Therefore, we aimed to explore the relevance of these parameters based on a literature review.

Methods: We conducted extensive literature research in the databases Embase and Medline to identify case reports and original studies that report data on the fasting test eg, fasting duration, blood glucose and insulin levels at the end of the fast, as well as data on C-peptide, proinsulin and beta-hydroxybutyrate, where available. Histology was seen as the diagnostic gold standard in the patients.

Results: Data of 522 individual patients and 36 individual controls with data on the fasting tests were identified. Whereas blood glucose, insulin and C-peptide are measured and reported in most cases, proinsulin and beta-hydroxybutyrate appeared in only 51% and 50% respectively. In combination with blood glucose, C-peptide reached higher diagnostic accuracy (AUC 0.97) than insulin (AUC 0.93), however, proinsulin and beta-hydroxybutyrate seem to be even better (both AUC = 0.99).

Conclusions:

- The fasting test is an excellent diagnostic test with very high sensitivity and specificity
- There is considerable variation in reporting and conducting fasting tests worldwide.
- Measurements of glucose and C-peptide at the end of the fasting test are sufficient to establish the diagnosis.
- Proinsulin and beta-hydroxybutyrate show very high diagnostic accuracy for diagnosing EHH but are not measured on a regular basis.

Abstract citation ID: lvag096.376

P204 - ECE_2482 - Clinical consequences of insulin overbasalization in hospitalized patients with type 2 diabetes mellitus: evidence for a basal insulin ceiling effect and long-term predictors

Feride Özkara Akkuş, Abdulkadir Sarı, Özge Baş Aksu, Mustafa Sahin, Rifat Emral and Demet Çorapçıoğlu
Endocrinology and Metabolic Diseases, Ankara Üniversitesi Tıp Fakültesi Hastaneleri, Ankara, Türkiye

Background: In the management of type 2 diabetes mellitus (T2DM), basal insulin titration is essential for achieving fasting plasma glucose (FPG) targets. However, escalation beyond a certain threshold—referred to as insulin overbasalization—may result in a clinical plateau where further dose increases fail to improve glycaemic control while promoting adverse metabolic effects. Although international guidelines recommend an upper limit of 0.5 U/kg/day, this threshold is frequently exceeded in routine practice. Data on the metabolic consequences in hospitalized patients admitted for glycaemic regulation remain

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

limited. This study evaluated the association between overbasalization and long-term metabolic parameters.

Methods: This retrospective, observational study included 100 adult patients with T2DM followed at Ankara University Faculty of Medicine between 2020 and 2025. Fifty overbasalized patients (basal insulin >0.5 U/kg/day with HbA1c >8%) were matched for age, sex, and BMI with fifty non-overbasalized patients. All patients had received insulin therapy for at least 12 months. Anthropometric and metabolic changes were assessed over a 12-month follow-up after hospitalization. ROC analysis was performed to identify predictors of overbasalization.

Results: Baseline demographic characteristics and HbA1c levels were comparable between groups. The overbasalization group had a significantly longer duration of insulin therapy (11.5 ± 6.6 vs 9.4 ± 6.7 years, $P = .016$) and a higher prevalence of hypertension ($P = .035$). During follow-up, overbasalized patients experienced a significant increase in body weight ($+3.5 \pm 11.1$ kg, $P = .028$), whereas the non-overbasalized group achieved a significant reduction (-3.2 ± 9.8 kg, $P = .024$). Improvements in HbA1c and FPG were observed exclusively in the non-overbasalization group (−1.5% and −44.5 mg/dL, respectively, $P < .001$). In the overbasalized cohort, basal insulin dose was not associated with glycaemic improvement but showed a negative association with BMI changes. ROC analysis identified insulin treatment duration as the sole significant predictor of overbasalization (AUC 0.663, $P = .005$; 95% CI 0.554-0.771), with a cut-off of 9.5 years.

Conclusions: In hospitalized patients with T2DM, insulin overbasalization is associated with weight gain and limited glycaemic benefit, consistent with a basal insulin "ceiling effect". Prolonged reliance on basal dose escalation despite inadequate control may reflect elements of clinical inertia in inpatient diabetes management. These findings highlight the importance of timely treatment intensification strategies with non-insulin agents rather than continued basal insulin escalation after approximately 9.5 years of therapy.

Abstract citation ID: lvag096.377

P207 - ECE_1706 - Maternal and neonatal vitamin d metabolite profiling and its long-term impact on childhood growth: findings from the KLOTHO birth cohort

Konstantinos Michalakis[1], Spyridon Karras[2], Maria Kypraiou[3], Dimitrios Goulis[4], Vikentia Harizopoulou[5], Antonios Vlastos[6], Marios Anemoulis[7], Georgios Tzimagiorgis[2], Maria Dalamaga[8], Neoklis Georgopoulos[9], Evanthia Kassi[10], Georgios Mastorakos[11], Kali Makedou[2], Dimitrios Skoutas[12] and Melpomeni Peppa[13]

[1]*Endocrine Practice, Department of Obesity and Metabolism, Athens 11521, Greece, Greece;* [2]*Laboratory of Biological Chemistry, Medical School, Aristotle University, Thessaloniki 55535, Greece;* [3]*Assisting Nature Centre of Reproduction and Genetics, Thessaloniki 57001, Greece;* [4]*Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Medical School, Faculty of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece;* [5]*Medical School, Aristotle University, Thessaloniki, Greece;* [6]*Department of Midwifery, Faculty of Health and Caring Sciences, University of West Attica, Athens, Greece;* [7]*Athens, Greece* [8]*Department of Biological Chemistry, National and Kapodistrian University of Athens, Athens 15771, Greece;* [9]*Division of Endocrinology, Department of Internal Medicine, School of Health Sciences, University of Patras, Patras 26504, Greece;* [10]*Department of Biological Chemistry, School of Medicine, National and Kapodistrian University of Athens Athens, Athens, Greece;* [11]*Second Department of Surgery, Medical School, Aretaieio Athens Hospital, National and Kapodistrian University of Athens, Athens 11528, Greece;* [12]*Thermi Clinic, Thessaloniki 57001, Greece;* [13]*Endocrine Unit, 2nd Propaedeutic Department of Internal Medicine, Attikon University Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece*

Background: Vitamin D is increasingly recognized as a key modulator of growth, metabolism, and body composition in early life. However, the long-term impact of maternal vitamin D status and its multiple circulating forms on childhood anthropometry remains poorly understood. The KLOTHO cohort provides a unique opportunity to investigate these associations using detailed multi-form vitamin D profiles.

Methods: Within the prospective KLOTHO cohort, serum concentrations of eight vitamin D metabolites [$25(OH)D_2$, $25(OH)D_3$, $1\alpha,25(OH)_2D_2$, $1\alpha,25(OH)_2D_3$, 3-epi-$25(OH)D_2$, 3-epi-$25(OH)D_3$, D_2, D_3] were quantified at birth by liquid chromatography–tandem mass spectrometry (LC–MS/MS). Anthropometric measurements were assessed at 10-11 years of age (height, weight, BMI, waist circumference, and skinfold thickness). Associations between $\log_{10}$-transformed metabolite levels and anthropometric outcomes were evaluated using Spearman's correlation and multivariable linear regression adjusted for available covariates (sex, birth weight, maternal BMI, and season). False discovery rate (FDR) correction was applied (q Results: Among 98 children with complete follow-up data, vitamin D metabolites at birth were significantly associated with anthropometric indices at 10-11 years. Specifically, total $25(OH)D_3$ and its epimer 3-epi-$25(OH)D_3$ correlated positively with height ($\rho = 0.28$, $q = 0.04$) and negatively with BMI and triceps skinfold thickness ($\rho \approx -0.25$ to -0.30, $q < 0.05$). In the adjusted models, $25(OH)D_3$ remained consistently associated with adiposity markers ($\beta_std = -.27$, $P = .008$), although this association did not remain statistically significant after false discovery rate correction ($q = 0.06$).

Conclusions: Multi-form vitamin D assessment at birth reveals distinct metabolic patterns associated with later childhood growth and adiposity. These findings suggest that specific vitamin D metabolites, particularly $25(OH)D_3$ and its epimer, may be associated with long-term influences on somatic growth trajectories, underscoring the potential importance ofearly vitamin D sufficiency for metabolic health.

Keywords vitamin D, metabolites, children's growth, KLOTHO birth cohort

Abstract citation ID: lvag096.378

P208 - ECE_2210 - Non–HDL cholesterol and HbA1c evaluation in Greek dyslipidaemic patients with diabetes mellitus after twelve-month treatment with ezetimibe/rosuvastatin fixed-dose combination. ZEUS study sub-analysis

Antonios Ziakas[1], Vasilios Vasilikos[2], Pavlos Stougiannos[3], Athanasios Anadiotis[4], Apostolos Kakkavas[5],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Dimitrios G. Chatzis[6], Eftychia Demerouti[7], Emmanouil Paximadakis[8], Konstantinos Kontsas[9], Katerina MacHtopoulou[10], Pavlos Rouskas[11], Alexandros Gkinis[12], Panagiotis Katrapas[12], Polyanthi Papanastasiou[12], Georgios Tsioumas[12] and Charalambos Vlachopoulos[13]

[1]1st Cardiology Department, AHEPA Hospital, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]3rd Cardiology Department, Hippokration Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]Department of Cardiology, Elpis General Hospital of Athens, Athens, Greece; [4]Cardiology Department, General Hospital of Nea Ionia "Konstantopoulio", Athens, Greece; [5]Department of Cardiology, Sismanogleio-Amalia Fleming General Hospital, Athens, Greece; [6]Private Cardiology Site "Dimitrios G. Chatzis", Athens, Greece; [7]Private Cardiology Site "Eftychia Demerouti", Athens, Greece; [8]Private Cardiology Site "Emmanouil Paximadakis", Athens, Greece; [9]Private Cardiology Site "Konstantinos Kontsas", Athens, Greece; [10]Private Cardiology Site "Katerina Machtopoulou", Thessaloniki, Greece; [11]Private Cardiology Site "Pavlos Rouskas", Thessaloniki, Greece; [12]Medical Department, ELPEN Pharmaceutical Co. Inc., Athens, Greece; [13]1st Cardiology Clinic, Hippokration General Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Background: The 2019 European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) dyslipidaemia guidelines, updated in 2025, identify non-High Density Lipoprotein Cholesterol (non-HDL-C) as a secondary therapeutic target providing complementary information on a patient's atherogenic lipid burden, particularly relevant in populations at increased cardiovascular risk, such as patients with dyslipidaemia and diabetes mellitus (DM). This sub-analysis of ZEUS study evaluated non-HDL-C target attainment and changes in HbA1c after 12 months of treatment with fixed-dose combination (FDC) of ezetimibe/rosuvastatin in Greek patients with dyslipidemia and DM under routine clinical practice.

Methods: ZEUS was a multicenter, prospective, non-interventional observational study (NCT03947866) enrolling 570 Greek adult patients with dyslipidaemia, of whom 113 had a concomitant diagnosis of DM. Among patients with DM, the majority were classified as very-high cardiovascular risk (78.76%), followed by high (18.58%) and moderate (2.65%) cardiovascular risk. Cardiovascular risk classification and lipid target assessment were performed according to the 2019 ESC/EAS guidelines. Due to the small sample size of patients classified as moderate cardiovascular risk, no robust conclusions could be drawn.

Results: Dyslipidaemic patients with DM, baseline mean (±SD) non-HDL-C levels were 143.10 mg/dL (±43.94) in very-high cardiovascular risk subgroup and 175.57 mg/dL (±48.02) in high-risk. After 12 months of treatment with the FDC of ezetimibe/rosuvastatin, non-HDL-C levels significantly decreased ($P < .001$) across these categories to 78.72 mg/dL (±18.12) in very-high-risk and to 83.63 mg/dL (±18.44) in high-risk patients with DM. According to the 2019 ESC/EAS guidelines, non–HDL-C target achievement rates at month 12 were 49.44% and 57.14%, respectively. Mean HbA1c, reduced significantly ($P = .03$) in very-high-risk patients with DM from 6.73% (±1.05) to 6.32% (±0.72) and in high-risk patients from 6.60% (±0.77) to 6.06% (±0.65), $P = .01$.

Conclusions: This subgroup analysis of ZEUS study in patients with DM showed that twelve-month treatment with FDC of ezetimibe/rosuvastatin led to statistically significant reductions in non-HDL-C and HbA1c across all cardiovascular-risk groups. The observed rates of non–HDL-C target achievement highlight the need for more complete application of guideline-recommended lipid management in routine clinical practice, particularly in patients at increased cardiovascular risk.

Abstract citation ID: lvag096.379

P210 - ECE_2254 - Unveiling the lipocalin-2/SLC22A17 axis in periprostatic adipose tissue: a metabolic-molecular link between obesity-related comorbidities and prostate cancer progression

Antonio Prats-Escribano[1,2,3], Jesús Pérez-Gómez[1,2,3], Ignacio Gil-Duque[1,2,3], Laura Arroyo-Millán[1,2,3], Mélanie Planque[4,5,6], Rocío Guzmán[1,2,3], Sarah-Maria Fendt[4,5], Manuel D. Gahete[1,2,3], André Sarmento-Cabral[1,2,3], Maria Malagon[1,2,3] and Raul M Luque[1,2,3]

[1]Department of Cell Biology, Physiology, and Immunology, University of Cordoba, Cordoba, Spain; [2]Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Cordoba, Spain; [3]Reina Sofia University Hospital (HURS), Cordoba, Spain; [4]Laboratory of Cellular Metabolism and Metabolic Regulation, VIB Center for Cancer Biology, VIB, Leuven, Belgium; [5]Laboratory of Cellular Metabolism and Metabolic Regulation, Department of Oncology, KU Leuven and Leuven Cancer Institute (LKI), Leuven, Belgium; [6]Spatial Metabolomics Expertise Center, VIB Center for Cancer Biology, VIB, Leuven, Belgium

Prostate cancer (PCa) is a hormone-dependent tumour and one of the most prevalent endocrine-related cancers in men worldwide. PCa progression is influenced by its interaction with the surrounding tumour-microenvironment, highlighting the role of periprostatic-adipose-tissue (PPAT) through the secretion of bioactive molecules (eg, adipokines); however, the nature/influence of this complex cell communication and signalling remains to be fully elucidated. To address this, we perform multiomic and bioinformatic approaches (integration of transcriptomic-proteomic-metabolomic data) into PPATs and their secretome using a well-characterized cohort of PPAT samples [75 PCa patients vs 21 control-subjects with benign prostatic hyperplasia (BPH)]. Different prostate cell models [normal-like prostate (PNT2) and PCa (PC3/DU145/LNCaP/22Rv1) cells] were used to test the role of lipocalin-2/receptors axis in PCa cell-behaviour via multiple functional and molecular analyses, including gain- and loss-of-function assays by overexpressing LCN2 and its associated receptor SLC22A17, as well as silencing the latter, to precisely characterize the modulation of this axis. As a result, a signature of significantly dysregulated adipokines profile was identified in the PPATs of PCa compared with those of BPH patients. Subsequent unsupervised clustering analyses allowed the identification of two distinct molecular phenotypes of PCa patients with a unique fingerprint of adipokines alterations that presented distinctive clinical/metabolic features (ie, BMI/diabetes/dyslipidemia), being lipocalin-2 the only adipokine showing consistent differences at the transcriptomic/proteomic levels. Lipocalin-2 treatment did not affect proliferation/apoptosis/colony-formation in PCa cells, but migration was significantly increased in PNT2 and decreased in DU145 cells, wherein a differential lipocalin-2 receptor expression profile (especially

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

SLC22A17) may directly contribute to these differential effects. This is further supported by our functional modulation experiments, which reinforce the critical role of the LCN2/SLC22A17 axis in PCa cell aggressiveness. Notably, expression of SLC22A17 receptor, but not LRP2, was significantly downregulated in different PCa patient cohorts and was associated with significantly poorer disease-free survival in PCa patients. Molecularly, lipocalin-2 treatment was associated with alterations in critical oncogenic/metabolic pathways, including neutrophil-degranulation, inflammation and autophagy, suggesting a connection with inflammasomes. Further analyses revealed a weight-dependent association between lipocalin-2 and individual inflammasome components. Additionally, arachidonic acid in the PPAT-secretome positively correlated with lipocalin-2 levels, specifically in obese PCa-patients, suggesting a metabolic link to lipocalin-2-mediated effects. In conclusion, these results demonstrate a profound dysregulation of the PPAT-derived adipokine profile in PCa, which is associated with obesity-related comorbidities, highlighting the multifaceted role of lipocalin-2/SLC22A17-receptor axis as a potential key player in the interaction between PPAT-PCa microenvironment, by influencing inflammation and tumour-cell behaviour.

Abstract citation ID: lvag096.380

P211 - ECE_2319 - Hematological toxicity of radioligand therapy based on personalized dosimetry: interim results of the multicenter DUONEN study

Marta Opalinska[1], Maclej Kolodziej[2], Grzegorz Kamiński[2], Marek Dedecjus[3], Aldona Kowalska[4], Marek Saracyn[2], Piotr Garnuszek[5], Wioletta Lenda-Tracz[1], Danuta Gąsior-Perczak[4], Anna Borkowska[1], Joanna Januszkiewicz-Caulier[3], Anna Budzyńska[2], Agata Kubik[2], Krzysztof Kacperski[2], Patrycja Szubstarska[2], Wioletta Chalewska[3], Izabela Cieszykowska[5], Renata Mikolajczak[5] and Alicja Hubalewska-Dydejczyk[1]

[1]Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [2]Department of Endocrinology and Isotope Therapy, Military Institute of Medicine—National Research Institute, Warsaw, Poland; [3]Department of Endocrine Oncology and Nuclear Medicine, National Institute of Oncology, Warsaw, Poland; [4]Collegium Medicum Jan Kochanowski University in Kielce, Kielce, Poland; [5]Radioisotope Centre POLATOM, National Centre for Nuclear Research, Otwock, Poland

Introduction: RTL targeted somatostatin receptors is increasingly available. Individual dosimetry performed during RLT of NET may enable to achieve better results of therapy with maintaining its safety. In theory, administering higher doses of RLT allows for greater radiation delivery to the tumor, potentially improving long-term treatment outcomes, but it also increases the risk of side effects, particularly myelotoxicity.

Aim: To evaluate the hematologic toxicity of personalized dosimetry in patients undergoing radioligand therapy.

Materials and Methods: Adult patients with advanced, unresectable well-differentiated (G1/G2) GEP-NETs progressing on long-acting SSA are randomized into four arms of personalized RLT:

A: [^{177}Lu]Lu-DOTATATE at a fixed 7400 MBq per cycle.

B: Combination of [^{177}Lu]Lu-DOTATATE and [^{90}Y]Y-DOTATATE (initially 3700:1850 MBq), with [^{90}Y]Y-DOTATATE dose adjusted by individual dosimetry to maximize tumor radiation.

C: Same as B, but [^{90}Y]Y-DOTATATE is fixed and [^{177}Lu]Lu-DOTATATE is adjusted by dosimetry.

D: [^{177}Lu]Lu-DOTATATE starting at 7400 MBq, with subsequent doses adjusted by individual dosimetry.

Critical doses to the kidneys and bone marrow for all patients in arms B-D have cumulative limits of <23 Gy for the kidneys and <2 Gy for the red bone marrow over 4 cycles.

Results: 55 patients already started RLT (arm: A-15, B-16, C-14, D-10 cases). In average, the RTL doses in the arm D were increased, in arm C decreased while in arm B remained similar across whole therapy.

Hematologic toxicities were assessed during and after RLT. Nadir values were generally recorded during RLT, with most patients showing partial or complete recovery over time. Persistent reductions (diagnosed if nadir was diagnosed during follow-up) were observed most frequently in neutrophils (18%) and platelets (14%), whereas hemoglobin and total white blood cells were less affected (12% and 8%, respectively).

Persistent anemia (Hb≤10 g/dL) was most frequently observed in group D (33%) and group C (18%). Thrombocytopenia (PLT < 150 x10^3/μL) persisted in 22%-27% of patients in groups C and D, although severe PLT < 50 x10^3/μL were observed only in one patient in arm C. Additionally, leukopenia (WBC < 4.0 x10^3/μL) and neutropenia (NEU < 2.0 x10^3/μL) were present in approximately 10%-22% of patients, with a slightly higher incidence in group D. Groups A and B showed lower rates of persistent hematologic impairments after treatment.

Conclusions: Dosimetry based RLT was associated with manageable hematologic toxicity, but a small subset of patients may experience clinically significant or life-threatening cytopenias.

The study is funded by the Medical Research Agency(Project number 2019/ABM/01/00077-00).

Abstract citation ID: lvag096.381

P212 - ECE_1407 - Periprostatic adipose tissue boosts prostate cancer progression via androgen receptor-mediated lipolytic reprogramming

Hannah Hui

Hong Kong, Hong Kong

Periprostatic adipose tissue (PPAT), a specialized fat depot surrounding the prostate gland, is linked to poor prostate cancer (PCa) prognosis. However, the mechanisms underlying the crosstalk between PPAT and PCa progression remain poorly understood. We found that PCa tumors, particularly aggressive ones, actively stimulated androgen receptor (AR) expression in PPAT, with upregulation of AR and its signaling in PPAT a hallmark of PCa aggressiveness. Adipocyte-specific AR overexpression was sufficient to promote PCa growth in vitro and in vivo. Mechanistically, AR directly suppressed E3 ligase *RNF213*, which stabilized hormone-sensitive lipase (HSL) to drive lipolysis. Consequently AR-driven lipolysis liberated free fatty acids (FFAs) to boost PCa cell growth and remodel the tumor microenvironment. Clinically, PPAT in high-risk PCa patients exhibited elevated lipolytic activity and reduced RNF213 expression. The PPAT conditioned medium (CM) of high-risk PCa patients

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

enhanced PCa cell proliferation, which was reversed by blocking fatty acid uptake. Targeting this axis with the antilipolytic drug Acipimox significantly attenuated PCa growth in vivo. Our findings reveal a critical feed-forward loop between PCa and PPAT, orchestrated by adipocyte AR signaling. This self-reinforcing cycle accelerates disease progression, and targeting PPAT lipolysis presents a promising therapeutic strategy.

Funding: This work is partially supported by Early Career Scheme of General Research Council (24110224).

Abstract citation ID: lvag096.382

P213 - ECE_3504 - Epidemiological profile of 134 patients with multiple endocrine neoplasia type 1 (MEN1)

Nektaria Papadopoulou-Marketou, Kosmas Daskalakis, Charikleia Christakou, Maria Eleni Chondrogianni, Marina Tsoli, Evanthia Kassi and Gregory Kaltsas
Endocrinology Unit, 1st Department of Propaedeutic Internal Medicine, National And Kapodistrian University Of Athens, ENETS–EURACAN Centre of Excellence for Neuroendocrine Tumors, Laiko General Hospital, Athens, Greece

Introduction: Patients with Multiple Endocrine Neoplasia type 1 (MEN1) exhibit marked clinical heterogeneity regarding tissue involvement, metastatic potential, disease stage at diagnosis, and overall mortality.

Aim: To evaluate the clinical manifestations and mortality associated with various neuroendocrine tumors (NETs) in a cohort of patients with MEN1.

Methods: We conducted a retrospective analysis of 134 patients with clinical and/or genetically confirmed MEN1 followed at the ENETS–EURACAN Centre of Excellence, Laiko General Hospital, Athens.

Results: Of 134 patients, 53.5% were male and 46.5% female. The mean follow-up from diagnosis to last data collection was 14.8years. At study conclusion, 121 patients (90.3%) were alive and 13 (9.7%) had died.

Genetic testing was performed in 58.9% of patients (79/134), with MEN1 mutations identified in 75 individuals, most frequently in exons 9 (22.8%), 10 (22.8%), and 3 (15.2%). The most common initial manifestation was primary hyperparathyroidism (88%), occurring before age 25 in 39.4%, between 25-40 in another 39.4%, and after age 40 in 19.2% of patients.

Gastroenteropancreatic NETs (GEP-NETs) were identified in 82 patients (75.9%). Firty-eight (50%) had G1, 23 (37.5%) G2 tumors (13% of which were stage III-IV), and one G3 tumor (2.7%, stage IV). Functioning GEP-NETs occurred in 15 patients (9 gastrinomas and 6 insulinomas).

Pituitary adenomas (pitNETs) were found in 67 patients (60.9%); 46 were microadenomas (57.5%) and 15 macroadenomas (18.8%).

Adrenal adenomas were observed in 30 patients (28.3%): 17 were unilateral (14.2%) and 19 bilateral (15.8%). Only 30% were functioning: 26.7% secreting cortisol, followed by aldosterone (3.3%).

Other neoplasias included meningiomas (11.8%), breast cancer (4.0%), and differentiated thyroid cancer (7.1%).

Pulmonary NETs (LungNETs) were found in 11 patients: 8 typical carcinoids (TC),3 atypical carcinoids (AC). Thymic carcinoids (ThC) were diagnosed in 5 patients: 2 with G2 tumors developed ACTH-dependent Cushing's syndrome.

Distant metastases from GEP-NETs, occurred in 16 patients (12.9%), all with G2 tumors >2 cm, mainly hepatic. Pancreatectomy was performed in 27 patients (24.1%); 38.0% received somatostatin analogs, and 13.4% PRRT. All patients with AC and/or ThC developed metastates, and 5 died. Additionally, seven patients died due to metastatic G2 PanNETs, and one from sepsis.

Conclusions: In one of the largest Greek MEN1 cohorts, we described the clinical phenotype, morbidity, and mortality of affected individuals. The study highlights the clinical and neoplastic heterogeneity of the syndrome and underscores the need for systematic, individualized follow-up in specialized centers with expertise in neuroendocrine tumors.

Abstract citation ID: lvag096.383

P215 - ECE_1904 - Computed tomography texture analysis of pheochromocytomas and abdominal paragangliomas: relationship with clinical, laboratory, and histopathological data

Natalya Tarbaeva, Almaz Manaev, Dmitry Beltsevich, Liliya Urusova, Kseniya Vysotskaya, Anna Roslyakova, Anastasia Chevais, Nadezhda Platonova, Ekaterina Troshina, Galina Melnichenko and Natalia Mokrysheva
Endocrinology Research Centre, Moscow, Russia

Objectives: Pheochromocytomas and paragangliomas (PPGLs) are heterogeneous chromaffin-cell tumors with diverse clinical course. Predicting the biological behavior of these tumors remains a critical challenge.

Aims: This study aimed to evaluate the feasibility of texture analysis of computed tomography (CT) images for predicting the clinical, biochemical, and histopathological features of PPGLs.

Materials and Methods: We conducted a retrospective single-center study. Preoperative four-phase contrast-enhanced CT images of 230 patients with a verified diagnosis of PPGL were analyzed. Clinical manifestations, including the presence and duration of arterial hypertension, carbohydrate metabolism disorders, dyslipidemia, and atherosclerosis were evaluated. In the first stage, comparative and correlation analyses were performed between hormonal parameters and contrast-enhanced CT findings. In the second stage, patients were stratified into two groups based on morphological characteristics: PASS scores <4 ($n = 155$) and PASS scores ≥ 4 ($n = 56$). Logistic regression analysis was conducted to assess the potential of predicting group classification based on clinical, laboratory, and contrast-enhanced CT imaging data.

Results: PPGLs characterized by isolated normetanephrine secretion demonstrated significantly greater contrast enhancement in both arterial and venous CT phases compared with other secretion types ($P < .001$). Correlation analysis revealed statistically significant moderate positive correlations between plasma free normetanephrine levels and the volume of viable tumor tissue without necrosis. In contrast, plasma free metanephrine levels showed moderate negative correlations with maximum

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

venous phase attenuation, the degree of venous contrast enhancement, and the 90th percentile of X-ray density within functioning tumor tissue during the venous phase of CT. Significant associations were observed between tumor size and the presence or absence of necrosis ($P < .001$), as well as between tumor structure and size ($P = .004$). CT imaging features demonstrated moderate predictive ability for PASS score–based group classification, with an AUC of 0.647 (95% CI: 0.471-0.797), sensitivity of 0.923 (95% CI: 0.727-1.000), specificity of 0.400 (95% CI: 0.250-0.548), positive predictive value of 0.333 (95% CI: 0.176-0.500), and negative predictive value of 0.941 (95% CI: 0.800-1.000).

Conclusions: Texture analysis of contrast-enhanced CT images provides a noninvasive, quantitative approach to aid in the characterization of the biochemical and histopathological features of PPGLs. Our study underscores the importance of further development of texture analysis methods to enhance diagnostic accuracy and improve prediction of the disease course.

Abstract citation ID: lvag096.384

P216 - ECE_3577 - A Taiwanese founder effect: distinct clinical phenotype of SDHD c.3G>C pathogenic variant in pheochromocytoma and paraganglioma

Wan-Chen Wu[1] and Pei-Lung Chen[2]
[1]*Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan;* [2]*National Taiwan University Hospital, Taipei, Taiwan*

Background: Germline mutations in *SDHD* (PGL1) are classically characterized by a high prevalence of head and neck paragangliomas (HNPGLs) and a strong paternal transmission pattern. While Western cohorts often exhibit an HNPGL-dominant phenotype with low rates of adrenal pheochromocytoma (PCC), we have identified a unique clinical profile in Taiwanese patients carrying a suspected founder variant at the start codon of *SDHD*.

Methods: We retrospectively analyzed 19 patients with confirmed germline *SDHD* pathogenic variant (PV). Phenotypes were classified into four groups: (1) Head and neck (H&N)—isolated carotid or other HNPGLs; (2) Extra-adrenal—sympathetic PGLs outside the H&N and adrenal regions; (3) Adrenal—unilateral or bilateral PCC; and (4) Multifocal—involvement of ≥2 of the above sub-groups.

Results: A striking founder effect was evident, with 18 of 19 patients (94.7%) harboring the *SDHD*, c.3G>C (p.0) variant; one patient carried the c.3G>A variant. The median age at diagnosis was 36.7 years (IQR 25.5-44.0). Distinct from Western reports, isolated H&N disease was found in only 31.6% ($n = 6$) of patients. In contrast, adrenal involvement (21.1%, $n = 4$) and multifocal presentations (42.1%, $n = 8$) were highly prevalent. Clinical symptoms were reported in 57.9% of the total cohort, rising significantly to 75.0% in the adrenal group and 87.5% in the multifocal groups. Biochemical evaluation revealed marked catecholamine excess with norepinephrine-predominant in the adrenal and multifocal groups (median 24-hr urine norepinephrine levels of 1052.2 and 669.7 μg/24h, respectively, compared to only 38.0 μg/24h in the H&N group). Metastatic disease occurred in four patients (21.1%). Paternal transmission was molecularly confirmed in three families (fathers carry the *SDHD* variant and mothers test negative). Interestingly, carrier screening identified two HNPGL cases (a father and a sister of index patients who both presented with bilateral adrenal PCCs), further illustrating the remarkable phenotypic heterogeneity of the *SDHD*, c.3G>C variant even within the same pedigree.

Conclusions: The *SDHD* c.3G>C founder variant in Taiwan is associated with a high degree of phenotypic diversity, specifically a high incidence of adrenal PCC and multifocal PGLs. These findings diverge from the HNPGL-centric paradigm, suggesting that for patients with this specific genotype, comprehensive systemic surveillance and aggressive cascade family screening are mandatory to detect both secretory and non-secretory tumors early.

Abstract citation ID: lvag096.385

P218 - ECE_3111 - Immunocytochemical studies in the diagnosis of thyroid and parathyroid tumors in outpatient endocrine practice

Marcin Nosal[1], Barbara Budzynowska[2] and Ewa Ogłodek[1]
[1]*Collegium Medicum, Jan Dlugosz Uniwersity, Częstochowa, Poland;* [2]*Gdów, Poland*

Background: Immunocytochemistry is an underutilized yet valuable diagnostic tool in outpatient endocrinology. Its use improves diagnostic accuracy in selected thyroid and parathyroid lesions, particularly in non-referral settings with limited access to advanced diagnostics. Early and precise diagnosis is essential for optimal surgical planning and for reducing diagnostic delay, especially in rare endocrine malignancies.

Materials and Methods: Between 2021 and 2025, 698 fine-needle aspiration biopsies (FNABs) of thyroid lesions were performed in a single-physician outpatient endocrine clinic in southern Poland. Until 2022, patient qualification followed the 2018 recommendations of the Polish Society of Endocrinology; from 2023 onward, the updated 2022 guidelines were applied. In clinically ambiguous cases, immunocytochemical staining was used as an adjunct diagnostic method. This analysis focuses on the diagnostic value of calcitonin and parathyroid hormone (PTH) immunostaining in medullary thyroid carcinoma (MTC) and parathyroid tumors.

Results: Medullary thyroid carcinoma accounts for approximately 1%-2% of all thyroid malignancies and may correspond cytologically to Bethesda categories III-VI, occasionally mimicking Hürthle cell neoplasms. Although serum calcitonin is a key diagnostic marker, its interpretation may be limited by preanalytical instability, the hook effect, or ectopic secretion. In the presented case, only mildly elevated calcitonin levels were detected, potentially delaying diagnosis. Immunocytochemical staining for calcitonin enabled definitive identification of MTC, later confirmed histopathologically, and allowed appropriate surgical management including lymphadenectomy. Parathyroid adenomas present similar diagnostic challenges. Cytological findings are often nonspecific, and serum calcium may remain normal, particularly in early or normocalcemic hyperparathyroidism. In addition, PTH instability may result in false-negative laboratory results. In the analyzed case, a lesion initially suspected to be thyroid in origin showed elevated PTH with normal calcium and low vitamin D. Immunocytochemical staining confirmed parathyroid origin, which was later verified histologically.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: Immunocytochemical detection of calcitonin and parathyroid hormone is a reliable, cost-effective diagnostic tool that improves accuracy in thyroid and parathyroid pathology. Its use is especially valuable in outpatient settings, facilitating earlier diagnosis, supporting surgical decision-making, and improving overall patient management.

References

1. Kong Z, Li Z, Cui XY, et al. CTR-FAPI PET enables precise treatment of medullary thyroid carcinoma. *Cancer Discov*. 2025;15(2):316-328. https://doi.org/10.1158/2159-8290.CD-24-0897
2. Yu YL, Liu ZY. Update on the pathology of medullary thyroid carcinoma. *Zhonghua Bing Li Xue Za Zhi*. 2025;54(10):1016-1021. https://doi.org/10.3760/cma.j.cn112151-20250128-00067
3. Shariq OA, Waguespack SG, Hamidi S, et al. Approach to the patient with hereditary medullary thyroid carcinoma. *J Clin Endocrinol Metab*. 2025;110(9):2685-2697. https://doi.org/10.1210/clinem/dgaf089

Abstract citation ID: lvag096.386

P219 - ECE_2258 - Periprostatic adipose tissue-secreted miR-6798-5p in obesity acts as a oncomiR regulating prostate cancer aggressiveness through the TAGLN2 gene

Laura Arroyo-Millán[1,2], Francisco Porcel-Pastrana[1,2], Ignacio Gil-Duque[1,2], Antonio Prats-Escribano[1,2], Miguel E. G-Garcia[1,2], María Ortega-Bellido[1,2], Antonio Jesús Martínez-Fuentes[1,2,3], Manuel D. Gahete[1,2,3], André Sarmento-Cabral[1,2,3] and Raul M. Luque[1,2,3]

[1]Department of Cell Biology, Physiology and Immunology, University of Córdoba, Cordoba, Spain; [2]Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), Reina Sofía University Hospital (HURS), Cordoba, Spain; [3]CIBER Pathophysiology of Obesity and Nutrition (CIBERobn), Cordoba, Spain

The periprostatic adipose tissue (PPAT) that surrounds two-thirds of the prostate has been postulated as a putative active player in the pathological interaction between obesity (OB) and prostate cancer (PCa); however, molecular bases underlying this PPAT-OB-PCa communication is scarce. This study was aimed at assessing for the first time the dysregulation of the whole human PPAT-secreted miRNome of PCa patients under normo-weight and OB, and to identify miRNAs with a potential critical role in the pathophysiological association between PPAT-OB-PCa. To that end, conditioned media (CM) from a discovery cohort of PPAT explants derived from PCa-patients with normo-weight ($n = 16$) or OB ($n = 12$) was determined and compared using an Affymetrix-miRNA array, showing that the expression of 33 miRNAs was significantly altered, wherein five exhibited a high discriminating capacity. Then, a systematic validation using a validation cohort [PCa-patients with normo-weight ($n = 15$) or OB ($n = 25$)] demonstrated that miR-6798-5p was profoundly altered in PCa-patients with OB. Functional assays, both *in vitro* [proliferation, migration, colony, and tumoursphere formation in various PCa cell models (LNCaP, 22Rv1, DU145, and PC-3)] and *in vivo* (tumours growth, MKI67 and mitosis number in a preclinical model), demonstrated the impact of miR-6798-5p modulation (overexpression and/or inhibition) on critical cancer hallmarks, suggesting a oncomiR role in PCa cells. Remarkably, an induced obesogenic milieu (high glucose and insulin) further amplified the miR-6798-5p-associated oncogenic effects *in vitro*. Mechanistically, proteomic and enrichment analyses revealed critical changes in protein expression upon miR-6798-5p modulation (ie miR-6798-5p overexpression promoted transcriptional activity and TP53 repression, while its inhibition reactivated ribosome biogenesis and rRNA processing pathways) through the regulation of TAGLN2 (an actin-binding protein). Altogether, our data demonstrates that the PPAT-secreted miR-6798-5p acts as a oncomiR in the interplay between OB and PCa, promoting tumour aggressiveness via TAGLN2 repression and translational reprogramming, and highlights that miR-6798-5p inhibition might be a promising therapeutic strategy in PCa.

Abstract citation ID: lvag096.387

P221 - ECE_3118 - Sequential [68Ga]Ga-PSMA-11 and [18F]FDG PET/CT in TENIS syndrome: a prospective comparison

Klaudia Zajkowska, Paulina Cegla, Marta Wojewódzka-Mirocha, Paweł Ochman, Agata Sackewicz, Joanna Januszkiewicz-Caulier and Marek Dedecjus

Department of Endocrine Oncology and Nuclear Medicine, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background: In patients with differentiated thyroid carcinoma (DTC) and biochemical evidence of persistent or recurrent disease with negative iodine scintigraphy (TENIS syndrome), [^{18}F]FDG PET/CT is regarded as the imaging gold standard. Prostate-specific membrane antigen (PSMA) is expressed by the neovasculature of several solid tumours, including DTC. Emerging evidence suggests that PSMA-targeted PET/CT may be useful in TENIS syndrome, demonstrating metastatic lesions in various anatomical sites, including those not visualised on [^{18}F]FDG PET/CT. The aim of this study was to compare the diagnostic performance of [^{68}Ga]Ga-PSMA-11 PET/CT and [^{18}F]FDG PET/CT in TENIS syndrome and to assess the optimal sequential imaging pathway.

Methods: Forty patients with TENIS syndrome were prospectively enrolled and randomly assigned to one of two diagnostic arms. In the first arm (PSMA–FDG), patients underwent [^{68}Ga]Ga-PSMA-11 PET/CT as the initial examination, followed by complementary [^{18}F]FDG PET/CT in cases with a negative result. In the second arm (FDG–PSMA), patients were first examined with [18F]FDG PET/CT and subsequently with [^{68}Ga]Ga-PSMA-11 PET/CT if the initial scan was negative. The two groups did not differ significantly with respect to serum thyroglobulin, disease stage or previous treatments. Endpoints were patient-level detection rates for each tracer and for each imaging pathway, as well as the incremental value of the complementary examination.

Results: In the PSMA–FDG arm, [^{68}Ga]Ga-PSMA-11 PET/CT was positive in 10/20 patients. Among the 10 patients with a negative PSMA scan, complementary [^{18}F]FDG PET/CT was positive in 2/

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

10. In the FDG–PSMA arm, [^{18}F]FDG PET/CT was positive in 16/20 patients. Among the four patients with a negative FDG scan, complementary [^{68}Ga]Ga-PSMA-11 PET/CT was positive in 1/4. Overall, the PSMA–FDG arm led to detection of pathological lesions in 12/20 (60%) patients, whereas the FDG–PSMA arm yielded positive findings in 17/20 (85%) patients. Patient-level detection rates were 45.8% (11/24) for [^{68}Ga]Ga-PSMA-11 PET/CT and 60% (18/30) for [^{18}F]FDG PET/CT. Complementary PET/CT after an initial negative result yielded additional clinically relevant information in 15% (3/20) of patients.

Conclusions: In patients with TENIS syndrome, [^{68}Ga]Ga-PSMA-11 PET/CT demonstrated inferior diagnostic performance compared with [^{18}F]FDG PET/CT, supporting the role of [^{18}F]FDG PET/CT as the reference imaging modality in this setting. A sequential FDG–PSMA strategy yielded a higher patient-level detection rate than the reverse pathway. Although complementary PSMA imaging may add incremental value after a negative FDG scan, [^{68}Ga]Ga-PSMA-11 should be considered an adjunct to, rather than a substitute for, [^{18}F]FDG PET/CT in TENIS syndrome.

Abstract citation ID: lvag096.388

P222 - ECE_2363 - Therapeutic outcomes, genetic background, and survival in metastatic pheochromocytoma and paraganglioma: a single-center cohort study

Nikolina Vučenović[1], Mirsala Solak[2], Ivana Kraljevic[2,3], Mirjana Đukić[4], Anja Barac Nekic[2], Tanja Skoric Polovina[2], Karin Zibar Tomšić[2], Annemarie Balaško[2], Hrvoje Popovac[2], Tina Dusek[2,3] and Darko Kastelan[2,3]

[1]Department of Endocrinology, General Hospital Šibenik, Šibenik, Croatia; [2]Department of Endocrinology, University Hospital Center Zagreb, Zagreb, Croatia; [3]School of Medicine University of Zagreb, Zagreb, Croatia; [4]Department of Endocrinology, General Hospital Sisak, Sisak, Croatia

Background: Metastatic pheochromocytoma and paraganglioma (mPPGL) are rare neuroendocrine tumors with heterogeneous clinical behavior, variable treatment responses, and limited prognostic data.

Methods: We performed a retrospective single-center analysis of patients with mPPGL. Demographic characteristics, timing of metastatic disease, treatment modalities, genetic findings, clinical outcomes, and survival data were collected and analyzed descriptively.

Results: Twelve patients with mPPGL were included (6 males and 6 females), with a median age at diagnosis of 49.5 years (range, 20-68) and a median follow-up duration of 86 months (range, 11-272). Nine patients had primary pheochromocytoma, whereas two had primary intra-abdominal paraganglioma and one had primary intrathoracic paraganglioma. Metastatic disease was present at initial diagnosis in 4/12 patients (33.3%), while 8/12 (66.7%) developed metastases during follow-up, with a median time to metastasis of 56 months (range, 10-171). The most frequent metastatic sites were bone, liver, lymph nodes, and lungs, often with multifocal involvement. Genetic testing was performed in 10/12 patients (83.3%). Pathogenic or likely pathogenic variants were identified in 6/12 patients (50%), including SDHB ($n=1$), SDHD ($n=1$), MEN2A ($n=1$), RET ($n=1$), as well as somatic mutations in RET ($n=1$) and ATRX ($n=1$).

All patients received multimodal treatment, including surgery ($n=11$), ^{131}I-MIBG ($n=10$), chemotherapy (CVD) ($n=7$), somatostatin analogues ($n=2$), peptide receptor radionuclide therapy (PRRT) ($n=1$), and temozolomide ($n=1$). At the last follow-up, complete response was observed in 2/12 (16.7%), partial response in 1/12 (8.3%), stable disease in 3/12 (25%), and progressive disease in 6/12 patients (50%). During long-term follow-up, 7/12 patients (58.3%) died. The cause of death was disease related in 5/7 patients (71.4%), while one patient experienced sudden death of unknown cause, and in one patient the cause of death was undocumented. Median overall survival was 86 months (range, 12-272).

Conclusions: Despite marked clinical heterogeneity and high disease-related mortality, a subset of patients with mPPGL can achieve durable disease control, highlighting the importance of individualized multimodal treatment in specialized centers.

Abstract citation ID: lvag096.389

P223 - ECE_3069 - SMAC-2 and SMAC-3 cells: characterization of two new ACC patient-derived cell lines

Andrea Abate[1], Mariangela Tamburello[1], Claudia Bonera[1], Guido Tiberio[2], Sara Baldelli[3], Mattia Carini[3], Alessia Inglesi[4], Maria Scatolini[4], Deborah Cosentini[5], Marta Laganà[5], Marta Leporati[6], Luigi Poliani[7], Domenico Cosseddù[6], Duilio Brugnoni[3], Alfredo Berruti[5] and Sandra Sigala[1]

[1]Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy; [2]Surgical Clinic, University of Brescia at ASST Spedali Civili di Brescia, Brescia, Italy; [3]ASST Spedali Civili di Brescia, Central Clinical Laboratory, Brescia, Italy; [4]Molecular Oncology Laboratory, Fondazione Edo ed Elvo Tempia, Ponderano, Italy; [5]Oncology, University of Brescia at ASST Spedali Civili di Brescia, Brescia, Italy; [6]Laboratory Medicine, AO Ordine Mauriziano, Torino, Italy; [7]Pathology Unit, University of Brescia at ASST Spedali Civili di Brescia, Brescia, Italy

Background: AdrenoCortical Carcinoma (ACC) is an aggressive, rare and heterogeneous malignancy that demands a broad spectrum of preclinical models. In this context, generating new cell lines is crucial. This work reports the establishment and characterization of two new patient-derived ACC cell lines, named SMAC-2 and SMAC-3 cells.

Materials and Methods: Cell cultures were established from two patients diagnosed with ACC and operated on. Mutational status was investigated by NGS and Sanger methods. Gene expression was analysed by qRT-PCR, while protein expression was evaluated by immunofluorescence. Hormonal secretion was investigated by LC-MS/MS. Cell proliferation was evaluated by BrdU-incorporation assay while cell viability was assessed by WST-1 assay.

Results: SMAC-2 originated from the primary adrenal tumor mass of a metastatic EDP-M-treated ACC in a female patient with Cushing's syndrome and hyperandrogenism, whereas SMAC-3 was derived from a male patient with a mitotane-treated local recurrence without clinical signs of hypercortisolism. Both lines harbored *TP53* mutations; SMAC-2 additionally carried a pathogenic *CTTNNB1* alteration and a *CDKN2A* deletion, while SMAC-3 showed a mutation in *MSH2*. Basal hormone profiling

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

revealed a cell line–specific fingerprint. Also, gene and protein expression of steroid hormone receptors presented a model-specific pattern. In line with the clinical manifestation of the original patient, SMAC-2 secretes high levels of cortisol. SMAC-3 is also able to secrete cortisol at baseline, although in a low amount. The reference drug in ACC, mitotane displayed in both cell lines a low potency in terms of reduction of cell viability and cell proliferation. Interestingly, treatment with low concentrations of mitotane (IC10, calculated based on cell viability) resulted in a significant reduction of cortisol in both cellular models. Experiments in a wide range of passages were carried out to study the stability of the two cell lines.

Conclusions: SMAC-2 and SMAC-3 therefore exhibit distinctive molecular and functional features that enlarge the panel of available ACC experimental models and constitute valuable tools for preclinical studies alongside existing cell lines.

Abstract citation ID: lvag096.390

P224 - ECE_2759 - Steroid hormones and endocrine disruptors in the prediction of prostate cancer aggressiveness

Jana Vitku[1], Tereza Skodova[1], Lucie Kolatorova[1], Anežka Varausová[1], Lukas Gadus[2,3], Ludmila Michnova[4] and Jiri Heracek[2,3]

[1]Department of Steroids and Proteofactors, Institute of Endocrinology, Prague, Czech Republic; [2]Department of Urology, Military University Hospital Prague, Prague, Czech Republic; [3]First Faculty of Medicine, Department of Urology, Charles University, Prague, Czech Republic; [4]Department of Pathology, Military University Hospital Prague, Prague, Czech Republic

Introduction: Prostate cancer (PCa) is a hormone-dependent disease in which steroid hormones and potentially also endocrine disruptors (EDs) may play an important role.

Aims: The study aimed to analyze steroid hormones (28 unconjugated, 17 conjugated) and EDs (15 unconjugated, 16 conjugated) in prostate tissue (cancerous and non-cancerous) and plasma in patients ($n = 163$) who underwent robotic radical prostatectomy for PCa, and to relate these profiles to tumor aggressiveness.

Methods: Quantification was performed using liquid chromatography–tandem mass spectrometry (LC-MS/MS). Cancerous and non-cancerous tissues from the same patients were compared using a paired t-test. Subsequently, individual steroids and EDs were compared between patient groups stratified by Gleason score, representing tumor aggressiveness, using ANOVA models. Finally, multivariate prediction models (bidirectional orthogonal projections to latent structures, O2PLS) were applied to evaluate complex relationships between steroids and EDs and PCa aggressiveness.

Results: Steroid hormones and EDs did not significantly differ between cancerous and non-cancerous tissue within the same patient, except for 17-hydroxyprogesterone ($P = .022$) and conjugated estriol ($P = .009$), both of which showed lower concentrations in cancerous tissue compared with non-cancerous tissue.

In the OPLS model constructed from prostate tissue samples, higher levels of conjugated pregnenolone, dehydroepiandrosterone (DHEA), 17-hydroxyprogesterone, corticosterone, 21-deoxycortisol, and both conjugated and unconjugated dihydrotestosterone were associated with lower Gleason score, suggesting a potential protective role. In contrast, higher Gleason score (ie greater cancer aggressiveness) was associated with increased levels of oxygenated DHEA metabolites (7α-hydroxyDHEA and conjugated 7-oxoDHEA), estrone, 5α-dihydroprogesterone, and glucocorticoids (cortisol and cortisone), indicating a shift toward alternative steroidogenic pathways, enhanced glucocorticoid activity, and increased estrogenic signaling in aggressive disease. Notably, both conjugated and unconjugated butylparaben were positively associated with higher Gleason score, suggesting that ED exposure may contribute to PCa progression. This tissue-based model explained a substantial proportion of Gleason score variability (32.5%, 26.7% after cross-validation), confirming the key role of intraprostatic steroid metabolism in PCa. In contrast, the OPLS model constructed from plasma samples explained considerably less variability in Gleason score (14.9%, 11.4% after cross-validation). Although some of the same steroids contributed to the model, their associations with Gleason score were predominantly negative.

Conclusions: This study provides the first integrated multisteroid and multiED analysis in prostate cancer tissue and plasma, highlighting the dominant role of intraprostatic steroid metabolism in determining tumor aggressiveness.

Acknowledgement: Supported by MH CZ—DRO, Institute of Endocrinology EÚ, 00023761 and Czech Health Research Council, project NU21J-01-00040.

Abstract citation ID: lvag096.391

P226 - ECE_3536 - Serum biomarkers as tools for disease recurrence detection and monitoring in patients with neuroendocrine tumors

Edyta Tkacz[1], Anna Kurzyńska[2], Agnieszka Stefańska[1], Małgorzata Szumińska[1], Karolina Węgrzyn[2], Anna Sowa Staszczak[2], Justyna Brodowicz[3], Katarzyna Gawlik[3], Bogdan Solnica[3], Marta Opalinska[2] and Alicja Hubalewska-Dydejczyk[2]

[1]Department of Endocrinology, Oncological Endocrinology, Nuclear Medicine and Internal Medicine, University Hospital in Krakow, Krakow, Poland; [2]Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [3]Department of Clinical Biochemistry, Jagiellonian University Medical College, Krakow, Poland

Introduction: A diverse group, which are neuroendocrine neoplasms (NENs) is characterized by variable secretory activity. Nevertheless, the spectrum of reliable biomarkers suitable for biochemical detection and monitoring is currently limited. Factors involved in angiogenesis, inflammatory processes, and extracellular matrix remodeling, such as tumor necrosis factor-aplha (TNF-α), fascin, matrix metalloproteinase 7 (MMP-7) and lipocalin-2, have been shown to contribute to tumor progression and metastasis in a multiple type of cancers. However, their clinical relevance in neuroendocrine tumors (NET) has not been fully clarified yet. The present study assessed serum concentrations of selected factors in patients with NETs in comparison with healthy controls.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Methods: The study involved eighty participants: 60 patients with advanced, histologically confirmed NETs and 20 healthy volunteers without a history of any malignancy. Serum levels of TNF-α, fascin, MMP-7, and lipocalin-2 were measured using enzyme-linked immunosorbent assay (ELISA) kits following the manufacturer's protocols. All samples were obtained under fasting conditions and analyzed in duplicate. Analysis of all measured factors was performed separately for pancreatic (Pan NETs), small intestine (Si NETs), and other NET cohort (rectum, stomach, lung), in comparison with healthy control groups. Statistical analysis of quantitative variables was performed using the ANOVA Kruskala-Wallisa test, ANOVA for independent groups test, with a significance threshold set at $P < .05$. Calculations were performed using Statistica 13 software.

Results: Serum concentrations of TNF-α, fascin, MMP-7, and lipocalin-2 were higher in NET patients compared with the control group: 16.91 vs 13.01 pg/mL ($P = .000025$); 23.81 vs 10.39 ng/mL ($P = .07$); 2.80 vs 1.65 ng/mL ($P = .000013$); and 196.97 vs 103.49 ng/mL ($P = .000002$), respectively. Only the difference in fascin levels did not reach statistical significance. In a comparative analysis of all measured factors, only MMP-7 showed an association with tumor origin. MMP-7 concentrations were significantly higher in patients with small intestine NETs compared with those with pancreatic NETs or other NET subtypes (3.39 vs 2.45 vs 2.8 ng/mL; $P = .002$).

Conclusions: The study confirmed significant differences in the serum concentrations of the analyzed factors between patients with neuroendocrine tumors (NETs) and healthy controls. The strongest associations with the presence of NETs were observed for TNF-α, MMP-7, and lipocalin-2. Additionally, MMP-7 concentrations varied depending on the primary tumor site. Further studies in larger, long-term cohorts are needed to fully determine the clinical relevance and potential utility of these analyzed factors.

Abstract citation ID: lvag096.392

P227 - ECE_3750 - Machine learning identifies hidden phenotypes and predicts somatostatin analogue response in gastroenteropancreatic neuroendocrine tumours

Fernando Vidal-Ostos De Lara[1], Sofiya Khoruzha Aleksandrovych[1], Jose Ignacio Busteros Moraza[2], Remedios Gomez Sanz[3], Bernard Theillac[4], Raquel Niddam Sanchez[1], Edinson Caviedes Sanchez[5], María Laura Villalobos Leon[5] and Concepcion Blanco Carrera[5]

[1]Endocrinology and Nutrition, Principe de Asturias University Hospital, Alcalá de Henares, Spain; [2]Pathological Anatomy, Principe de Asturias University Hospital, Alcalá de Henares, Spain; [3]General Surgery, Principe de Asturias University Hospital, Alcalá de Henares, Spain; [4]Nuclear Medicine, Principe de Asturias University Hospital, Alcalá de Henares, Spain; [5]Oncology, Principe de Asturias University Hospital, Alcalá de Henares, Spain

Introduction: Gastroenteropancreatic neuroendocrine tumours (GEP-NETs) display marked clinical heterogeneity. Conventional TNM staging and histological grading inadequately capture prognostic diversity, and reliable prediction of somatostatin analogue (SSA) response remains limited. Machine learning approaches may uncover hidden phenotypes and improve treatment selection.

Material and Methods: We conducted a retrospective cohort study of 115 GEP-NET patients diagnosed and treated in a multidisciplinary unit (2001-2024). Demographic data, tumour characteristics (location, size, TNM stage, grade), biomarkers (Ki-67, chromogranin A, angioinvasion), treatment details, and outcomes were collected. We applied unsupervised K-means clustering (18 variables) to identify phenotypes and supervised Random Forest classification to predict SSA response in 65 patients receiving SSA as first-line therapy. Model performance was compared using AUC-ROC, C-index, cross-validation (5-fold), and feature importance analysis (SHAP values).

Results: K-means clustering identified four distinct GEP-NET phenotypes: (1) "Indolent Incidental" ($n = 28$, 24%): small pancreatic NETs, no metastases, 5-year overall survival (OS) 95%; (2) "Gastric Indolent" ($n = 30$, 26%): gastric NETs, well-differentiated, 5-year OS 92%; (3) "Carcinoid Intestinal" ($n = 35$, 30%): multifocal small-bowel carcinoids with 46% metastatic disease, 5-year OS 68%; (4) "Aggressive Metastatic" ($n = 22$, 19%): large T3-T4N1M1 tumours, 5-year OS 32%. Machine learning clustering improved prognostic discrimination (C-index 0.71) compared to conventional TNM staging (C-index 0.62), a relative improvement of 14% ($P < .001$ by log-rank test). For SSA response prediction, Random Forest achieved superior performance (AUC 0.79, 95% CI 0.68-0.90) compared to standard logistic regression (AUC 0.68, 95% CI 0.54-0.82). Top predictive variables were: histological grade (importance 0.24), baseline chromogranin A (0.19), tumour location (0.15), angioinvasion (0.12), and tumour size (0.10). A simplified clinical nomogram (0-5 point risk score) stratified patients into risk categories predicting SSA response probability: low risk 95%, intermediate risk 65%, high risk 15%.

Conclusions: Machine learning identifies four GEP-NET phenotypes reflecting distinct biological behaviours superior to conventional TNM staging. Random Forest prediction of SSA response enables personalized treatment selection and avoids unnecessary SSA exposure in resistant patients. This approach integrates non-linear variable interactions missed by traditional statistical methods. Further external validation in multicentric cohorts is warranted to implement these tools in routine clinical practice.

Abstract citation ID: lvag096.393

P228 - ECE_2751 - An exploratory assessment of the GloBE-reg registry for studying the safety of long-acting growth hormone in cancer survivors (the SAFE-survivors study)

Monica Logan[1], Joseph McElvaney[1], Malika Alimussina[1], Navoda Atapattu[2], Suet Ching Chen[1,3], Ying Ki Chung[4], Peter Clayton[5], Angela Delaney[6], Maria Fleseriu[7], Antony Fu[8], Andrew Hoffman[9], Violeta Iotova[10], Gudmundur Johannsson[11], Annie Leong[12], Elena Lundberg[13], Bradley Miller[14], Mariami Oniani[15], Sebastian Neggers[16], Nurshadia Saminga[17], Lars Sävendahl[18], Katharina Schilbach[19], Sumudu Seneviratne[20], M. Guftar Shaikh[3], Lloyd Tack[21], Diana Vitali[22], Kent Ho-Chung Yau[23], Kevin Cj Yuen[24], Faisal Ahmed[1,3] and Judith Gebauer[25]

[1]Office for Rare Conditions Registries, University of Glasgow, Glasgow, United Kingdom; [2]Endocrine and Diabetic Unit, Lady Ridgeway Hospital For Children, Colombo, Sri Lanka;

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[3]Developmental Endocrinology Research Group, University of Glasgow, Glasgow, United Kingdom; [4]Caritas Medical Centre, 九龙, Hong Kong; [5]University of Manchester, Manchester, United Kingdom; [6]Division of Endocrinology, Saint Jude Children's Research Hospital, Memphis, United States; [7]Departments of Medicine and Neurological Surgery, Oregon Health & Science University, Portland, United States; [8]Department of Paediatrics & Adolescent Medicine, Princess Margaret Hospital, Kwai Chung, Hong Kong; [9]Division of Endocrinology, Metabolism and Gerontology, Stanford University School of Medicine, Palo Alto, United States; [10]Department of Paediatrics, Medical University Varna, Varna, Bulgaria; [11]Endocrinology, Sahlgrenska University Hospital, Gothenburg, Sweden; [12]Department of Paediatrics, University Malaya Medical Centre, Kuala Lumpur, Malaysia; [13]Umea University Hospital, Umea, Sweden; [14]MHealth Fairview Masonic Children's Hospital, Minneapolis, United States; [15]M.Iashvili Children Central Hospital, Tbilsi, Georgia; [16]Section Endocrinology and Pituitary Center, Rotterdam, The Netherlands; [17]University Malaya Medical Centre, Kuala Lumpur, Malaysia; [18]Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden; [19]LMU University Hospital, Munich, Germany; [20]University of Colombo, Colombo, Sri Lanka; [21]Department of Paediatric Endocrinology, Ghent University Hospital, Ghent, Belgium; [22]SOD Italia, Rome, Italy; [23]Prince of Wales Hospital, Shatin, Hong Kong; [24]Barrow Pituitary Center, University Arizona College of Medicine and Creighton University School of Medicine, Phoenix, United States; [25]University Cancer Center Leipzig and Department of Oncology, Leipzig, Germany

Introduction: Growth hormone (GH) treatment is approved for cancer survivors with GH deficiency. Alongside daily GH, long-acting GH (LAGH) has been recently approved for the treatment of GHD. Given its different mechanistic action to daily GH, the safety of LAGH in this group needs further study.

Methods: The Global Registry for Novel Therapies in Rare Bone and Endocrine Conditions (https://globe-reg.net/) was initiated in 2022 to collect real world data on safety and effectiveness of GH therapy. In late 2025, a non-interventional, retrospective and prospective study, SAFE-Survivors was launched with the aim of using GloBE-Reg to study cases of all ages who receive daily GH or LAGH following a cancer diagnosis; longitudinal data shall be analysed at 12, 24, 60, and 120 months after initiation of GH. The study will recruit for 10 years and this report presents the preliminary analysis of the first data tranche.

Results: Since its launch in late 2022, 44 centres from 24 countries in 5 continents have enrolled 5075 cases with a median current age of 12.2 (10^{th}, 90^{th} centile: 6.3, 18.1). Of these, 2928 (58%) had growth hormone deficiency (GHD). Among this cohort, 92 (3%) cases from 16 centres received GH following a cancer diagnosis. Of these, 10 (11%) were receiving LAGH, 2 had stopped GH and the remainder were on daily GH. In the first data tranche at study launch, data was available for 74 (80%) cases from 11 centres. The median age at start of therapy and the current age was 11 yrs (6.4, 14.8) and 14.5 yrs (9.8, 19.2), respectively. This cohort consisted of 64 reports of intracranial tumours including craniopharyngiomas (n,23) and pituitary tumours (n,8). Therapy data was available in 64 cases and the broad groups were surgery only (10), radiation only (3), chemotherapy only (3) and combined (48). Median follow-up after GH initiation was 28 months(4.5, 96) with data at 12, 24, 60 and 120 months in 23, 19, 9 and 3 cases respectively.

Conclusions: This initial analysis offers an early view of the long-term safety of LAGH in comparison to daily GH treatment in cancer survivors with GHD. No new cancers or recurrences were found in this cohort. However, this is based on a small sample and short follow up time and requires further data clarification. Increased patient recruitment and data collection of the GloBE-Reg over time will be crucial to fully assess safety and guide clinical practice.

Abstract citation ID: lvag096.394

P230 - ECE_3166 - Seminal microbiota as an endocrine modulator: lactobacillus-dependent reprogramming of hormonal networks in male idiopathic infertility

Fudulu Alina[1], Adrian Albulescu[1], Anca Botezatu[1], Dinu Draganescu Daniela[2], Suzana Vladoiu[2,3], Cristina Stancu[2,4], Andrei Muresan[2], Dinu Draganescu Daria[5] and Corin Badiu[2,6]
[1]Department of Molecular Virology, Ştefan S. Nicolau Institute of Virology, Bucureşti, Romania; [2]Research Department , Endocrinology IV, C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania; [3]"C.I.Parhon" National Institute of Endocrinology, Bucharest, Romania; [4]Laboratory of Molecular, Cellular and Structural Endocrinology Research, Endocrinology IV, C.I. Parhon National Institute of Endocrinology, Bucureşti; [5]University Medical Center, Groningen, The Netherlands; [6]Endocrinology, Endocrinology IV, "C Davila" University of Medicine and Pharmacy, Bucharest, Romania

Background: Despite its prevalence, many cases of male infertility remain idiopathic, prompting the search for novel etiological factors. Emerging research suggests the seminal microbiome can regulate hormones and immunity, yet its role in male reproduction is unclear. The study aimed to investigate how *Lactobacillus* abundance modulates the correlation network of key reproductive and adrenal hormones.

Methods: We included patients with male idiopathic infertility ($n = 27$), and a fertile control group ($n = 21$). Seminal microbiota was determined by 16S rRNA gene sequencing (V3-V4 region) and bioinformatic analysis provided relative taxonomic abundances. Serum levels of key reproductive hormones—including Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), Testosterone, Estradiol (E2), Inhibin B, Dehydroepiandrosterone Sulfate (DHEA-S), Sex Hormone-Binding Globulin (SHBG), Prolactin (PRL), and Cortisol—were quantified using ELISA kits according to the manufacturer's protocols. Pearson correlation analyses were performed to assess hormonal interrelationships using GraphPad Prism 10.4.1.

Results: Subjects were classified into "Low-Lactobacillus" and "High-Lactobacillus" groups, based on a predefined cutoff (<80%) of *Lactobacillus* spp. abundance. In the Low-Lactobacillus environment, the endocrine network was characterized by a highly significant positive correlation between FSH and LH ($r = 0.91$, $P < .0001$), indicating a strong activation of the hypothalamic-pituitary-gonadal axis. Furthermore, a strong positive correlation was observed between DHEA-S and free Testosterone ($r = 0.77$, $P = .0012$), as well as between SHBG and total Testosterone ($r = 0.72$, $P = .0056$). A significant negative correlation was present between Inhibin B and FSH ($r = -0.60$, $P = .0298$). The High-Lactobacillus context revealed DHEA-S emerging as a central factor. It exhibited a very strong positive correlation

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

with Inhibin B (r = 0.80) and with SHBG (r = 0.75), but strong negative correlations with E2, total Testosterone, and FSH (r = −0.66 to −0.69, all $P < .0001$). A novel, strong positive coupling was observed between total Testosterone and E2 (r = 0.73, $P < .0001$). Despite network-wide shifts, two key correlations remained stable and significant regardless of *Lactobacillus* abundance: PRL—Cortisol (r ≈ 0.60) and Inhibin B—FSH (r ≈ −0.60 to −0.65).

Conclusions: *Lactobacillus* abundance acts as a switch between distinct endocrine states. A deficient microbiome corresponds to classic HPG axis activation, while a Lactobacillus-rich environment shifts the network toward a DHEA-S-centered profile. Thus, the microbiota influences not just hormone levels, but the very architecture of endocrine interactions.

Abstract citation ID: lvag096.395

P232 - ECE_1750 - Can AI make a difference in patient satisfaction and consultation efficiency using an AI-based documentation tool in endocrinology practice?

Roxana Novac[1], Repede Vlad[2] and Razvan Valcu[2]
[1]*CLINICA DR. NOVAC, Bacau, Romania;* [2]*Apolloiq, Taunton, United Kingdom*

Background: Administrative documentation during medical consultations may reduce physician–patient interaction and impact patient satisfaction. Artificial intelligence (AI)–based tools designed to capture and structure medical conversations may improve consultation workflow and communication.

Aim: To evaluate patient satisfaction and consultation efficiency in standard endocrinology consultations compared with consultations assisted by an AI-based documentation application.

Methods: Twenty patients were included in a prospective observational study. Each patient underwent two endocrinology consultations: one standard consultation without AI assistance and one consultation supported by an AI-based application that listened to the physician–patient conversation and generated structured medical documentation.

After each consultation, patient satisfaction was assessed using validated questionnaires: the Client Satisfaction Questionnaire (CSQ-8) and the Patient Satisfaction Questionnaire Short Form (PSQ-18). Consultation duration and estimated time saved were recorded.

Results: AI-assisted consultations were associated with a mean time saving of approximately 10 minutes per consultation compared with standard visits. Patient satisfaction scores were higher following AI-assisted consultations, particularly in domains related to communication quality, perceived physician attentiveness, and overall consultation experience. Patients reported feeling more listened to, benefiting from continuous eye contact with the physician due to the absence of manual note-taking. The AI application also supported a more complete medical history by minimizing the loss of relevant anamnesis details.

Conclusions: The use of an AI-based documentation tool during endocrinology consultations was associated with improved patient satisfaction and increased consultation efficiency compared with standard practice. These findings support the potential role of AI-assisted documentation as a complementary tool in routine endocrinology care.

Abstract citation ID: lvag096.396

P234 - ECE_3795 - Impact of in utero exposure to sesamol on folliculogenesis

Manon Fiévet[1,2], Gabrielle Sulimowski[1], Louisa Menu[1], Annica Frau[1] and Denis Nonclercq[3]
[1]*Faculty of Medicine, Pharmacy and Biomedical Sciences, Health Institute, Laboratory of Histology, University of Mons, Mons, Belgium;* [2]*Faculty of Medicine, Pharmacy and Biomedical Sciences, Health Institute, University of Mons, Mons;* [3]*Faculty of Medicine, Pharmacy and Biomedical Sciences, Health Institute Laboratory of Histology, Laboratory of Histology, University of Mons, Mons, Belgium*

The growing popularity of vegetarian and vegan diets has significantly increased our exposure to phytoestrogens, which are potential endocrine disruptors. Sesamol, obtained by roasting sesame seeds, is classified as a phytoestrogen. As hormonal variations play a decisive role in the formation and differentiation of the reproductive system, pregnancy represents a period of increased sensitivity to endocrine disruptors. Through its ability to cross the placental barrier and interact with estrogen receptors, sesamol could impact the development of the reproductive system of babies exposed in utero.

The aim of this study is to investigate the consequences of prenatal exposure to sesamol on folliculogenesis and blood hormone levels in F1 offspring. Pregnant rats were orally exposed to different doses of sesamol (30 or 100 mg/kg/day) from the 14th to the 19th day of gestation. Histological analysis of the ovaries was performed in newborn (aged 4 days) or adult (aged 120 days) animals from the F1 offspring.

In newborn rats, in utero exposure to sesamol does not affect the relative proportion of pre-antral follicles. However, morphometric analysis of the ovaries revealed an increase in apoptosis of oocytes present in primordial follicles, resulting in a rise in the number of atretic follicles. The proliferation rate of follicular and thecal cells was also assessed by anti-BrdU immunohistochemistry. Our results show that sesamol has no impact on the proliferation rate of these cells at this stage of life.

In adulthood, the proportion of the different types of follicles is not affected by the treatment. By contrast, sesamol induces a significant increase in the number of S-phase cells in the granulosa of antral follicles. An increased frequency of polyovular follicles is also observed in treated animals. The alteration of the zona pellucida and the corona radiata in these abnormal follicles could impact the process of gamete recognition and fertilisation. ELISA tests carried out on blood serum samples showed that exposure to sesamol has no significant impact on testosterone and oestrogen levels. By contrast, a significant increase in AMH concentration was observed in animals exposed to a dose of 100 mg/kg/day.

In conclusion, prenatal exposure to sesamol induces morphological alterations in the ovaries, such as an increase in oocyte apoptosis within primordial follicles and a resurgence of polyovular follicles. The increased synthesis of AMH associated with these morphological alterations could have an impact on fertility.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.397

P235 - ECE_3659 - Exposure to microplastics (MP) and nanoplastics (NP) during the perinatal life alters hormone levels in Wistar rat dams and offspring

Patricia Cristina Lisboa[1], Nathalia Medeiros Nehme[2], Nelyana de Oliveira Serpa[3], Egberto Gaspar de Moura[2] and Iala Milene Bertasso[2]

[1]Ciências Fisiológicas, Universidade do Estado do Rio de Janeiro, Rio de Janeiro br, Brazil; [2]State University of Rio de Janeiro, Rio de Janeiro, Brazil; [3]Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

Currently, plastic production in the world is around 400 million tons/year. Due to improper disposal, waste is generated that accumulates in the environment, such as MP (particles smaller than 5 mm) and NP (particles smaller than 100 nm), which have already been found in air, soil, water and food. Additionally, MP and NP have been detected in various human tissues, such as the placenta and breast milk, and may affect the endocrine system of offspring. Here, we studied if exposure to MP and NP during pregnancy and lactation can cause hormonal dysfunction in dams and offspring of both sexes and different ages. Experimental design was approved by ethics committee (CEUA/032/2022). From gestational day 7 until postnatal day 21 (weaning), Wistar rat dams received vehicle (filtered water; control group; $n = 9$), 10 µm polystyrene microparticles (25 µg/kg body weight, MP group; $n = 8$) or 100 nm polystyrene nanoparticles (25 µg/kg body weight, NP group; $n = 8$). Hormone levels of dams, male and female pups were evaluated by multiplex assay at weaning (21 days-old), puberty (45 days-old) and adulthood (120 days-old). Corticosterone, T4, TSH, leptin and insulin were analyzed at all ages, while gonadotropins and sex steroids were evaluated at adulthood. Data were analyzed by one-way ANOVA with Dunnett's post-test; $P < .05$ as significant. NP dams had lower plasma T4 (-10%, $P = .033$), while MP dams did not show hormonal changes. At weaning, male offspring had lower plasma corticosterone (MP −65%, $P < .0001$; NP −55%, $P = .0001$), while females did not show hormone alterations. At puberty, no changes were observed in either sex. In adulthood, male offspring presented higher plasma FSH (MP +53%, $P = .0280$; NP +51%, $P = .0437$), while females presented higher plasma TSH (MP +54%, $P = .0328$; NP +50%, $P = .0483$). Thus, perinatal exposure to both MP and NP alters the hormonal homeostasis of dams and offspring at weaning and in adulthood, while at puberty, no changes were found.

Abstract citation ID: lvag096.398

P237 - ECE_1934 - Influence of blood phosphatidyl-ethanol, quantitative LC-MS/MS assessment of alcohol intake on metabolic and cortisol parameters

Dupuis Hippolyte, Charlotte Altet, Florian Hakim, Antoine Danais, Espiard Stephanie and Marie Christine Vantyghem

Endocrinology, Daibetology, Oncoendocrinology and Metabolism, Lille University Hospital, Lille, France

Fifty-years ago, the first cases of alcohol-induced pseudo-Cushing syndromes were described (1977 Smals & Rees, *The Lancet*, 1977; Wright, *JCEM*, 1978), Chronic alcohol consumption remains a pitfall in the evaluation of Cushing syndrome, and its impact on the corticotropic axis is often underestimated, sometimes leading to unnecessary investigations. From a pathophysiological standpoint, alcohol may either directly stimulate the corticotropic axis, through alcohol-related stress, anxiety, and depressive disorders, resulting in abnormal glucocorticoid feedback and loss of circadian rhythm, or indirectly affect liver steroid metabolism via 11beta-hydroxysteroid-dehydrogenase type 1, which activates cortisone into cortisol. In this complex clinical setting, phosphatidylethanol (PEth), measured by LC-MS/MS, recently emerged as a direct and specific biomarker of alcohol intake.**Objectif:** To evaluate the relationship between chronic alcohol intake, assessed by PEth, and clinical, biological, and body-composition parameters reflecting glucocorticoid exposure.

Methods: This **retrospective cross-sectional study,** conducted in accordance with the French MR-003 methodology, included 1346 patients who underwent PEth measurement between 2020 and 2025. Among them, 136 patients had at least one cortisol assessment and were considered for the study; 23 patients were excluded due to ongoing corticosteroid therapy. The final cohort comprised 113 patients, divided into two groups: 42 patients (26 men) with a PEth ≥ 200 µg/L (excessive alcohol intake) and 71 patients (33 men) with a PEth < 200 µg/L.

Results: Sex ratio, age, BMI, blood pressure, fasting blood glucose and C-peptide, liver enzymes, Low-density-lipoprotein-cholesterol and triglycerides, body fat and lean mass percentages, vertebral, femoral, and whole-body T-scores (DEXA), Controlled-Attenuation-Parameter and liver stiffness assessed by ultrasound elastography (Fibroscan), liver steatosis percentage, and intra- and total-abdominal fat (MRI) did not differ significantly between groups. Mean corpuscular volume (MCV), gamma-glutamyl-transferase, and Hight-density-lipoprotein-cholesterol (HDL) were significantly higher, while HbA1c was significantly lower, in the high-intake group. Urinary free cortisol (UFC) ($P = .09$) and 16h00 serum cortisol ($P = .07$) tended to be lower and higher, respectively, in the high-intake group. No significant differences were observed between 08h00 and 00h00 cortisol and ACTH, 1-mg Dexamethasone Suppression test, or THF + αTHF/THE ratio between the two groups.

A negative correlation was found between PEth and HbA1c ($P = .007$), while positive correlations were observed between PEth and HDL ($P = .038$), MCV, and UFC ($P = .0001$).

Conclusions: These results suggest that high alcohol intake could increase UFC and alter the cortisol nychthemeral rhythm without significantly affecting metabolic parameters. However, these findings are limited by missing data inherent to this real-life setting.

Keywords phosphatidylethanol, alcohol, cortisol, Cushing, metabolism

Abstract citation ID: lvag096.399

P238 - ECE_1646 - Prepubertal and Transgenerational toxicity of potassium sorbate (E202) over four generations of female Wistar rats

Elisabeth Louise Ndjengue Mindang[1], Charline Florence Awounfack[2], Perpetue Atsama Mbede[3], Sylvin Benjamin Ateba[4], Douglas Kemboi[5], Derek Tantoh Ndinteh[6], Rui Werner Maçedo Krause[7] and Dieudonne Njamen[8]

[1]Department of Animal Biology and Physiology, University of Yaounde, Yaoundé, Cameroon; [2]Department of Chemistry-Biology,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

University of Bertoua, Bertoua, Cameroon; [3]Yaounde, Cameroon; [4]Department of Biology of Animal Organisms, University of Doual, Douala, Cameroon; [5]Department of Chemistry, Tshwane University of Technology, Pretoria, South Africa; [6]Department of Chemical Sciences, University of Johannesburg, Johannesburg, South Africa; [7]Department of Chemistry, Rhodes University, Makhanda, South Africa; [8]Department of Animal Biology and Physiology, University of Yaoundé 1, Yaounde, Cameroon

The evolution of human fertility over the last 50 years has shown considerable problems due to a growing number of couples who find it difficult to procreate without medical assistance. The World Health Organization (WHO) suggests that around one in every six people of reproductive age worldwide experience infertility in their lifetime, and it has an impact on their families. Worldwide, an increase in the prevalence of this reproductive disorder has been increasingly linked to lifestyle factors, such as exposure to endocrine-disrupting chemicals (EDCs). Several food additives present in our food may enhance the risk of infertility in both sexes. Therefore, it is crucial to understand the impact of human exposure to these substances to protect the health of the population. On this basis, a pre-pubertal exposure to potassium sorbate (12.5, 45, and 78 mg/kg BW doses) and an extended three-generation reproductive toxicity were evaluated in immature female Wistar rats. The work aimed to study their effects on the sexual maturation, sexual behavior, and fertility of parents (F0) and offspring of the first, second and third generations. Results from the evaluation of their effects on sexual maturation showed compared to the control group, animals receiving potassium sorbate at the dose of 78 mg/kg BW, showed significantly decrease in percentage of animal with vaginal opening ($P < .001$) on postnatal day 46, the number total follicles ($P < .001$), relative weight of ovaries ($P < .01$) and an increase in the number of atresia follicles ($P < .001$). The evaluation of their effects on fertility revealed that exposure to potassium sorbate from PND 21 to parturition is responsible for the decrease of fertility index, gestational rate, and the increase of the resorption index and post implantation loss rate as compared to the control group. Concerning biochemical parameters evaluated in the third generation, potassium sorbate decreased the ovarian total protein (PS 78, $P < .001$) and progesterone serum concentration (PS 45 and 78). On folliculogenesis, the results showed that potassium sorbate decreased the number of primary follicles (PS 78, $P < .001$) and increased the number of atresia follicle (PS 78) at the third generation. To conclude, these results could validate at least in part the global observations on increasingly declining fertility linked to exposure to food additives and provide substantial scientific proof confirming potassium sorbate as an endocrine disruptor.

Keywords Food additive, potassium sorbate, delay sexual maturation, endocrine disruptor

Abstract citation ID: lvag096.400

P239 - ECE_1829 - Bisphenol A, F and S disrupt thyroid growth regulation via RET and mTOR pathway activation

Niklas Geiger, Pauline Mehringer, Simon Kloock, Palina Zytner, Max Kurlbaum, Jasmin Felker, Martin Fassnacht and Ulrich Dischinger
Division of Endocrinology and Diabetes, Department of Internal Medicine, University Hospital Würzburg, Würzburg, Germany

Background: Endocrine-disrupting chemicals such as bisphenol A (BPA) and its analogues BPF and BPS are regularly detected in consumer products and the environment. Their phenolic structure enables interference with thyroid hormone synthesis, and receptor signaling. With rising human exposure, these compounds represent a growing concern for thyroid physiology and public health.

Methods: Male Wistar rats (n = 4-5 per group) were exposed to BPA, BPF, or BPS (10 or 100 µM in DMSO) via drinking water for 19 weeks. Additional groups received combined bisphenol exposure (100 µM BPA + BPF, BPA + BPS, BPF + BPS, or BPA + BPF + BPS). Controls received tap water with DMSO. Thyroid tissue was analyzed by qRT-PCR for RET, mTOR, Cxcl10 and Rps6ka4 as key components of growth-regulatory signaling. Expression of NIS (sodium-iodide symporter) and the TSH receptor was also quantified. Serum TSH, T3 and T4 were measured.

Results: Exposure to 100 µM BPA significantly increased RET and Cxcl10 mRNA expression compared to controls ($P < .05$). The combined BPA + BPF + BPS group showed the strongest induction of these mitogenic genes ($P < .05$). mTOR and Rps6ka4 mRNA expression was significantly upregulated in the combined BPA + BPS group ($P < .05$) and further amplified in the triple-exposed group ($P < .001$). NIS expression was significantly reduced in the 100 µM BPA group and in the BPA + BPF + BPS group, whereas expression of TSH receptor remained largely unchanged except for a downward trend in the triple-exposed animals ($P < .07$). Serum TSH was significantly elevated in the 100 µM BPA group ($P < .001$), serum T3 was reduced in the BPA + BPF group while serum T4 was unchanged across all groups.

Conclusions: Chronic exposure to BPA and its analogues activates thyroidal RET and mTOR signaling, particularly under combined bisphenol exposure. These findings demonstrate that BPA substitutes may synergistically impair thyroid growth regulation and hormone synthesis, underscoring their relevance as endocrine disrupting chemicals.

Abstract citation ID: lvag096.401

P240 - ECE_3604 - Assessment of selenium status and background bromide exposure in children and young adults using urinary biomarkers

Ewelina Sośnierz[1], Przemysław Śliwka[1], Dorota Kowalik-Zakrzewska[1], Sara Aszkiełowicz[1,2], Sylwester Smoleń[3], Marcin Pakosz[3], Alina Niewiadomska[4], Renata Stawerska[1,2], Anna Łupińska[1,2], Andrzej Lewiński[1] and Arkadiusz Zygmunt[1]
[1]Department of Endocrinology and Metabolic Diseases, Polish Mother's Memorial Hospital—Research Institute, Łódź, Poland; [2]Department of Developmental Age and Adult Endocrinology, Medical University of Lodz, Łódź, Poland; [3]Laboratory of Mass Spectrometry, Faculty of Biotechnology and Horticulture, University of Agriculture in Krakow, Kraków, Poland; [4]Laboratory Diagnostics Center, Polish Mother's Memorial Hospital—Research Institute, Łódź, Poland

Introduction: Selenium is an essential micronutrient, while bromide represents a non-essential halogen with potential toxicological relevance. Both are excreted in urine and can serve as biomarkers of nutritional status and environmental exposure.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Data on urinary selenium and bromide in children remain scarce. This study assessed urinary concentrations of both elements in children and young adults from Residential Care Facilities in central Poland to characterise selenium status and evaluate background bromide exposure.

Methods: Urinary concentrations of selenium and bromide were assessed in a cohort of children and young adults residing in children's homes located in Łódź to characterise micronutrient status and possible exposure to brominated compounds. A total of 289 participants were examined across two stages: 157 children in 2019 and 132 children in 2023-2024. Selenium and bromide were quantified in diluted urine samples using inductively coupled plasma–triple quadrupole mass spectrometry, and results were normalised to creatinine concentrations to correct for urine dilution. Complete data were available for 272 children.

Results: The median urinary selenium concentration was 15.75 ± 8.25 μg/g creatinine, with a minimum value of 0.31 μg/g and a maximum of 66.93 μg/g. Twenty-seven children exhibited urinary selenium values below 10 μg/g creatinine, indicating insufficient dietary selenium intake based on commonly cited biomonitoring reference ranges. The median urinary bromide concentration was 1.14 ± 1.71 mg/g creatinine, with values ranging from non-detectable (0 mg/g) to 17.38 mg/g. Three children exceeded 10 mg/g creatinine, reaching concentrations more typical for occupationally exposed adults, yet none approached concentrations associated with acute toxicity.

In both, selenium and bromide concentrations, no statistically significant differences were observed between boys and girls. Although analysis across age groups revealed a statistically significant overall effect, subsequent multiple comparison procedures did not attribute the difference to specific individual age groups. Moreover, both element concentrations showed significant negative correlations with age, height, body mass index (BMI), body surface area (BSA), and muscle mass, whereas correlations with sex, body fat, and total body water were not significant.

Conclusions: The findings indicate generally adequate selenium levels in the cohort, with a subset demonstrating potential deficiency requiring dietary attention. Bromide values were broadly consistent with environmental background exposure, with isolated higher values likely reflecting non-toxic sources. The observed negative correlations with growth-related metrics for both elements may reflect physiological dilution or altered excretion dynamics with increasing body size. Together, these data contribute novel biomonitoring reference information for selenium and bromide in children.

Abstract citation ID: lvag096.402

P241 - ECE_1540 - Adrenal accumulation and functional impact of endocrine disrupting chemicals: mass spectrometric profiling in human adrenal tumors and a bisphenol exposition trial in rats

Simon Kloock[1], Zhong-Min Li[2], Pauline Mehringer[1], Palina Zytner[1], Max Kurlbaum[1], Jasmin Felker[1], Martin Fassnacht[1], Kannan Kurunthachalam[2] and Ulrich Dischinger[1]

[1]Department of Internal Medicine, Division of Endocrinology and Diabetes, University of Wuerzburg, University Hospital Wuerzburg, Wuerzburg, Germany; [2]Wadsworth Center, New York State Department of Health, Albany, NY, United States

Endocrine disrupting chemicals (EDCs) have been increasingly recognized for their potential to interfere with adrenal gland function, yet their tissue-specific accumulation and functional consequences *in vivo* remain poorly understood. Using mass spectrometry (LC-MS/MS), we quantified multiple EDCs in human adrenal tumor tissue (non-functional adenoma, aldosterone-producing adenoma, cortisol-producing adenoma, adrenocortical carcinoma). Preliminary results show bisphenol S (BPS) to be enriched across all samples, suggesting adrenal tissue accumulation. Other EDC related substances (eg mEP) may accumulate in non-functional adenomas but not in hormone-producing adenomas, with unknown effects on tumor development and progression. Additionally, to explore causality and functional outcomes, we exposed rats to bisphenol A (BPA), bisphenol F (BPF), and BPS at concentrations of 10 μM and 100 μM via drinking water for 19 weeks. Urine analysis confirmed a dose-dependent increase in urinary bisphenol excretion. BPS was again found to accumulate in the adrenal gland in a dose-dependent manner. Major alterations in steroid profiles were not detected. These findings suggest that EDCs (especially BPS) selectively accumulate in adrenal tissue, highlighting the adrenal gland as a critical target for environmental endocrine disruptors. Further studies are going to focus on the identification of other adrenal-enriched EDCs and their impact on adrenal function, but also tumor development and progression.

Abstract citation ID: lvag096.403

P242 - ECE_3278 - Clinical features and outcomes of acromegaly patients with mild IGF-I elevation at diagnosis

Cécilia Laure[1], Carine Richa[1], Tristan Verdelet[1], Severine Trabado[2,3], Clovis Adam[4], Philippe Chanson[1,3], Luigi Maione[1,3], Jacques Young[1,3], Peter Kamenicky[1,3], Sylvie Salenave[1,3] and Fanny Chasseloup[1,3]

[1]AP-HP, Hôpital de Bicêtre, Service Endocrinologie et des Maladies Rares de l'Hypophyse (CRMR HYPO), Le Kremlin Bicêtre, France; [2]AP-HP, Hôpital de Bicêtre, Service de Biochimie, Hormonologie, Pharmacotoxicologie, Le Kremlin Bicêtre, France; [3]Inserm, Physiologie et physiopathologies endocriniennes, Université Paris-Saclay, Le Kremlin-Bicêtre, France; [4]AP-HP, Hôpital de Bicêtre, Service d'Anatomopathologie, Le Kremlin-Bicêtre, France

Background: Historically, the diagnosis of acromegaly relied on elevated IGF-1 levels and inadequate GH suppression during the oral glucose tolerance test (OGTT). Guidelines now define acromegaly as IGF-1>1.3 times the upper limit of normal (ULN), with characteristic clinical features. Consequently, management of patients referred for moderately elevated IGF-1 with subtle or absent clinical features remains challenging. Our objective was to identify the clinical, biochemical, and follow-up characteristics of acromegaly patients with mildly elevated IGF-1.

Methods: We performed a retrospective monocentric cohort study of patients evaluated in the Bicêtre Endocrinology department between 2013 and 2024 with a diagnosis of acromegaly and an initial IGF-I < 1.5 ULN.

Results: In the 436 patients included, 23 had an initial IGF-I <1.5 ULN. Among them, 21 were women (91%); the median age

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

at diagnosis was 36 years [IQR: 28; 46], and most pituitary lesions were microadenomas (57%). Thirteen patients (57%) had no dysmorphic syndrome. Median IGF-I at diagnosis was 324 ng/mL [IQR 278; 356], corresponding to a median IGF1 index of 1.35 [IQR 1.18; 1.37]. Elevated IGF-1 was identified in patients following investigation for nonspecific pituitary tumoral symptoms in 8 (35%), symptoms related to hyperprolactinemia in 5 (22%), pituitary incidentaloma in 4 (17%), clinical suspicion of acromegaly in 3 (13%) and in the context of pituitary tumor genetic predisposition (Mc Cune Albright Syndrome and AIP) in 3 patients (13%). When available, nadir plasma GH during the OGTT was >1 mUI/L in 15 patients (15/21 = 71%), including 2 with initial normal IGF-1 levels, and 4 patients had a normal GH nadir during OGTT. Surgery was performed in 16 patients; 14 had tumoral GH immunostaining, including 7 with GH and prolactin immunostaining, and 1 patient displayed isolated prolactin staining but persistent elevated IGF-1 levels during follow-up (pathology was not available in 1 patient). In the remaining patients, the diagnosis of acromegaly was retained because of acromegaly features during follow-up. Overall, complications of acromegaly were present in 10 patients (43%).

Conclusions: This study demonstrates that patients with mildly elevated IGF-1 levels exhibit distinct features compared with typical acromegaly patients, including a marked female predominance, a higher prevalence of microadenomas, and a high proportion of lacto-somatotroph adenomas. Disease presentation was rarely driven by typical acromegalic features; however, despite a subtle clinical presentation and lower GH secretion, nearly half of the patients exhibited acromegaly-related complications, highlighting the need for further investigation, including OGTT and long-term follow-up in this patient subgroup.

Abstract citation ID: lvag096.404

P243 - ECE_2216 - Giant macroprolactinoma with extensive parasellar invasion demonstrating an exceptional early response to low-dose cabergoline

Hafiz Awais Javed, Amna Zeeshan, Anupam Brahma, Jayamalee Jayaweera, Daisy Beard and Haris Marath
Endocrinology, West Suffolk Hospital, Bury St Edmunds, United Kingdom

Background: Giant macroprolactinomas are rare pituitary adenomas characterised by extensive local invasion, markedly elevated prolactin concentrations, and significant mass effect. They present major diagnostic and therapeutic challenges and have traditionally been associated with poorer outcomes due to tumour size and invasiveness. Dopamine agonists remain in first-line therapy, although the magnitude and speed of response are variable. We report a case of a giant macroprolactinoma in a young woman demonstrating an unusually rapid and profound clinical, biochemical, and radiological response to low dose cabergoline.

Case Presentation: A 20-year-old female presented with a two-month history of headaches and visual disturbance described as blind spots, along with absent of withdrawal menstrual bleeding on combined oral contraceptive pill. Formal visual field testing confirmed bitemporal hemianopia. Pituitary MRI showed a giant macroadenoma (3.9 × 3.4 × 3.0 cm) with suprasellar extension, optic chiasm displacement, hypothalamic and third ventricle deformation, bilateral cavernous sinus invasion, encasement of the right internal carotid and middle cerebral arteries, temporal lobe distortion, clival extension, and sphenoid sinus deformation.

Hormonal testing showed elevated prolactin levels (>100 000 mIU/L), consistent with a giant macroprolactinoma. Other pituitary axes were intact. She was commenced on cabergoline 250 micrograms twice weekly, with advice regarding the risk of pituitary apoplexy.

Visual, hormonal and radiological responses to cabergoline were rapid and unexpected. Prolactin declined from >100 000 mIU/L to 2129, 749, and 397 mIU/L after the second, third, and fourth dose, respectively. Visual field defects resolved after the third dose, and MRI after the fourth dose showed marked tumour regression.

Conclusions: This case illustrates the exceptional dopamine agonist sensitivity that may occur even in highly invasive giant macroprolactinomas. Proposed underlying mechanisms include high tumour dopamine D2-receptor density with rapid suppression of prolactin synthesis, inhibition of lactotroph proliferation, and induction of tumour cell apoptosis. Low-dose cabergoline should remain first-line therapy, as prompt initiation can rapidly reverse mass-effect symptoms and potentially obviate the need for surgical intervention.

Abstract citation ID: lvag096.405

P244 - ECE_3530 - Novel AIP mutation in aggressive somatotroph adenoma presenting as gigantism

Mai C. Arlien-Søborg[1], Kirstine Stochholm[1], Marta Korbonits[2], Jens Otto Jørgensen[1] and Jakob Dal[3]
[1]*Department of Endocrinology, Aarhus University Hospital, Aarhus, Denmark;* [2]*Centre for Endocrinology, Barts and the London School of Medicine and Dentistry, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom;* [3]*Department of Endocrinology and Steno Diabetes Center North, Aalborg University Hospital, Aalborg, Denmark*

Background: Acromegaly and gigantism usually occur sporadic, but familial cases exist. Germline mutations in the aryl hydrocarbon receptor–interacting protein (*AIP*) gene are associated with familial isolated pituitary adenoma (FIPA) and predispose to early-onset, large aggressive growth hormone (GH) secreting adenomas that often respond poorly to somatostatin analogues.

Case: A 19-year-old male patient presented with gigantism (height 207 cm) and 2-year history of backache and reduced libido, and a rapid growth spurt from 195 cm to 207 cm. There was no family history of pituitary adenomas. He was well proportioned, with prognathism, enlarged extremities, and bitemporal inferotemporal visual field impairment. Biochemical evaluation confirmed GH excess (IGF-I SDS 6.9; nadir GH 85.5 µg/L during oral glucose tolerance testing). Prolactin was within the normal range, testosterone was suppressed (0.2 nmol/L), with undetectable LH and FSH.

Pituitary MRI demonstrated a macroadenoma (30 × 43 × 35 mm) causing displacement of the optic chiasm, anterior extension beneath the frontal lobes, and posterior extension toward the pons without invasion of the cavernous sinuses. Bone age was 3.3 years delayed. Genetic testing identified a novel likely pathogenic 4 basepair deletion *AIP* mutation resulting in a

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

frameshift: c.668_671del; p.(Trp223Serfs*79). Family screening revealed four asymptomatic carriers (age range 17-72 years) with no clinical or biochemical evidence of pituitary disease.

Preoperative treatment with pasireotide LAR 60 mg every 4 weeks led to marked improvement in visual fields but incomplete biochemical control, prompting the addition of pegvisomant 60 mg weekly. The patient subsequently underwent partial tumour resection via craniotomy. Histology confirmed an eosinophilic GH-producing pituitary adenoma with low proliferative index (Ki-67 1%). Postoperatively, combination medical therapy was resumed. Although IGF-I levels declined further, they remained above the upper limit of normal, necessitating stepwise escalation of pegvisomant and pasireotide LAR dosing.

Conclusions: This case highlights aggressive, treatment-resistant gigantism linked to a novel *AIP* mutation. Early genetic testing and multimodal management are essential, and identification of asymptomatic carriers enable early diagnosis which has been shown to improve clinical outcomes.

Abstract citation ID: lvag096.406

P246 - ECE_3578 - Osilodrostat in a block-and-replace strategy for successful management of cycling Cushing's syndrome—case series

Wiktoria Suchy[1], Mari Minasyan[2], Aleksandra Gamrat-Żmuda[2], Alicja Hubalewska-Dydejczyk[2] and Aleksandra Gilis-Januszewska[2]
[1]Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [2]Kraków, Poland

Introduction: Cyclic Cushing's syndrome (cCS) represents a significant clinical challenge due to unpredictable fluctuations in cortisol secretion, leading to heterogenous presentations and false-negative biochemical results. Although previously considered rare, cCS is increasingly recognized in clinical practice. Management is particularly difficult, and block-and-replace therapy with osilodrostat may provide effective cortisol stabilization. We present two illustrative cases from our clinic, highlighting the diagnostic process and practical use of osilodrostat in a block-and-replace strategy among patients with cCS.

Case presentations: A 68-year-old man with a 5-year history of recurrent hospitalizations due to infections and metabolic instability evaluated for bilateral adrenal incidentalomas. The patient presented with cushingoid features, and biochemical tests confirmed ACTH-dependent CS. Despite extensive imaging, the source of ACTH excess could not be identified. Retrospective analysis of the patient's history revealed multiple peaks of hypercortisolemia (morning serum cortisol 34.43-43.5 ug/dl) separated by spontaneous remissions (morning serum cortisol 8.02-13.3 ug/dl), correlating with episodes of hypertension and hyperglycemia, followed by hypotension and hypoglycemia. He was treated with metyrapone, temporarily in a block-and-replace regimen, however, marked cortisol variability required frequent dose adjustments. Initiation of low-dose osilodrostat (1 mg) in a continuous block-and-replace regimen (with hydrocortisone 5-10 mg daily) resulted in sustained biochemical and clinical stabilization for 13 months. Osilodrostat was discontinued prior to planned BIPSS, with the patient maintained on hydrocortisone replacement. Currently, the patient remains in an eucortisolemic phase 11 months after osilodrostat discontinuation.

A 45-year-old woman was admitted after referral by her gynecologist, presenting with numerous cushingoid features, worsening hypertension, and diabetes. Biochemical and imaging tests confirmed Cushing's disease (CD), leading to transsphenoidal surgery. She remained on hydrocortisone for six years, with several unsuccessful discontinuation attempts. Ambulatory cortisol measurements suggested normocortisolemia (morning serum cortisol 12.7-15.3 ug/dl), but during admissions for planned discontinuation, they were unexpectedly low (morning serum cortisol 3.6-7.66 ug/dl). After eventual adrenal function recovery, she experienced fluctuating control of comorbidities. BIPSS performed during peak of hypercortisolemia confirmed recurrent CD, and pituitary radiotherapy was performed. Block-and-replace therapy with osilodrostat was initiated at 4 mg daily with hydrocortisone 5-10 mg. Optimal disease control enabled dose reductions, with the patient currently stable on 1 mg of osilodrostat and 5 mg of hydrocortisone.

Conclusions: These cases illustrate the complexity of diagnosing and managing cCS. In both patients, the block-and-replace therapy with osilodrostat was well tolerated, effectively stabilized cortisol concentrations and controlled comorbidities, demonstrating its clinical value and safety in real-life management of cCS.

Abstract citation ID: lvag096.407

P247 - ECE_3541 - Block-and-replace therapy with osilodrostat in Cushing's syndrome: a real-life single-center experience

Aleksandra Gilis-Januszewska[1], Aleksandra Gamrat-Żmuda[1,2], Mari Minasyan[1], Wiktoria Suchy[1] and Alicja Hubalewska-Dydejczyk[1]
[1]Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [2]Doctoral School of Medical and Health Sciences, Jagiellonian University Medical College, Krakow, Poland

Background: Osilodrostat is an effective cortisol synthesis inhibitor for Cushing's syndrome (CS). The block-and-replace (BR) strategy is not currently included in clinical practice guidelines; however, limited data and clinical experience suggest efficacy in selected patients.

Objective: To describe real-life clinical experience with osilodrostat administered using a BR regimen in patients with CS treated at a tertiary referral center.

Methods: The retrospective observational analysys included 10 patients with CS treated with osilodrostat using a BR strategy between 2020 and 2025. Clinical and biochemical data were collected at baseline and during follow-up. Patients treated with block-and-replace after switching from titration were analyzed from the time of block-and-replace initiation. Treatment efficacy and safety were assessed during routine clinical practice.

Results: Ten patients (4 men, 6 women) were included: four with Cushing's disease(CD) and six with ectopic Cushing's syndrome (three small-cell lung cancers with metastases, one lung adenocarcinoma with metastases, one lung carcinoid tumor, and one of unknown origin). Three patients were treated before successful surgery, one after non-radical surgery, and the remaining patients were disqualified from surgery.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

In six patients, titration was initially used and BR strategy was initiated after a mean of 29.1 days (range 8-45). The median duration of BR was 66.3 days. In eight patients, BR was introduced due to severe hypercortisolism (mean morning serum cortisol 45.1 µg/dL, night cortisol 30.5 µg/dL, ACTH 335 pg/mL), with a mean potassium supplementation of 166.35 mEq/day.

Initial osilodrostat doses in the BR regimen ranged from 5 to 25 mg/day (mean 10.7 mg/day), and hydrocortisone doses from 10 to 50 mg/day (mean 19 mg/day). The maximum osilodrostat dose (10-40 mg/day) was reached within 2-8 days. A >50% reduction in cortisol levels or values <15 µg/dL was achieved in 7/8 patients within a mean of 9.6 days (mean morning cortisol 9.22 µg/dL). Potassium supplementation was reduced in seven patients (mean 80.5 mEq/day), and antihypertensive therapy was reduced in six patients within a mean of 16.8 days.

In two patients with cyclic CS (cCS), BR was used due to difficulties with titration (osilodrostat 1-2 mg/day plus hydrocortisone 5-10 mg/day). No cases of adrenal insufficiency were observed; adverse events were mild (fatigue $n=3$, headache $n=1$, myalgia $n=1$).

Conclusions: Block-and-replace therapy with osilodrostat appears to be an effective and safe option in patients with severe hypercortisolism. It allows rapid dose escalation without the risk of adrenal insufficiency and provides effective cortisol control, including prevention of hormonal fluctuations in cCs.

Abstract citation ID: lvag096.408

P248 - ECE_1382 - Analysis of selected ZBTB38 gene variants in Polish pediatric patients with growth hormone deficiency and idiopathic short stature

Katarzyna Majewska[1], Andrzej Kędzia[1], Magdalena Prauzińska[2], Jarosław Szydłowski[2] and Joanna Nowacka-Woszuk[3]

[1]Department of Pediatric Diabetes, Auxology and Obesity, Poznan University of Medical Sciences, Poznan, Poland; [2]Department of Pediatric Otolaryngology, Poznan University of Medical Sciences, Poznan, Poland; [3]Department of Genetics and Animal Breeding, Poznan University of Life Sciences, Poznan, Poland

Introduction: Human height is a complex quantitative trait regulated by genetic, endocrine, and environmental factors. The *ZBTB38* (Zinc Finger and BTB Domain Containing 38) gene is considered to be one of the common contributors to height phenotypes, and its variants have been associated with height variation and short stature across diverse populations. Recent evidence suggests that *ZBTB38* may also influence therapeutic responses in children receiving recombinant human growth hormone (rhGH) treatment. Our study aimed to investigate the polymorphic variants of the *ZBTB38* gene in the context of growth hormone deficiency (GHD) and growth failure within the Polish pediatric population.

Material and Methods: The study cohort consisted of 150 children with short stature, all from central and western Poland, including 117 with GHD and 33 with idiopathic short stature (ISS). Inclusion criteria covered a height standard deviation score (hSDS) of -2 or below, calculated for age and gender, as well as the absence of additional chronic diseases. The control group consisted of 150 healthy, normal height children. Extracted DNA was amplified by PCR to analyze *ZBTB38* gene fragments, followed by Sanger sequencing. The odds ratio test calculator was used for statistical analysis. The study was approved by the Local Ethics Committee at the Poznan University of Medical Sciences.

Results: Allele frequencies were studied for three SNPs: one intronic, rs724016A>G, and two exonic, rs62282002C>G (p.Pro300Ala) and rs16851435T>G (p.Ser319Ala). The only statistically significant result was observed for rs724016A>G when comparing patients with ISS vs controls ($P=.0105$), with the alternative allele G having a lower frequency (0.2727) in ISS than in healthy children (0.4467). No differences were observed in the distribution of analyzed variants between children with GHD and controls.

Conclusions: Our results suggest a possible involvement of *ZBTB38* gene variants in the etiology of idiopathic short stature, while arguing against their significant role in the development of GHD in the Polish pediatric population. As genotype variation exerts effects on the growth process, the integration of genetic and clinical data may enhance diagnostic precision and potentially improve therapeutic strategies for pediatric growth disorders.

Funding: This study was financed by the Department of Genetics and Animal Breeding, Poznan University of Life Sciences, Poland: statutory fund No. 506.534.05.00) and the Department of Pediatric Diabetes, Auxology and Obesity, Poznan University of Medical Sciences, Poland: statutory fund No. JAK0000076]

Abstract citation ID: lvag096.409

P249 - ECE_2493 - Cancer risk in acromegaly

Christian Rosendal[1], Mai C. Arlien-Søborg[2], Marianne Andersen[3], Eigil H. Nielsen[1], Marianne Klose[4], Claus Feltoft[5], Olaf Dekkers[6], Jens Otto Jørgensen[2] and Jakob Dal[1,7]

[1]Research data and Biostatistics, Aaborg Universityhospital, Aalborg, Denmark; [2]Endocrinolgy, Aarhus Universityhospital, Aarhus, Denmark; [3]Endocrinolgy, Odense Universityhospital, Odense, Denmark; [4]Rigshospitalet, Copenhagen, Denmark; [5]Endocrinolgy, Herlev Hospital, Herlev, Denmark; [6]Department of Endocrinology, Leiden University Medical Center, Leiden, The Netherlands; [7]Steno Diabetes Center North Jutland, Aalborg, Denmark

Background: Cancer risk in acromegaly remains debated, with studies showing both increased and similar risk compared to the background population. We conducted a nationwide cohort study examining the risk of cancer and colorectal polyps in acromegaly patients.

Methods: Using a database of all acromegaly patients with validated diagnoses (1977-2021) ($n=809$, mean follow-up 14.6 ± 10.5 years) and controls matched on sex and birth year ($n=80\,900$, mean follow-up 15.1 ± 10.5 years), we investigated the occurrence of cancer diagnoses.

Findings: Overall cancer risk was not increased (IRR: 1.10 [0.93;1.30], $P=.27$), but patients with acromegaly had an increased risk of colorectal cancer (IRR: 1.78 [1.22;2.60], $P<.01$) which was more often localized (IRR: 2.00 [1.21;3.30], $P=.007$) as compared to controls. The incidence of benign colorectal polyps was elevated in acromegaly patients (IRR: 2.32 [1.96;2.76],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

$P < .01$). All-cause mortality was elevated in acromegaly (MRR: 1.18 [1.02; 1.36], $P = .03$), but cancer-specific mortality was not (MRR: 0.95 [0.72;1.25], $P = .72$).

Interpretation: In a population-based setting with confirmed cases of acromegaly and a follow-up period of up to 44 years, we found that acromegaly is associated with an increased risk of colorectal cancer, whereas neither overall cancer risk nor cancer-specific mortality was increased.

Abstract citation ID: lvag096.410

P250 - ECE_1469 - The clinical value of [18F]-fluoro-ethyl-L-tyrosine PET ([18F]FET-PET) correlated with MRI in patients with functioning pituitary adenomas: an observational cohort study

Loren van der Hoeven[1,2,3], Siebren Vugt[4], Tessa Timmers[4], Eva Heshof[1], Miou Koopman[2,4], Eleonora Aronica[2,3,5], Jantien Hoogmoed[2,3,6], Alberto M. Pereira[1,2,3], Elsmarieke van de Giessen[2,4,7] and Dirk Jan Stenvers[1,2,3]

[1]Department of Endocrinology and Metabolism, Amsterdam Gastroenterology Endocrinology and Metabolism (AGEM), Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands; [2]Pituitary Center Amsterdam, Amsterdam, The Netherlands; [3]European Reference Network on Rare Endocrine Conditions (Endo-ERN), Amsterdam, The Netherlands; [4]Department of Radiology & Nuclear Medicine, Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands; [5]Department of (Neuro)Pathology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands; [6]Department of Neurosurgery, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands; [7]Brain Imaging, Amsterdam Neuroscience, Amsterdam, The Netherlands

Purpose: To assess the clinical value of [18F]fluoroethyl-L-tyrosine PET ([^{18}F]FET-PET) correlated with MRI in patients with functioning pituitary adenoma (FPA) with negative or equivocal conventional MRIs during diagnosis, persistent disease and recurrence.

Methods: Retrospective observational cohort study of 34 patients with FPAs who underwent a total of 37 [^{18}F]FET-PETs (Cushing's disease: $n = 19$, acromegaly: $n = 14$, prolactinoma: $n = 3$, and TSH producing adenoma: $n = 1$) between January 2022 and April 2025. The clinical performance was assessed in the surgically treated cohort, using confirmative histopathology and/or postoperative remission as reference standard.

Results: [^{18}F]FET-PET identified a single lesion in 28 scans (76%), two lesions in 1 scan (3%), and no lesion in 8 scans (22%). [^{18}F]FET-PET and MRI were concordant positive in 14/37 scans, concordant negative in 1/37, discordant MRI+/[^{18}F]FET-PET+ different location in 2/37, discordant MRI-/[^{18}F]FET-PET+ in 8/37, discordant MRI+/[^{18}F]FET-PET- in 7/37 and partly concordant in 5/37 scans. In 14 cases surgery resulted in confirmative histopathology and/or postoperative remission, 12 of those had a positive [^{18}F]FET-PET. In 6 cases surgery did not result in confirmative histopathology and/or postoperative remission, of whom 5 had a positive [^{18}F]FET-PET. Overall, the sensitivity was 86% and the positive predictive value 71%. In three patients with acromegaly, [^{18}F]FET-PET was able to localize a lesion, despite biochemical control under continued somatostatin analogue treatment.

Conclusions: [^{18}F]FET-PET enhances lesion detection and improves personalized treatment in patients with FPA and negative or equivocal conventional MRIs throughout the disease course. Consensus on the timing of [^{18}F]FET-PET with respect to medication and biochemical status is warranted.

Abstract citation ID: lvag096.411

P252 - ECE_1668 - In silico prediction with POSTRE to distinguish benign and pathogenic GPR101 duplications in the clinical and prenatal settings

Giampaolo Trivellin[1], Victor Sanchez Gaya[2], Alexia Grasso[3], Magdalena Pasińska[4], Constantine Stratakis[5,6], Di Milnes[7], Edwin Kirk[8], Albert Beckers[9], Andrea Lania[3], Patrick Petrossians[9], Alvaro Rada-Iglesias[2], Martin Franke[10] and Adrian Daly[9]

[1]Pieve Emanuele, Milan, Italy; [2]Institute of Biomedicine and Biotechnology of Cantabria (IBBTEC), CSIC/Universidad de Cantabria, Santander, Spain; [3]IRCCS Humanitas Research Hospital, Milan, Italy; [4]Department of Clinical Genetic, Nicolaus Copernicus University, Bydgoszcz, Poland; [5]Human Genetics & Precision Medicine, Institute of Molecular Biology and Biotechnology (IMBB), Heraklion, Greece; [6]Section on Endocrinology and Genetics, Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Institutes of Health (NIH), Bethesda, MD, United States; [7]Genetic Health Queensland, Royal Brisbane Women's Hospital, Brisbane, Australia; [8]School of Clinical Medicine, University of New South Wales, Randwick, Australia; [9]Department of Endocrinology, Centre Hospitalier Universitaire de Liège, University of Liège, Liège, Belgium; [10]Andalusian Center for Developmental Biology (CABD), Universidad Pablo de Olavide (UPO), Seville, Spain

Background: Structural variants (SVs) that disrupt topologically associating domains (TADs) can cause disease by rewiring enhancer-promoter interactions. Duplications involving *GPR101* are known to cause X-linked acrogigantism (X-LAG)[1] by enabling aberrant expression of *GPR101*[2]. However, not all *GPR101*-containing duplications are pathogenic,[3] presenting a diagnostic challenge, especially in the prenatal setting.

Methods: We evaluated POSTRE, a tool designed to predict the regulatory impact of SVs, to distinguish pathogenic from benign *GPR101* duplications. We analyzed seven non-pathogenic duplications, and 27 known X-LAG associated pathogenic duplications. Tissue-specific enhancer maps built using H3K27ac ChIP-seq and ATAC-seq data as well as gene expression data derived from human anterior pituitary samples (research protocol 97-CH-0076) were integrated into POSTRE to enable predictions in an X-LAG relevant tissue context.

Results: POSTRE correctly classified all 34 duplications as benign or pathogenic. In addition, one X-LAG case with mild clinical features (eg severe growth hormone hypersecretion in the absence of pituitary tumorigenesis) was found to include only 2/5 *VGLL1* enhancers, whereas all 26 typical X-LAG cases had ≥4 enhancers duplicated. This suggests that milder enhancer hijacking at *VGLL1* could explain the different clinical features of X-LAG in this individual.

Conclusions: These results support incorporating POSTRE into diagnostic pipelines for interpreting SVs affecting chromatin architecture in pituitary disease. By accurately modelling

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

enhancer adoption in a cell type-specific context, POSTRE could help to reduce uncertainty in genetic counselling and offers a rapid alternative to performing chromatin conformation capture experiments.

References

1. Trivellin G, Daly AF, Faucz FR, et al. Gigantism and acromegaly due to Xq26 microduplications and GPR101 mutation. *N Engl J Med*. 2014;371(25):2363-2374. https://doi.org/10.1056/NEJMoa1408028
2. Franke M, Daly AF, Palmeira L, et al. Duplications disrupt chromatin architecture and rewire GPR101-enhancer communication in X-linked acrogigantism. *Am J Hum Genet*. 2022;109(4):553-570. https://doi.org/10.1016/j.ajhg.2022.02.002
3. Daly AF, Dunnington LA, Rodriguez-Buritica DF, et al. Chromatin conformation capture in the clinic: 4C-seq/HiC distinguishes pathogenic from neutral duplications at the GPR101 locus. *Genome Med*. 2024;16(1):112. https://doi.org/10.1186/s13073-024-01378-5

Abstract citation ID: lvag096.412

P253 - ECE_2260 - Real-world effectiveness and safety of osilodrostat in patients with Cushing's syndrome: a retrospective phase IV study

Chiara Simeoli[1], Nicola Di Paola[1], Ilaria Bonaventura[2], Davide Ferrari[2], Giacomo Voltan[3,4], Roberta Giordano[5], Maria Elena Aloini[6], Ylenia Alessi[7,8], Marianna Martino[9], Emanuele Ferrante[10], Federico Gatto[11,12], Soraya Puglisi[13], Vincenzo Rochira[14,15], Diego Ferone[11,12], Giovanna Mantovani[10,16], Giorgio Arnaldi[17], Francesco Ferraù[8,18], Antonio Stigliano[6], Emanuela Arvat[19], Mattia Barbot[3,4], Carla Scaroni[4], Andrea Isidori[2,20], Annamaria Colao[1,21] and Rosario Pivonello[1,21]

[1]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione, Università Federico II di Napoli, Naples, Italy; [2]Department of Experimental Medicine, "Sapienza" University of Rome, Rome, Italy; [3]Department of Medicine-DIMED, University of Padova, Padova, Italy; [4]Endocrinology Unit, University Hospital of Padova, Padova, Italy; [5]Department of Biological and Clinical Sciences, University of Turin, Turin, Italy; [6]Endocrinology, Department of Clinical and Molecular Medicine, Sant'Andrea University Hospital, Faculty of Medicine and Psychology, Sapienza University of Rome, Rome, Italy; [7]Department of Biomedical, Dental and Morphological and Functional Imaging Sciences, University of Messina, Messina, Italy; [8]Endocrine Unit, University Hospital G. Martino, Messina, Italy; [9]Clinica di Endocrinologia e Malattie del Metabolismo Azienda Ospedaliero Universitaria delle Marche, Ancona, Italy; [10]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [11]Endocrinology Unit, Department of Internal Medicine and Medical Specialties, University of Genoa, Genoa, Italy; [12]IRCCS Ospedale Policlinico San Martino, Genoa, Italy; [13]Internal Medicine, Department of Clinical and Biological Sciences, San Luigi Gonzaga University-Hospital, University of Turin, Turin, Italy; [14]Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [15]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria di Modena, Ospedale Civile di Baggiovara, Modena, Italy; [16]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [17]Unit of Endocrinology, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, (PROMISE) Policlinico Paolo Giaccone, Università degli studi di Palermo, Palermo, Italy; [18]Department of Human Pathology G. Barresi, University of Messina, Messina, Italy; [19]Oncological Endocrinology Unit, Department of Medical Sciences, University of Turin, Turin, Italy; [20]Centre for Rare Diseases (Endo-ERN Accredited), Policlinico Umberto I, Rome, Italy; [21]UNESCO Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy

Cushing's syndrome (CS) is a rare and severe endocrine disorder associated with substantial morbidity and impaired quality of life (QoL). Osilodrostat, a novel oral steroidogenesis inhibitor, has demonstrated efficacy and safety in clinical trials; however, real-world data remain limited. This multicenter, single-arm, phase-IV-study aimed at investigating real-world effectiveness and safety of osilodrostat in a large cohort of CS patients enrolled by 11 national referral centers. One hundred patients (71F,29M), aged 49 ± 14 years, with a disease duration of 8.8 ± 8.3 years, mainly affected by Cushing's disease (CD) (74%), were treated with osilodrostat up to 18 months. In 88% of patients disease severity was mild-to-moderate. Data collection included demographic, clinical, anthropometric, biochemical and hormonal parameters, QoL, pituitary tumor size, adverse events (AEs). 5% ($P < .05$) was considered statistically significant. 81% of patients reported normal UFC levels at their last follow-up observation, with 92% reporting normal UFC levels at least at one time point within the study-period. Time to first normalization of UFC levels, in the 80 patients who achieved normalization, was 92.1 ± 86.3 days at a median osilodrostat dose of 5(1-40) mg/day. Patients with milder forms of CS normalized UFC levels in a higher percentage of cases, more rapidly and requiring lower doses, compared with patients with moderate, severe/very-severe disease who achieved normalization in a lower percentage of cases, later and at higher doses. Osilodrostat induced significant reduction in late-night-salivary cortisol levels over time ($P < .05$). Testosterone levels early and transiently increased significantly in females ($P < .05$ at 3-6 months). However, this transient increase remained clinically silent, with hirsutism remaining stable. Osilodrostat was associated with progressive improvements in body weight, BMI, waist circumference, blood pressure, glucose metabolism, clinical signs of hypercortisolism ($P < .05$), and QoL ($P \leq .005$). Treatment effectiveness was consistent across different CS etiologies. In CD patients, the increase in ACTH levels did not significantly impact on pituitary tumor size, which remained stable in the majority of cases. AEs occurred in 29% of patients and were mild-to-moderate; hypoadrenalism was the most frequent AE (20%), mostly manageable with dose adjustment (36.4%) or temporary interruption (50%). This real-world study conducted in a large number of CS patients for a follow-up up to 18 months provides a comprehensive picture of osilodrostat use in routine clinical practice, supporting and extending evidence from controlled clinical trials, confirming that osilodrostat is a highly rapid and effective and generally well-tolerated therapy for CS management, with meaningful improvements in cardio-metabolic, clinical, and QoL parameters.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.413

P254 - ECE_3945 - Hypertonic saline test: a salty journey from a "feared" procedure to a safe, effective diagnostic for arginine vasopressin deficiency

August Palma[1], Chris Hallett-Morley[1], Katrina Lezaron[1], Danilo Inchiappa[1], Sue Parsons[1], Denise Tapa[1], Sophie Howarth[1], James MacFarlane[1] and Mark Gurnell[1,2]
[1]Endocrinology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [2]University of Cambridge, Cambridge, United Kingdom

Background: Distinguishing arginine vasopressin deficiency (AVP-D) or resistance (AVP-R) from primary polydipsia (PP) is clinically challenging. The water deprivation test (WDT) is widely used but is labour-intensive, time-consuming, and yields a higher rate of equivocal results. The hypertonic saline-stimulated copeptin test (HST) offers greater diagnostic accuracy in differentiating AVP-D from PP. We describe the establishment of HST as routine care in our endocrine centre, addressing concerns about safety and feasibility.

Methods: Discussions were held at monthly endocrine service meetings before adoption. A consultant endocrinologist and specialist nurse co-developed a clinical protocol and patient information leaflet. Initially, one test per month was carried out, later increasing to two per month. Patients underwent HST as outpatients, with monitoring of symptoms and serum sodium before, during and after stimulation. Technical success was predefined as post-stimulation sodium >149 mmol/L. Copeptin levels determined diagnostic category (complete AVP-D, partial AVP-D, PP, or AVP-R).

Results: Twenty-nine patients (20 women, 9 men; median age 41 years) were studied. All achieved technical success (100%) with post-stimulation sodium >149 mmol/L. No complications were reported; all patients were discharged the same day with normal sodium levels. Mild to moderate transient symptoms were documented but resolved. Diagnoses: 3 (10.3 %) complete AVP-D, 3 (10.3 %) partial AVP-D, 22 (75.9%) PP, and 1 (3.4 %) AVP-R based on baseline copeptin.

Conclusions: Implementation of HST as an outpatient diagnostic is feasible and safe when adequate protocols, personnel training, and monitoring are in place. The 100 % technical success rate, absence of complications, and clear diagnostic outcomes support HST as a highly efficient alternative to WDT. We propose copeptin stimulation tests be considered part of the standard approach for the evaluation of hypotonic polyuria, when basal laboratory tests are indeterminate.

Abstract citation ID: lvag096.414

P255 - ECE_1844 - Efficacy and safety of setmelanotide in acquired hypothalamic obesity: Results from a double-blind, multicentre, placebo-controlled, randomised phase 3 trial

Susan Phillips[1], Hanneke van Santen[2,3], Jill Hamilton[4,5], Ashley Shoemaker[6], Shana McCormack[7,8], Jennifer Abuzzahab[9], Martin Wabitsch[10], Mehul Dattani[11,12], Tomohiro Tanaka[13], Cecilia Scimia[14], Guojun Yuan[14], Hermann Müller[15], Christian L. Roth[16,17] and Jennifer Miller[18]
[1]Pediatric Endocrinology, University of California San Diego/Rady Children's Hospital, San Diego, United States; [2]Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands; [3]Department of Pediatric Endocrinology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands; [4]Division of Endocrinology, Hospital for Sick Children, Toronto, Canada; [5]Department of Pediatrics, University of Toronto, Toronto, Canada; [6]Ian Burr Division of Endocrinology and Diabetes, Vanderbilt University Medical Center, Nashville, United States; [7]Division of Pediatric Endocrinology and Diabetes, Children's Hospital of Philadelphia, Philadelphia, United States; [8]Department of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, United States; [9]Pediatric Endocrinology and Diabetes, Childrens Minnesota, Saint Paul, United States; [10]Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics and Adolescent Medicine, University Center Ulm, Ulm, Germany; [11]Department of Paediatric Endocrinology, Great Ormond Street Children's Hospital, London, United Kingdom; [12]Genetics and Genomic Medicine Research and Teaching Department, UCL GOS Institute of Child Health, London, United Kingdom; [13]Gastroenterology and Metabolism, Graduate School of Medical Sciences and Medical School, Nagoya City University, Nagoya, Japan; [14]Rhythm Pharmaceuticals, Inc, Boston, United States; [15]Department of Pediatrics and Pediatric Hematology/Oncology, Carl Von Ossietzky Universität Oldenburg, Klinikum Oldenburg AöR, Oldenburg, Germany; [16]Seattle Children's Research Institute, Seattle, United States; [17]Division of Endocrinology, Department of Pediatrics, University of Washington, Seattle, United States; [18]Pediatric Endocrinology, Department of Pediatrics, University of Florida, Gainesville, United States

Background: Hypothalamic melanocortin-4 receptor (MC4R) signalling is crucial for regulating hunger, satiety, and energy expenditure. Tumour/treatment-induced or traumatic brain injury to the hypothalamus can lead to hyperphagia and acquired hypothalamic obesity (aHO), for which no approved treatments exist. We present results of an international Phase 3 trial of the MC4R agonist setmelanotide in aHO (NCT05774756).

Methods: Patients aged ≥4 years with BMI ≥95th percentile (<18 years) or ≥30 kg/m^2 (≥18 years) and aHO were included. Patients were randomized 2:1 to setmelanotide (0.5 mg subcutaneously once daily [QD], titrated to 1.5-3.0 mg QD) or placebo for up to 60 weeks. The primary endpoint was a modified intent-to-treat analysis of the percentage change in BMI at 52 weeks. Secondary endpoints included the proportion of patients with ≥5% BMI reduction and the change in maximal daily hunger score (scored 0-10 in patients ≥12 years). Safety was also assessed.

Results: Of 120 patients included, 81 and 39 received setmelanotide or placebo, respectively (female, 60.0%; mean [SD] age, 19.9 [13.8] years; BMI z-score in patients <18 years, 3.61 [1.66]; BMI in patients ≥18 years, 41.2 [9.7] kg/m^2). Fourteen patients discontinued treatment before end of trial. The primary endpoint, mean (SE) change in BMI at 52 weeks, was −16.5% (1.4%) for setmelanotide vs +3.3% (2.0%) for placebo, with a significant placebo-adjusted difference of −19.8% (95% CI: −24.6%, −15.1%; $P < .0001$). A significantly greater proportion of patients who received setmelanotide vs placebo achieved a BMI reduction of ≥5% (79.5% vs 10.4%, $P < .0001$). The mean (SE) change in the weekly average of the maximal daily hunger score was −2.73 (0.28) for setmelanotide vs −1.45 (0.40) for placebo ($P = .0086$). Overall, 81 (100%) vs 35 (89.7%) patients receiving setmelanotide vs placebo experienced AEs, the most common of which were

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

skin hyperpigmentation (55.6% vs 7.7%), nausea (50.6% vs 30.8%), vomiting (39.5% vs 17.9%), and headache (38.3% vs 30.8%). In the setmelanotide arm, one death due to seizures (treatment-unrelated) was reported and one serious treatment-related AE of hypernatremia due to vomiting and inability to tolerate desmopressin; after 2 days setmelanotide was reinitiated upon hospital discharge.

Conclusions: In the largest randomised, placebo-controlled trial in aHO to date, setmelanotide demonstrated significant effects over placebo in the primary and key secondary efficacy endpoints at 52 weeks, with no new safety signals. Setmelanotide may represent an important treatment option for patients with aHO aged ≥4 years, for which currently no approved treatments exist.

Abstract citation ID: lvag096.415

P256 - ECE_2728 - Impact of setmelanotide on metabolic index scores in Phase 3 trial participants with acquired hypothalamic obesity

Hanneke van Santen[1,2], Susan Phillips[3], Jill Hamilton[4,5], Ashley Shoemaker[6], Shana McCormack[7,8], Jennifer Abuzzahab[9], Martin Wabitsch[10,11], Nicolas Touchot[12], Cecilia Scimia[12], Shuang Hu[12], Mehul Dattani[13], Tomohiro Tanaka[14], Christian L. Roth[15,16], Hermann L Müller[17] and Jennifer Miller[18]

[1]Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands; [2]Department of Pediatric Endocrinology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands; [3]Pediatric Endocrinology, University of California San Diego/Rady Children's Hospital, San Diego, United States; [4]Division of Endocrinology, Hospital for Sick Children, Toronto, Canada; [5]Department of Pediatrics, University of Toronto, Toronto, Canada; [6]Ian Burr Division of Endocrinology and Diabetes, Vanderbilt University Medical Center, Nashville, United States; [7]Division of Pediatric Endocrinology and Diabetes, Children's Hospital of Philadelphia, Philadelphia, United States; [8]Department of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, United States; [9]Pediatric Endocrinology and Diabetes, Childrens Minnesota, Saint Paul, United States; [10]Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics and Adolescent Medicine, University Center Ulm, Ulm, Germany; [11]German Center for Child and Adolescent Health (DZKJ), Ulm, Germany; [12]Rhythm Pharmaceuticals, Inc, Boston, United States; [13]Genetics and Genomic Medicine Research and Teaching Department, UCL GOS Institute of Child Health, London, United Kingdom; [14]Gastroenterology and Metabolism, Graduate School of Medical Sciences and Medical School, Nagoya City University, Nagoya, Japan; [15]Seattle Children's Research Institute, Seattle, United States; [16]Division of Endocrinology, Department of Pediatrics, University of Washington, Seattle, United States; [17]Klinikum Oldenburg, University Children's Hospital, Oldenburg, Germany; [18]Pediatric Endocrinology, Department of Pediatrics, University of Florida, Gainesville, United States

Introduction: Acquired hypothalamic obesity (aHO) is a rare complex disease characterized by hyperphagia and reduced energy expenditure, leading to accelerated and sustained weight gain. Commonly associated with pituitary hormone deficiencies, fatigue, or sleep disturbances, aHO puts patients at high risk for metabolic complications like insulin resistance, dyslipidemia, and hepatic steatosis. Non-invasive metabolic markers enable early detection and quantification of cardiometabolic risk, allowing timely, targeted interventions. In the international Phase 3 trial of MC4R agonist setmelanotide (NCT05774756), the primary endpoint of percent change in BMI at Week 52 was met. This post-hoc analysis assessed setmelanotide impact on metabolic index scores.

Methods: Patients with aHO aged ≥4 years in the Phase 3, double-blind TRANSCEND trial were randomized 2:1 to receive setmelanotide (0.5 mg subcutaneously once daily [QD], titrated up to 1.5-3.0 mg QD) or placebo for up to 60 weeks. The modified intent-to-treat (mITT) population was analyzed for changes in lipid accumulation product (LAP), triglyceride-glucose waist circumference index (TYG-WC), visceral adiposity index (VAI), fatty liver index (FLI), and metabolic syndrome z-score (MetS z-score) after 52 weeks of therapeutic dose. Only participants with baseline and week 52 values available were included.

Results: Overall, 120 participants were included in the pivotal cohort (81 setmelanotide, 39 placebo), with a mean (SD) age of 19.9 (13.8; range: 4-66) y, a mean BMI in participants ≥18 y of 41.2 (9.7) kg/m^2, and a BMI z-score in participants <18 y of 3.61 (1.66). In the mITT population ($n = 81$), baseline metabolic index scores for each marker were indicative of metabolic dysfunction. The mean (SD) change from baseline to week 52 in the setmelanotide-treated group vs placebo was greater across all indices: for LAP ($n = 68$ vs $n = 36$) the change was -36.4 (58.8) vs −2.6 (37.0), $P < .0001$; TYG-WC ($n = 63$ vs $n = 35$) was -138.3 (140.1) vs +21.2 (73.2), $P < .0001$; VAI ($n = 67$ vs $n = 35$) was −1.5 (2.8) vs −0.4 (1.7), $P = .0009$; FLI ($n = 65$ vs $n = 35$) was −24.2 (26.7) vs +4.4 (11.1), $P < .0001$; and reductions in MetS z-score ($n = 53$ vs $n = 31$) were −0.9 (1.0) vs −0.2 (0.4), $P < 0.0001$, respectively.

Conclusions: Setmelanotide treatment in patients with aHO led to significant improvements in multiple metabolic index scores vs placebo. These data suggest reductions in visceral fat burden, hepatic steatosis, and overall cardiometabolic risk. The findings highlight the broad metabolic benefits and strong clinically meaningful efficacy of setmelanotide in this population, supporting its potential as a therapeutic option for patients with aHO.

Abstract citation ID: lvag096.416

P258 - ECE_3609 - Surgical vs medical remission in Cushing's disease: a medium-term comparative analysis

Ylenia Alessi[1], Francesco Ferraù[2], Carla Paola Costa[3], Elena Sofia Blanca[3], Giordana Siracusano[3], Alessandra Piccione[3], Filippo Flavio Angileri[1], Angela Alibrandi[4], Francesca Pecori Giraldi[5] and Salvatore Cannavò[2]

[1]Department of Biomedical, Dental and Morphological and Functional Imaging Sciences, University of Messina, Messina, Italy; [2]Department of Human Pathology of Adulthood and Childhood, University of Messina, Messina, Italy; [3]Endocrine Unit, "Gaetano Martino" University Hospital of Messina, Messina, Italy; [4]Department of Economics, University of Messina, Messina, Italy; [5]Department of Clinical and Community Sciences, University of Milan, Milano, Italy

Background: Cushing's disease (CD) is a rare endocrine disorder caused by chronic cortisol excess, associated with increased cardiometabolic morbidity and mortality. Although normalization of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hypercortisolism represents the main therapeutic goal, clinical features and comorbidities may persist after biochemical remission. Transsphenoidal pituitary surgery is the first-line treatment, while medical therapy is used in patients with persistent, recurrent, or inoperable disease. Data comparing medium-term outcomes of surgical vs medical remission are limited.

Aims: The aim of this study was to evaluate differences in anthropometric/clinical/hormonal and metabolic parameters, including related-comorbidities, between patients achieving remission after surgical treatment and those achieving remission through medical therapy, with additional gender-specific analyses.

Methods: We retrospectively evaluated 57 patients with CD in remission (45 females): 36 treated surgically (S) and 21 under pharmacological treatment (P). Anthropometric/clinical/biochemical parameters and related-comorbidities were assessed at baseline (T0), 1 year and 2 years after remission (T1 and T2 respectively). Comparisons were performed between treatment groups and across timepoints. Gender-stratified analyses were conducted within each group.

Results: At T1, S showed a significantly greater improvement in clinical features of hypercortisolism compared with P, including a reduction in waist circumference, striae rubrae, easy bruising and facial rubor. Biochemically, S exhibited lower triglycerides, total cholesterol and HbA1c, but a higher rate of growth hormone deficiency (GHD). At T2, myopathy and facial rubor were significantly more pronounced in P, with no significant differences in other clinical/biochemical/cardiometabolic parameters. Gender-specific analyses indicated a more severe phenotype in males, particularly in P, where a higher prevalence of cardiomyopathy and diabetes mellitus was observed at T1, with the latter also trending towards significance at T2. In S, males showed a more favorable lipid profile at T2 but had a higher prevalence of GHD and hypogonadism compared to females at both T1 and T2. In contrast, females exhibited a higher prevalence of psychiatric disorders at T1 and greater central obesity at T2.

Conclusions: In patients with CD in remission, surgical treatment provides faster and more sustained improvements in clinical phenotype and metabolic profile compared to medical therapy. However, several comorbidities persist up to two years post-remission, indicating the need for long-term, multidisciplinary follow-up. Additionally, gender-specific differences reveal that males in P group experience more severe cardiometabolic comorbidities while females show greater central obesity and psychiatric disorders. These findings highlight the importance of individualized management strategies that address both treatment type and sex differences to optimize patient outcomes beyond biochemical remission.

Abstract citation ID: lvag096.417

P259 - ECE_3757 - An artificial intelligence assisted risk-stratification approach to endocrine surveillance in adult survivors of primary, non-pituitary brain tumour treated with radiotherapy

Darran Mc Donald[1,2], Liam O'connell[3], Maria Tomkins[1,2], Tara McDonnell[1,2], Niamh Mc Dermott[2], Jack Lee[2], Claire Carthy[2], Mary Moore[2], Amar Agha[1,2], Donncha O'brien[1,2], Kieron Sweeney[4], Stephen McNally[4], Mohsen Javadpour[4], Clare Faul[3], David Fitzpatrick[3], Michael W. O'reilly[1,2] and Mark Sherlock[1,2]

[1]Department of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland; [2]Department of Endocrinology, Beaumont Hospital, Dublin, Ireland; [3]St Luke's Radiation Oncology Network, Dublin, Ireland; [4]Department of Neurosurgery, Beaumont Hospital, Dublin, Ireland

Background: There is no established guidance on the optimal approach to screening for radiotherapy-induced hypopituitarism in survivors of primary, non-pituitary brain tumours arising in adulthood. While pituitary radiation dose exposure is a recognised risk factor, its incorporation into screening protocols remains uncertain. We therefore, evaluated a risk-stratification approach to endocrine surveillance based on pituitary radiation dose exposure.

Methods: Pituitary function was assessed in adult brain tumour survivors, treated with intensity-modulated radiotherapy who were attending Beaumont Hospital (the Irish National Neurosurgical Centre) between 2012 and 2022. Hormone assessments included a pituitary profile, short synacthen test and dynamic testing of GH axis with either a glucagon stimulation or insulin tolerance test in selected cases. M Vision® artificial intelligence software was utilised to contour the hypothalamic-pituitary axis. Mean radiation dose to the pituitary gland and hypothalamus were then autogenerated by the radiotherapy planning system. Participants were categorised into low (LD, <30Gy), intermediate (ID, 30-44.9Gy) and high (HD, >45Gy) dose exposure groups. Kruskal-Wallis test evaluated differences across these groups with post-hoc analysis using Dunn's test performed when significant differences were observed.

Results: Pituitary function was assessed in 140 brain tumour survivors (prospective cohort $n = 54$, retrospective cohort $n = 86$). Median age at radiotherapy was 39.7 years (IQR 30.5-49.8) with a median post-radiotherapy interval of 60.5 months (IQR 36.0-83.0). Groups comprised LD group ($n = 33$), ID group ($n = 30$) and HD ($n = 74$) survivors. The prevalence of GH deficiency was LD-35%, ID-30% and HD-78%. Gonadotropin, adrenocorticotrophic hormone (ACTH) and thyroid stimulating hormone (TSH) deficiency did not arise in the LD. Gonadotropin deficiency occurred in ID-3% and HD-18%. ACTH deficiency occurred in ID-16% and HD-15%. TSH deficiency occurred in ID-3% and HD-14%. A composite of gonadotropin, ACTH and TSH deficiency occurred in 0%, 17% and 23% in the LD, ID and HD groups, respectively. Panhypopituitarism was only observed in the HD group ($n = 3/40$, 8%). Pituitary radiation dose thresholds (lowest dose at which specific hormone deficits occurred) were GH axis >12.2Gy, gonadotropin axis >37.1Gy, ACTH axis >36.9Gy and thyroid axis >43.4Gy.

Conclusions: Integrating artificial intelligence to rapidly generate pituitary radiation dosimetry allows for the optimisation and personalisation of radiotherapy-induced hypopituitarism screening protocols. Screening is unnecessary in survivors exposed to less than 30Gy (if not GH replacement candidates), while reduced surveillance frequency appears reasonable for intermediate dose exposure (30-44.9Gy). This risk stratification approach has the potential to reduce the burden of endocrine surveillance in up to 50% of adult brain tumour survivors.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.418

P260 - ECE_1902 - Effect of growth hormone treatment on muscle strength in adults with Prader-Willi syndrome (PWS)

Rosalie Poldervaart[1], Janneke Baan[1], Karlijn Pellikaan[1], Jacqueline Goos[1] and Laura De Graaff[1,2]
[1]Rotterdam, The Netherlands; [2]Department of Endocrinology, Radboud University Medical Center, Nijmegen, The Netherlands

Introduction: Prader-Willi syndrome (PWS) is a rare genetic syndrome characterized by hypothalamic dysfunction, intellectual disability, hypotonia and hyperphagia. Individuals with PWS display features of growth hormone (GH) deficiency, including short stature, increased fat mass, and low muscle mass and strength. Reduced muscle mass results in a low basal metabolic rate (BMR). Combined with hyperphagia, this often results in severe obesity. As obesity is the primary contributor to increased morbidity and mortality in adults with PWS, addressing it is essential for long-term health in this population.

GH treatment improves body composition and muscle strength in children with PWS. Smaller studies suggest similar improvements in body composition in adults. However, the effect of GH treatment on muscle strength in adults with PWS has not yet been demonstrated. We have studied the effect of GH treatment on muscle strength in a Dutch population of GH-naïve adults with PWS.

Methods: At the Dutch Center of Reference for PWS, 24 GH-naïve patients with PWS were included in this open-label prospective cohort study. We measured muscle strength before the start of GH treatment (0.6 mg once daily) and after 3, 6 and 12 months of therapy. Muscle strength was quantified using a handgrip dynamometer for hand and forearm strength, as well as the 30-second sit-to-stand test and the 5× sit-to-stand test for leg muscle strength. In addition, subjective improvements in muscle and side-effects were assessed. All tests were validated for adult individuals with an intellectual disability.

Results: Ten females and fourteen males were included (17 deletion and 7 mUPD, age range 22-63 years, BMI range 23-38 kg/m^2). Overall, patients, parents and caregivers reported notable improvements in muscle strength. Most remarkable subjective changes were increased walking speed and increased ability to get out of chairs, walk without help or climb the stairs. They also reported a decrease in fatigue and daytime sleepiness. Objective improvements were significant increases in muscle strength as measured by the handgrip dynamometer ($P = .042$), the 30-second sit-to-stand test ($P = .002$), and the 5× sit-to-stand test ($P = .032$).

Conclusions: GH treatment significantly improves muscle strength in adults with PWS. As improved muscle strength improves exercise tolerance, it enables a healthier lifestyle needed to reduce obesity and cardiovascular complications in this vulnerable population.

Abstract citation ID: lvag096.419

P261 - ECE_3746 - Impact of stringent IGF-I control on glycemic outcomes in acromegaly: a real-world evidence study in the United States

Suwei Wang[1], Raffaella Colzani[1], Janetricks Okeyo[1] and Nicholas Tritos[2]
[1]Crinetics Pharmaceuticals, Inc., San Diego, United States; [2]Harvard Medical School, Boston, United States

Background: Acromegaly is a chronic endocrine disorder characterized by excess secretion of growth hormone (GH), leading to elevated insulin-like growth factor 1 (IGF-I) and an increased risk of metabolic complications, including insulin resistance and diabetes mellitus (DM). While normalization of IGF-I is the standard therapeutic goal, the evidence regarding possible incremental glycemic benefits associated with achieving IGF-I levels below conventional thresholds appears to be limited. This study investigates whether more stringent IGF-I control confers additional improvements in glycemic outcomes among patients with acromegaly.

Methods: A retrospective cohort study was performed utilizing a de-identified, linked dataset from Komodo US claims and Prognos Health Laboratory records. The study population comprised adults with acromegaly who attained IGF-I ≤1.3× upper limit of normal (ULN) and had at least one post-treatment HbA1c measurement between January 2020 and November 2025. Participants were categorized into three groups based on IGF-I levels: Optimal (0.8-1.0 × ULN), Suboptimal (1.0-1.3 × ULN), and Stringent (≤0.8 × ULN). Primary endpoints included changes in HbA1c following achievement of IGF-I targets and glycemic control in patients with DM. Statistical analyses included descriptive statistics, analysis of variance (ANOVA), multivariable regression, and mixed-effects modeling.

Results: The study included 3783 patients (56.5% female; mean age 54.3 years). The Stringent IGF-I group ($n = 2176$, 57.5%) demonstrated a reduction in HbA1c (mean change −0.05, SD 0.74), compared with the Optimal ($n = 701$, 18.5%; mean change 0.02, SD 0.55) and Suboptimal ($n = 906$, 23.9%; mean change −0.0003, SD 0.68) groups (overall ANOVA, $P = .029$). Longitudinal mixed-effects modeling revealed a significant decline in HbA1c over time in the Stringent group ($P = .012$) compared with the other groups. Multivariable regression analysis confirmed that stringent IGF I control was significantly associated with greater HbA1c reduction ($\beta = -.15$, 95% CI −0.18 to −0.11, $P = .11$) and increased odds of achieving glycemic control, defined as HbA1c <6.5% (OR = 1.04, 95% CI 1.01-1.08, $P = .009$) in patients with DM over the study period. Notably, increasing age was associated with lower likelihood of achieving glycemic control (OR = 0.98, 95% CI 0.97-0.99, $P < .001$).

Conclusions: Patients who achieved stringent IGF-I control experienced greater reductions in HbA1c and a higher likelihood of glycemic control in diabetes. These findings support the implementation of more stringent IGF-I targets to improve glycemic control in patients with acromegaly.

Abstract citation ID: lvag096.420

P262 - ECE_3860 - Pituitary tumors in the course of pituitary adenoma and pheochromocytoma/paraganglioma association (3PAs). A single-center case series

Anna Bogusławska[1], Ewelina Rzepka[1], Anna Nogieć[2], Alicja Hubalewska-Dydejczyk[1] and Aleksandra Gilis-Januszewska[1]
[1]Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland; [2]Kraków, Poland

The coexistence of pituitary adenoma and pheochromocytoma/paraganglioma is extremely rare condition known as 3PAs association. Approximately 30% of reported cases harbor pathogenic germline variants, most commonly in *SDHx* genes (particularly

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

SDHB). An additional 31% of patients present clinical features suggestive of hereditary disease despite negative genetic testing

We present three cases of pituitary adenoma in the course of 3PAs.

Patient 1. A 50-year-old woman diagnosed with a prolactinoma, initially presenting with irregular menses. Pituitary MRI showed invasive macroadenoma with concomitant hyperprolactinemia (at the age of 29 years). Due to tumor progression and poor tolerance of high-dose cabergoline, transsphenoidal surgery was performed. Histopathology confirmed oncocytic acidophil stem cell adenoma GH(-),PRL(+),ACTH(-),TSH(-),FSH(-),LH(-), alfasubunit(-), MIB1<1%. In 2022, recurrence as a pituitary microadenoma was detected and dopamine agonist was reintroduced (cabergoline 0.5 mg/week). Subsequently, abdominal imaging showed right adrenal mass and CT confirmed 56 × 40 × 52 mm adrenal lesion with heterogeneous contrast enhancement. Biochemical testing showed markedly elevated urinary normetanephrines. Right adrenalectomy confirmed pheochromocytoma (PASS score 7, Ki-67 6%) and genetic testing revealed a pathogenic *SDHB* missense mutation (p.Cys192Arg). Family history revealed paraganglioma in both her son and mother.

Patient 2. A 47-year-old man, presented at the age of 36 with severe headaches and loss of libido. MRI showed pituitary macrodenoma 49 × 16 × 27 mm invading local structures which was surgically removed without hormonal assessment. Histopathology revealed adenoma hypophysis AE1/AE3, synaptophysin(+), CD56(−), TTF1(−). Due to persistent hyperprolactinemia cabergoline was implemented (0.5 mg/week). Last MRI showed residual tumour in turkish saddle. In routine abdominal ultrasound right adrenal mass was found. CT showed adrenal tumor (24 × 22 mm) with native contrast enhancement of 41 HU. Urinal metoxycatecholamines were elevated and right adrenalectomy was performed. Histopathology confirmed pheochromocytoma with PASS = 5 and Ki67<1%. Genetic testing for *SDH, MAX, VHL, MEN1, CDKN1b* mutations were negative.

Patient 3. In 2014 the patient underwent right adrenalectomy due to pheochromocytoma at the age of 50. One year later, recurrence of symptoms were noted. Biochemical and imaging studies demonstrated recurrent and disseminated disease. Additionally, PET/CT with Ga68 revealed increased tracer uptake in pituitary gland and MRI confirmed pituitary macroadenoma 11 × 11 × 8 mm. Biochemically, GH was elevated and IGF-1 within normal range. Due to disseminated process, patient died and no genetic testing was available.

3PAs syndrome should be considered in patients with pituitary adenoma and coexisting or subsequent paraganglioma/pheochromocytoma. Although SDHx mutations are uncommon in PitNETs, their presence is more likely in patients with concomitant pheochromocytoma/paraganglioma or a positive family history.

Abstract citation ID: lvag096.421

P263 - ECE_2227 - Preoperative score to distinguish silent corticotroph tumors from gonadotroph tumors before surgery

Cristina Guillen, Elena García, Jorge Frances, Francisca María Peiró-Marqués, Maria Rodríguez-Bedoya, Johana Sottile, Jorge Navarro, Javier Abarca Olivas, Joaquin Serrano and Antonio Pico

Instituto de Investigación Biomédica de Alicante (ISABIAL), Instituto de Investigación Biomédica de Alicante (ISABIAL), Alicante, Spain

Introduction: Silent Corticotroph Tumors (SCTs) are aggressive tumors that are clinically indistinguishable from Silent Gonadotroph Tumors (SGTs) before pathology results are available. Given the higher risk of recurrence in SCTs, preoperative identification is important. Our goal was to create a non-invasive, multiparametric score that combines imaging features and hormonal results to accurately predict SCT lineage.

Methods: We analyzed a retrospective cohort of 59 patients with clinically non-functioning tumors, including 27 SCTs and 31 SGTs. We compared specific T2-weighted MRI features, such as the Signal Intensity Ratio (SIR) and the presence of microcystic changes. These features were combined with baseline hormonal markers (ACTH, Cortisol, IGF-1, GH) to create a predictive score.

Results: SCTs were significantly brighter on T2-weighted MRI. The quantitative SIR was nearly double in SCTs compared to SGTs (2.43 ± 1.01 vs 1.31 ± 0.30, $P = .0049$). In qualitative terms, 75% of SCTs showed characteristic T2-microcystic areas, while only 15% of SGTs showed this ($P < .0001$). Even though they are clinically silent, basal cortisol was significantly higher in SCTs than SGTs (14.17 ± 4.6 vs 9.84 ± 4.8 µg/dL, $P = .005$). ACTH (52.0 vs 24.7 pg/mL), IGF-1 (175.1 vs 105.8 ng/mL), and basal GH levels showed a trend of almost doubling (0.42 ± 0.5 vs 0.19 ± 0.1 ng/mL, $P = .22$). Based on these findings, we propose a 4-point preoperative score: Radiology: SIR >1.5 (+1 point) OR Presence of T2-Microcysts (+1point). Hormones: Basal ACTH > 40 pg/mL (+1 point) AND IGF-1 >130 ng/mL (+1 point). A score of ≥3 points predicts the Corticotroph lineage with high diagnostic accuracy (AUC 0.98).

Conclusions: We present a combined score for the preoperative diagnosis of Silent Corticotroph Tumors. By using simple T2-MRI markers (High SIR/Microcysts) with baseline hormonal levels (High ACTH/IGF-1), doctors can reliably tell apart high-risk SCTs from less aggressive SGTs. This tool helps neurosurgeons decide on the level of resection needed and how to monitor patients afterward for this challenging condition.

Abstract citation ID: lvag096.422

P264 - ECE_3480 - The DA-resistance in prolactinomas according to current definitions

Maria Aleksandra Komisarz-Calik[1,2], Anna Bogusławska[1], Alicja Hubalewska-Dydejczyk[1] and Aleksandra Gilis-Januszewska[1]

[1]*Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland;* [2]*Doctoral School of Medical and Health Sciences, Jagiellonian University Medical College, Kraków, Poland*

Objectives: Dopamine agonists (DA) are the first-line therapy for prolactinomas; however, a subset of patients exhibits resistance or incomplete response. The approach to the concept of resistance has evolved over the years, and a precise definition of resistance is needed.

Methods: This retrospective study included 85 patients (out of 125 screened patients) with prolactinoma treated with DA, followed for a median of 52.0 months. We compared clinical, biochemical, and radiological parameters (at baseline, 6, and 12

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

months) and the incidence of resistance, using two definitions. **1) Resistance**—failure to normalize serum prolactin concentration (PRL) or achieve ≥30% reduction in tumor maximal diameter (MTD) after standard (7.5-10 mg per day of bromocriptine or 2.0 mg per week of cabergoline) or maximally tolerated DA doses. **2) Resistance**—failure to normalize PRL and inability to reduce tumor size (TV) by 50% despite the maximally tolerated DA doses. **Responsiveness** was defined as PRL normalization and either≥30% reduction in MTD or >50% TV reduction, depending on the approach. Patients who did not meet the criteria for DA resistance and responsiveness were classified as **partial responders.**

Results: The cohort comprised 54 males (63.5%), with a mean age of 41.5 ± 17.2 years. After 6 and 12 months of treatment, 24.7% and 40% achieved PRL normalization, 29.4% and 41.2% demonstrated ≥50% reductions in TV, and 16.0% and 28% achieved ≥30% reductions in MTV. At 6 months, we identified 29.5% vs 41.2% DA-resistant tumors (*P* = *.064*), at 12 months, 31.8% vs 30.6% (*P* = *.078*), and at last follow-up, 23.5% vs 23.5% (*P* = *1.000*) according to definitions 1) and 2), respectively. Incidence of responsive tumors was 7.0% vs 10.6% at 6 months (*P* = *.375*), 10.6% vs 16.5% at 12 months (*P* = *.125*), and 25.9% vs 35.3% at the last follow-up (*P* = *.039*). Partially responsive tumors constituted 63.5% at 6 months vs 48.2% (*P* = *.024*), 57.6% at 12 months vs 52.9% (*P* = *.618*), and 50.6% at the last follow-up vs 41.2% (*P* = *.185*). In both resistant groups, resistant tumors were associated with higher PRL at 6 and 12 months and at the last follow-up *(P* < *.001*).

Conclusions: Using definition 2, a higher proportion of responsive tumors was observed across all time points. The 1 definition is associated with a higher percentage of partially resistant tumors, especially at 6 months. Further studies are needed to unify the definition of DA-resistant prolactinomas.

Abstract citation ID: lvag096.423

P265 - ECE_2692 - Paradoxical growth hormone increase during OGTT in acromegaly is linked to smaller adenomas with a more aggressive biochemical profile

Mathilde Damm, Jon Rasmussen, Yeliz Bulut, Caroline Kistorp and Mikkel Andreassen
Rigshospitalet, University of Copenhagen, København Ø, Denmark

Introduction: It is estimated that a paradoxical rise in growth hormone (GH) during oral glucose tolerance test (OGTT) occurs in approximately 30% of patients with acromegaly. The phenomenon is likely related to ectopic expression of glucose-dependent insulinotropic polypeptide (GIP) receptors in the GH-secreting pituitary adenoma. The clinical significance of paradoxical GH increase remains poorly studied; however, one study has suggested that it may be associated with smaller adenomas at baseline, but higher random GH levels when adjusted for tumor size.

Aims: To compare endocrine, radiological, and metabolic characteristics at diagnosis between patients with a paradoxical GH increase and those without a paradoxical increase

Methods: This retrospective, single-center study included consecutive patients with an available baseline GH profile during an OGTT. A paradoxical GH increase was defined as a peak-to-basal GH ratio exceeding 120%

Results: A total of 109 patients with acromegaly were included; 44 (40%) exhibited a paradoxical GH increase during OGTT and 65 (60%) did not. Patients with paradoxical increase were of similar age compared with those without (mean (SD) 54 ± 15 vs 51 ± 13 years; *P* = .243). Baseline GH at t = 0 was also comparable between groups (median 16 [IQR 11-35] vs 15[5-39] µg/L; *P* = .58). The paradoxical group had higher IGF-1 levels (688 ± 275 vs 578 ± 253 µg/L; *P* = .06) and a significantly higher IGF-1 SDS (8.8 ± 3.9 vs 7.2 ± 3.8; *P* = .049). Maximum adenoma width tended to be smaller in the paradoxical group, but this was not statistically significant (median 15 [11-24] vs 19 [12-25] mm; *P* = .143). IGF-1 adjusted for adenoma size (IGF-1/maximum diameter) was significantly higher in patients with paradoxical increase (median 49 [31-70.] vs 31 [20-47]; *P* < .01. HbA1c was similar between groups (39.0 ± 4.0 vs 38.0 ± 4.8 mmol/mol; *P* = .615). Systolic blood pressure (137 ± 19 vs 134 ± 23 mmHg; *P* = .62) and diastolic blood pressure (85 ± 11 vs 84 ± 17 mmHg; *P* = .75) did also not differ between groups.

Discussion: Compared with previous reports, we observed a slightly higher prevalence of paradoxical GH increase, affecting 40% of patients. Our findings support that patients exhibiting a paradoxical GH rise have more hormonally active tumors, reflected by higher IGF-1 levels and IGF-1 SDS, and by significantly higher IGF-1 when adjusted for tumor size. With respect to glucose metabolism and blood presure we did observe any differencies between the 2 groups.

Abstract citation ID: lvag096.424

P266 - ECE_1022 - Long-term safety, biochemical control and symptom management with CAM2029 in the 52-week ACROINNOVA 2 open-label extension

Diego Ferone[1], Beverly M.K. Biller[2], Timo Deutschbein[3], Maria Fleseriu[4], Mônica Gadelha[5], Aleksandra Gilis-Januszewska[6], Pietro Maffei[7], Robert D Murray[8], Jochen Seufert[9], Julie M. Silverstein[10], Jacob Råstam[11], Maria Harrie[11], Agneta Svedberg[11], Alberto M. Pedroncelli[11], Fredrik Tiberg[11] and Joanna L. Spencer-Segal[12]
[1]*Endocrinology Unit, Department of Internal Medicine, IRCCS Ospedale Policlinico San Martino, Genova, Italy;* [2]*Neuroendocrine and Pituitary Tumor Clinical Center, Massachusetts General Hospital, Boston, MA, United States;* [3]*Medicover Oldenburg MVZ, Oldenburg, Germany;* [4]*Pituitary Center, Departments of Medicine and Neurological Surgery, Oregon Health and Science University, Portland, OR, United States;* [5]*Neuroendocrinology Research Center/ Endocrinology Division, Medical School and Hospital Universitario Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil;* [6]*Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland;* [7]*Department of Medicine, Padua University Hospital, Padua, Italy;* [8]*Department of Endocrinology, St James's University Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom;* [9]*Division of Endocrinology and Diabetology, Department of Medicine II, Medical Centre—University of Freiburg, Freiburg, Germany;* [10]*Division of Endocrinology, Metabolism and Lipid Research, Department of Neurosurgery, Washington University School of Medicine, St. Louis, MO, United States;* [11]*Camurus AB, Lund, Sweden;* [12]*Department of Internal Medicine and Michigan Neuroscience Institute, University of Michigan, Ann Arbor, MI, United States*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Long-term biochemical control of acromegaly is essential to reduce mortality and morbidity. CAM2029 is a long-acting, octreotide subcutaneous depot for self-administration. ACROINNOVA 2 demonstrated long-term safety and efficacy of CAM2029, including patients biochemically uncontrolled on standard-of-care (SoC) somatostatin receptor ligands. Here we report results of the 52-week ACROINNOVA 2 extension.

Methods: ACROINNOVA 2 was an open-label, 52-week (W) trial (core phase) with 52W extension. Patients who completed W48 CAM2029 treatment and W52 assessment could directly continue (DC) to the extension. Patients could restart CAM2029 after completing the core phase and either after return to SoC or after >4 weeks elapsed. CAM2029 20 mg was administered every 4W ± 1W via pre-filled pen. Primary endpoint was safety. Secondary endpoints included biochemical control (insulin-like growth factor I [IGF-I] ≤upper limit of normal [ULN] per age and sex) rate and symptoms (Acromegaly Index of Severity [AIS] score).

Results: Forty-three patients were included in the ACROINNOVA 2 extension safety analysis (DC $n = 20$, restarted $n = 23$). Mean (standard deviation [SD]) CAM2029 exposure in the extension was 54.0 (9.5) weeks. CAM2029 was well tolerated with no new safety signals. CAM2029-related adverse events (AEs) were reported by 17 (39.5%) patients; the most frequent were injection site AEs (12 [27.9%]). In the efficacy analysis set ($N = 42$; DC $n = 19$, restarted $n = 23$), biochemical control rate increased from start (52.4%) to end (70.7%) of extension. Similar trends were observed for the DC and restarted groups (Table). Notably, the biochemical control rate for the restarted group decreased from end of core phase to start of extension. Upon restarting CAM2029, the biochemical control rate increased at extension end. AIS overall score was stable throughout the extension.

Efficacy analysis set	Overall	Restarted	DC
Patients with IGF-I ≤ULN, *n*/*N* (%)			
SoC baseline	23/42 (54.8)	11/23 (47.8)	12/19 (63.2)
Core phase end (W50/52 mean)	29/42 (69.0)	14/23 (60.9)	15/19 (78.9)
Extension start	22/42 (52.4)	8/23 (34.8)	14/19 (73.7)
Extension end (W102/104 mean)	29/41 (70.7)	13/22 (59.1)	16/19 (84.2)
Mean AIS overall score (SD)			
SoC baseline	($n = 42$) 4.2 (3.3)	($n = 23$) 4.5 (3.1)	($n = 19$) 3.7 (3.5)
Core phase end (W52)	($n = 41$) 3.0 (3.1)	($n = 23$) 3.0 (3.3)	($n = 18$) 2.8 (3.0)
Extension start	($n = 42$) 2.8 (2.7)	($n = 23$) 2.8 (2.5)	($n = 19$) 2.9 (2.9)
Extension end (W104)	($n = 41$) 2.5 (2.3)	($n = 22$) 2.7 (2.2)	($n = 19$) 2.3 (2.5)

Conclusions: Long-term CAM2029 improves biochemical and symptom control of acromegaly over time, and restores biochemical control when restarted in patients switched to SoC.

Abstract citation ID: lvag096.425

P267 - ECE_1010 - Glucocorticoid-induced positive feedback in Cushing disease: insights from a multicenter cohort

Betina Biagetti[1], Andres Cardona-Arias[1], Alfonso Soto[2], M. Dolores Ollero[3], Maria Dolores Moure Rodriguez[4], Laura Gonzalez Fernandez[5], Ana Castro[6], Fernando Guerrero[7], Pedro Iglesias[8], Rosa Camara-Gómez[9], Miguel Paja[10], Victoria Alcázar Lázaro[11], Andreu Simó-Servat[12], Claudia Lozano-Aida[13], Ana Irigaray[3], Lucía Manzano Valero[6], Rocio Villar Taibo[14], Ignacio Bernabeu[14], Carmen Fajardo-Montañana[15], Anna Aulinas[16], Rogelio García Centeno[5,7], Felicia Alexandra Hanzu[18] and Marta Araujo Castro[19]

[1]Hospital Universitario Vall d'Hebron, Barcelona, Spain; [2]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [3]Complejo Hospitalario de Navarra, Navarra, Spain; [4]Hospital Universitario de Cruces, Bilbao, Spain; [5]Hospital Gregorio Marañon, Madrid, Spain; [6]Hospital UNiversitario de Toledo, Toledo, Spain; [7]Hospital Universitario de Bellvitge, Barcelona, Spain; [8]Hospital Puerta de Hierro, Madrid, Spain; [9]Hospital la Fé de Valencia, Valencia, Spain; [10]Hospital Universitario de Basurto, Bilbao, Spain; [11]Hospital Universitario Severo Ochoa, Madrid, Spain; [12]Hospital Mutua de Terrasa, Terrasa, Spain; [13]Hospital Universitario Central de Asturias., Asturias, Spain; [14]Hospital Universitario de Santiago de Compostela, Santiago de Compostela, Spain; [15]Hospital Universitario La Ribera, Valencia, Spain; [16]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [17]Endocrinólogo, Gregorio Marañon Hospital, Madrid, Spain; [18]Hospital Clinic de Barcelona, Barcelona, Spain; [19]Hospital Universitario Ramón y Cajal., Madrid, Spain

Background and Objective: Cushing disease (CD) is characterized by impaired glucocorticoid negative feedback. In rare cases, patients exhibit glucocorticoid-induced positive feedback (GIPF), which may represent a distinct corticotroph adenoma phenotype. We aimed to investigate the prevalence, clinical and biochemical features, and surgical outcomes of GIPF in a large multicenter cohort.

Design: Retrospective cohort study from the SPAIN-CUSHING registry.

Methods: We included 139 patients with CD who had complete overnight 1-mg dexamethasone suppression test. GIPF was defined as a paradoxical cortisol response, corresponding to an increase of at least 25% in serum cortisol levels after dexamethasone compared with baseline. Clinical, biochemical, and radiological characteristics as well as surgical outcomes were compared between groups. Recurrence was evaluated in patients undergoing transsphenoidal surgery, with recurrence-free survival assessed by Kaplan–Meier analysis.

Results: Thirteen patients (9.3%) showed GIPF. These patients had lower BMI (26.4 vs 29.8 kg/m^2, $P = .032$), higher urinary free cortisol expressed as the upper limit of normal ratio (4.7 vs 2.8 ULN, $P = .047$), and a markedly greater ACTH response to desmopressin (525.0 vs 63.1 pg/mL, $P = .022$). Tumor size, proportion of macroadenomas, and cavernous sinus invasion did not

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

differ. Despite this, after surgery remission was significantly lower in GIPF (28.6% vs 70.2%, $P = .036$), and Kaplan–Meier analysis showed reduced recurrence-free survival in GIPF patients (log-rank $P = .04$). Clinical phenotypes and comorbidities were otherwise similar.

Conclusions: GIPF occurs in up to 9% of patients with CD and is associated with poorer surgical outcomes and lower remission rates. This phenotype likely represents a distinct subtype of corticotroph adenoma, highlighting the need for closer follow-up and molecular characterization.

Abstract citation ID: lvag096.426

P268 - ECE_1951 - Depression and anxiety in patients with endogenous Cushing Syndrome: a nationwide matched cohort study using affective drug dispensations

Keren Kaminer[1,2], Ilan Shimon[1,2], Yaron Rudman[1,2], Talia Diker-Cohen[1,2], Shiri Kushnir[3], Tzipora Shochat[4], Yuval Zeev Sufaro[5], Noa Tal[6], Merav Serebro[7], Maria Fleseriu[8] and Amit Akirov[1,2]

[1]Department of Endocrinology, Diabetes & Metabolism, Rabin Medical Center, Beilinson Campus, Petah Tikva, Israel; [2]Gray Faculty of Medical & Health Sciences, Tel Aviv University, Tel Aviv-Yafo, Israel; [3]Rabin Medical Center, Beilinson Campus, Research Authority, Petah Tikva, Israel; [4]Biostatistics Unit, Rabin Medical Center, Beilinson Campus, Petah Tikva, Israel; [5]Neurosurgery Department, Rabin Medical Center, Beilinson Campus, Skull Base Surgery Service, Petah Tikva, Israel; [6]Pacific Neuroscience Institute, Pacific Pituitary Disorders Center, Santa Monica, United States; [7]Endocrinology, Ichilov Sourasky Hospital, Tel Aviv-Yafo, Israel; [8]Departments of Medicine and Neurological Surgery, Oregon Health & Science University, Pituitary Center, Portland, United States

Objective: Cushing syndrome (CS) is associated with depression and anxiety. This study compared treated mood and anxiety disorders between patients with CS and controls, assessing differences by etiology and remission status.

Methods: A retrospective matched cohort study of patients with endogenous CS (2000-2024) from the Clalit Health Services database. Each patient was matched with five controls by age, sex, socioeconomic status, and BMI. Mood and anxiety disorders were identified through affective drug dispensations (ADD). Drug discontinuation was defined as ≥1 month without dispensations.

Results: The cohort included 540 patients with CS (mean age 47.8 ± 17.0 years; 64.4% women) and 2517 controls, with a median follow-up of 13.3 years (IQR 8.3-18.5). At baseline, patients with CS had nearly twice the odds of receiving ADD than controls (OR = 1.9, 95% CI,1.3-2.6), with a significant excess in women (12.9% vs 6.9%, OR = 1.9, 95% CI, 1.3-2.8). During follow up, drug discontinuation rates did not differ (HR = 0.7, 95% CI: 0.5-1.0), whereas the risk of new-onset ADD was twofold higher in CS (HR = 2.2, 95% CI, 1.8-2.6), persisting in patients who achieved remission (HR = 2.1, 95% CI, 1.5-2.7) and those who did not (HR = 2.3, 95% CI, 1.6-3.5). Compared to controls, the risk of new-onset ADD was similarly elevated in Cushing disease (HR = 2.4, 95% CI: 1.9-3.1) and adrenal CS (HR = 2.1, 95% CI, 1.9-3.1).

Conclusions: Endogenous CS is associated with a higher risk of treated affective disorders at diagnosis and throughout long-term follow-up, with persistence after remission, underscoring the need for ongoing psychological care.

Abstract citation ID: lvag096.427

P269 - ECE_2444 - Implementation of long-acting growth hormone therapy in real-world clinical practice: findings from the INSIGHTS-GHT registry

Ilonka Kreitschmann-Andermahr[1], Joachim Woelfle[2], Christof Land[3], Alexander Mann[4], Günter Karl Stalla[5], Wolfram Karges[6], Katharina Schilbach[7], Timo Deutschbein[8], Erwin Lankes[9], David Pittrow[10], Christine Pausch[11], Christian J. Strasburger[12] and Dirk Schnabel[9]

[1]Department of Neurosurgery and Spine Surgery, University Hospital Essen, Essen, Germany; [2]Department of Pediatrics and Adolescent Medicine, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany; [3]Endokrinologie Gauting, Zentrum für Kinder- und Jugendendokrinologie, Gauting, Germany; [4]Endokrinologikum, Frankfurt am Main, Germany; [5]Medicover Neuroendocrinology, München, Germany; [6]Endocrinology and Diabetes Section, University Hospital RWTH Aachen, Aachen, Germany; [7]Department of Endocrinology, Diabetology and Metabolism, LMU München, Internal Medicine IV, München, Germany; [8]Medicover Oldenburg MVZ, Oldenburg, Germany; [9]Pediatric Endocrinology, Charité University Medicine, Center for Chronically Sick Children, Berlin, Germany; [10]Institute for Clinical Pharmacology, Technical University Dresden, Dresden, Germany; [11]GWT-TUD, Innovationszentrum Real-World Evidence, Dresden, Germany; [12]Department of Endocrinology, Diabetes and Nutrition, Charité University Medicine Berlin, Berlin, Germany

Background: INSIGHTS-GHT is a German nationwide, product-independent registry endorsed by scientific societies that captures real-world use of growth hormone (GH) therapies in both children and adults, including long-acting GH (LAGH). LAGH reduces injection frequency and may improve adherence in replacement therapy for growth hormone deficiency (GHD). We present updated baseline utilisation and treatment patterns in paediatric/adolescent and adult patients initiating LAGH.

Methods: This interim cross-sectional analysis included registry patients with GHD who initiated LAGH from 2023 onwards. Demographics, prior GH exposure, starting dose at LAGH initiation (categorised relative to product label), and baseline IGF-I/IGFBP-3 were summarised by age group.

Results: At database analysis on December 3rd, 2025, 2218 patients were enrolled into the register study, 191 of whom received LAGH preparations.

Paediatric/Adolescent Cohort: Among 114 patients aged <18 years initiating LAGH, mean age at initiation was 9.5 ± 3.8 years; 77.2% were male and 74.5% were prepubertal. Fifty-eight percent switched from daily GH (median prior duration 2.9 years). At initiation, 80.6% received a starting dose below the product-label recommendation; the median dose was 92% of the recommended dose. In switch patients, IGF-I SDS was −2.1 (SD 1.2) before any GH and 0.1 (SD 1.6) at LAGH initiation.

Adult Cohort: Seventy-two adults initiated somapacitan treatment, the only approved LAGH for the adult indication in Germany at the time. Mean age at initiation was 42.4 (SD 16.2) years; 55.6% were male. Most patients (90.1%) had organic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

GHD, and 45.5% had childhood-onset disease. Ninety-one percent switched from daily GH (median prior duration 10.7 years). Starting dose relative to label was below in 39.3%, in label in 53.6%, and above in 7.1%; mean dose was 87.9% (SD 30.2) of the recommended dose (median 100%; range 30%-200%).

No new safety signals were detected in either cohort. Registry data contribute to post-authorisation safety (PASS) requirements.

Conclusions: In routine practice, LAGH is commonly initiated with conservative starting doses relative to product labels in both paediatric/adolescent and adult patients, suggesting cautious titration during early adoption. Longitudinal follow-up in INSIGHTS-GHT will assess how these initial dosing strategies translate into IGF-I trajectories, effectiveness, adherence, and safety under real-world conditions.

Reference

1. Woelfle J, Kreitschmann-Andermahr I, Strasburger CJ, et al. First 100 patients receiving long-acting growth hormone therapy: real-world evaluation from INSIGHTS-GHT registry. *Orphanet J Rare Dis*. 2025;20(1):372. https://doi.org/10.1186/s13023-025-03898-8

Abstract citation ID: lvag096.428

P270 - ECE_3177 - Prognostic impact of somatic mutations in corticotroph and lactotroph pituitary tumours

Anna Carretti[1,2,3], Jonathan Lopez[3,4,5,6], Alexandre Vasiljevic[7,8,9], Emmanuel Jouanneau[3,6,10] and Gerald Raverot[2,3,6]

[1]*Experimental Medicine, Sapienza University of Rome, Rome, Italy;* [2]*Endocrinology Department, Reference Center for Rare Pituitary Diseases HYPO, "Groupement Hospitalier Est" Hospices Civils de Lyon, Bron, France;* [3]*Claude Bernard Lyon 1 University, Villeurbanne, France;* [4]*Hospices Civils de Lyon, Lyon, France;* [5]*Department of Biochemistry and Molecular Biology, Lyon Sud University Hospital, Lyon, France;* [6]*Cancer Research Center of Lyon, INSERM U1052, CNRS UMR5286, Lyon, France;* [7]*Cancer Research Center of Lyon, Inserm U1052, CNRS UMR5286, Lyon, France;* [8]*Pathology Department, "Groupement Hospitalier Est" Hospices Civils de Lyon, Bron, France;* [9]*Lyon 1 University, Villeurbanne, France;* [10]*Neurosurgery Department, Reference Center for Rare Pituitary Diseases HYPO, "Groupement Hospitalier Est" Hospices Civils de Lyon, Bron, France*

Introduction: Lactotroph and corticotroph pituitary tumours (lactoPiT and corticoPiT) represent the most common secreting aggressive pituitary tumours (APT) and pituitary carcinomas (PC), characterised by a worse prognosis and reduced survival. Known markers of aggressiveness (invasion, Ki-67, mitotic count, p53) are not always able to predict tumour behaviour.

Studies showed that somatic mutations in *SF3B1* in lactoPiT and in *ATRX* and *TP53* in corticoPit and lactoPiT are associated with greater aggressiveness, resistance to traditional treatments, and reduced overall survival. The latest European guidelines suggest molecular screening for somatic mutations in these genes in lactoPiT and corticoPiT with suggestive features of aggressiveness to facilitate early identification and intervention.

Aim: To evaluate the recommendation of the European guidelines, to define the incidence of said somatic mutations, to investigate the association with other known markers of aggressiveness.

Methods: Clinical study on a cohort of consecutive patients affected by macro-lactoPiT and macro-corticoPiT, surgically treated between 2023 and 2025 and histologically confirmed. Somatic mutation research was performed using next-generation sequencing (NGS) with the « Solid Tumour Solution » from Sophia Genetics, including *TP53*, *ATRX*, and *SF3B1* genes on Illumina™ NextSeq500® or Novaseq® instruments.

Results: 64 patients were included (41 women and 45 corticoPiT), operated between January 2023 and October 2025. 47 of them underwent NGS, for the remaining 17 analysis is ongoing. Low quality was seen in 8 samples, results are available for 39 (26 women, 28 corticoPiT, median age 47 years (range 16-88)). Somatic mutations were found in 6/39 (15%). *ATRX* and *SF3B1* genes were not altered in those tumours. *TP53* pathogenic variants were found in two patients. Incidentally, *ATM* variants were identified in two cases, one associated with a *TP53* variant. Two patients showed *FANCA* and *NBN* variants, respectively. The last case displayed pathogenic variants in *BRCA2* and *RB1*. All mutated tumours were corticoPiT (three women). Four were invasive, four proliferative, and five had a Ki-67 score higher than 3% (median 7.2%, range 6-9.5).

Conclusions: In this cohort, we did not identify somatic mutations in *ATRX* or *SF3B1* genes, whereas *TP53* variants appeared to be more common. The broad inclusion criteria for molecular testing may be a reason for this low percentage. NGS enabled us to identify additional pathogenic variants in pituitary tumours, notably in the *ATM* gene, which has been associated with *SF3B1* variants in other malignancies. This incidental finding may represent another genetic mechanism involved in pituitary tumorigenesis, warranting further study.

Abstract citation ID: lvag096.429

P271 - ECE_3771 - Comparative analysis of masseter and temporal muscle thickness and quality in patients with Cushing's syndrome and non-functioning pituitary tumors

Anna Arecco[1], Loris Peirano[2], Claudia Campana[1], Bianca Bignotti[3], Oleksandr Starovatskyi[4], Ilaria Patelli[1], Mara Boschetti[1,5], Diego Ferone[1,5], Alberto Tagliafico[3,4] and Federico Gatto[1,5]

[1]*Endocrinology Unit, Department of Internal Medicine and Medical Specialties (DIMI), Centre of Excellence for Biomedical Research (CEBR), University of Genova, Genoa, Italy;* [2]*University of Genoa, Genoa, Italy;* [3]*Celle Ligure, Italy;* [4]*Department of Radiology, IRCCS Ospedale Policlinico San Martino, Genoa, Italy;* [5]*Endocrinology Unit, IRCCS Ospedale Policlinico San Martino, Genoa, Italy*

Background: Cushing's syndrome (CS) is bourdened by a peculiar myopathy characterized by atrophy of type 2 muscle fibres and increased intramuscular fat infiltration. Previous studies have demonstrated masseter and temporal muscles as reliable proxies of muscle mass and quality.

Aims: We compared masseter thickness (MMT), temporal thickness (TMT) as well as masseter and temporal muscle quality (simplified Goutallier score: 0 = normal, 1 = fatty infiltration) in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

patients with CS and non-functioning pituitary tumours (NF-PitNETs) matched for sex and age. Brain/sella turcica MRIs performed at diagnosis and/or follow-up were retrospectively evaluated to define MMT, TMT and facial muscles quality. In patients with CS, available abdominal CT scans were used to evaluate iliopsoas muscle area (the gold standard to define sarcopenia) and iliopsoas density.

Results: Both groups included 43 patients (28 females, 65%) with a median age of 58 years. In the CS group, 40 subjects had an ACTH-PitNET and only 3 an adrenal CS.

Median MMT was 16.5 mm [IQR 6.54] in the CS group and 15.3 mm [IQR 3.60] in the NF-PitNET group ($P = .264$); median TMT was 5.35 mm [IQR 1.72] vs 5.80 mm [IQR 1.97], respectively ($P = .086$).

Masseter quality was poorer in the CS group compared to the NF-PitNET group, with 64.7% patients having a Goutallier grade 1 vs 26.2% in the NF-PitNET group ($P < .001$). Temporal quality was similar (Goutallier score 1: 67.4% in CS vs 34.9% in NF-PitNET group; $P = .003$).

Male patients had significantly higher MMT and TMT than females in the NF-PitNET group ($P = .002$ for both muscles), while in the CS group only TMT was higher in male patients ($P = .007$). Muscle quality was not affected by gender in both groups ($P > .05$).

In CS patients, no difference was found in masseter ($P = .236$) and temporal quality ($P = .151$) between controlled (UFC < 1.0xULN) and active CS patients (UFC ≥ 1.0xULN).

No correlation was found between MMT, TMT and cortisol or UFC values ($P > .05$).

Of note, in CS patients, iliopsoas area had a significant direct correlation with both MMT (rho = .529, $P = .024$) and TMT (rho = .498, $P = .016$). Iliopsoas density was lower in subjects with poor masseter quality ($P = .005$) and temporal quality ($P = .006$).

Conclusions: CS patients have poorer masseter and temporal muscle quality than the NF-PitNET group. MMT and TMT correlated with iliopsoas area; poorer masseter and temporal muscle quality were associated with lower iliopsoas density. These findings support the role of facial muscle evaluation by brain/sella turcica MRI to investigate muscle mass and quality in patients with CS.

Abstract citation ID: lvag096.430

P272 - ECE_1911 - LINC 7 secondary analysis: osilodrostat treatment outcomes across various aetiologies and severities of Cushing's syndrome

Nicolas Scheyer[1], Jérôme Bertherat[2], Justine Cristante[3], Benedicte Decoudier[4], Lasolle Hélène[5], Hervé Lefebvre[6], Delphine Drui[7], Charly Vaillant[8], Julia Morera[9], Frederic Castinetti[10], Nicolas Chevalier[11], Andrea Piacentini[12], Wence Agbotounou[13], Mario Maldonado[13] and Antoine Tabarin[14]

[1]*Département d'Endocrinologie, Diabétologie et Nutrition, CHRU de Nancy, Hôpital Brabois et Université de Lorraine, Vandœuvre-lès-Nancy, France;* [2]*Hôpital Cochin, AP-HP, and Université Paris-Cité, Centre de Référence des Maladies Rares de la Surrénale, Paris, France;* [3]*CHU Grenoble Alpes, Service d'Endocrinologie, Université Grenoble Alpes, Grenoble, France;* [4]*Department of Endocrinology, CHU de Reims, Reims, France;* [5]*Department of Endocrinology, Hôpital Louis Pradel, Hospices Civils de Lyon Bron Cedex, Lyon 1 University, Lyon, France;* [6]*Department of Endocrinology, Diabetes and Metabolic Diseases, Université de Rouen Normandie, INSERM, NorDiC UMR 1239, CHU Rouen, Rouen, France;* [7]*CHU de Nantes, Nantes, France;* [8]*CH du Mans, Le Mans, France;* [9]*CHU de Caen, Caen, France;* [10]*Department of Endocrinology, Aix-Marseille University, INSERM, MMG, La Conception Hospital, Assistance Publique Hopitaux de Marseille, Marseille, France;* [11]*CHU de Nice, Nice, France;* [12]*Recordati SpA, Milan, Italy;* [13]*Recordati AG, Basel, Switzerland;* [14]*CHU de Bordeaux and Centre de Référence des Maladies Rares de la Surrénale, Bordeaux, France*

Introduction: Endogenous Cushing's syndrome (CS) is a rare disease caused by excess cortisol production. LINC 7 (NCT05633953), a retrospective observational study, assessed osilodrostat safety and effectiveness in adrenal (adenomas, carcinomas, bilateral adrenal nodular disease [BND]) and ectopic adrenocorticotropic hormone secretion (EAS) aetiologies of CS. This analysis evaluated osilodrostat safety and effectiveness by CS aetiology and severity.

Methods: Patients with CS who initiated osilodrostat under the French Autorisation Temporaire d'Utilisation scheme or, once approved, in routine clinical practice were followed up retrospectively for ≤36 months (Tabarin *et al. J Clin Endocrinol Metab* 2025). Patients were specified as having: (1) mild benign adrenal CS (M_bACS; any cortisol measure [ACM; mean urinary free cortisol, late-night salivary cortisol, or morning serum cortisol] at baseline ≤2 times the upper limit of normal [ULN], with adrenal adenoma or BND); (2) mild malignant CS (M_mCS; baseline ACM ≤2xULN, with adrenocortical carcinoma or EAS); or (3) moderate-severe CS (MSCS; baseline ACM >2xULN, all aetiologies). Analyses are descriptive only.

Results: 91/103 patients had ACM data available at baseline (M_bACS, $n = 20$; M_mCS, $n = 19$; MSCS, $n = 52$). Initial median (min–max) osilodrostat dose was 4 (1-10), 4 (1-40), and 10 (2-60) mg/day, respectively; at week (W)24, this was 4 (1-12), 15 (3-40), and 20 (0-120) mg/day. At W12 and W24, ACM ≤ULN was achieved in $n = 8/9$ and $n = 4/4$ patients with M_bACS, respectively; equivalent values were $n = 7/10$ and $n = 7/7$ for M_mCS and $n = 15/28$ and $n = 9/15$ for MSCS. Among patients with hypertension ($n = 75/91$ [82.4%]), mean baseline systolic blood pressure (SBP; mmHg) was 139.9 (M_bACS, $n = 17$), 141.1 (M_mCS, $n = 15$), and 148.4 (MSCS, $n = 34$). By W24, SBP had decreased in M_mCS (130.5, $n = 6$) and MSCS (134.9, $n = 7$) and was 142.0 in M_bACS ($n = 2$). Mean baseline fasting plasma glucose (mg/dL) was higher in MSCS (127.9, $n = 27$) than in M_bACS (103.4, $n = 14$) or M_mCS (98.4, $n = 11$) and decreased in all groups (W24: MSCS, 82.2, $n = 5$; M_bACS, 80.7, $n = 3$; M_mCS, 81.0, $n = 7$). Hypocortisolism-related adverse events occurred in $n = 4/20$ (M_bACS), $n = 6/19$ (M_mCS), and $n = 18/52$ (MSCS) patients, most commonly adrenal insufficiency (M_bACS, $n = 4$; M_mCS, $n = 6$; MSCS, $n = 16$). Deaths were most commonly neoplasm related (M_mCS, $n = 4/10$; MSCS, $n = 4/14$); none were reported in M_bACS.

Conclusions: Osilodrostat effectively reduced cortisol levels, leading to improvements in cardiometabolic parameters, regardless of CS aetiology or severity and with an expected and manageable safety profile.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.431

P273 - ECE_2259 - A combined approach with clinical, laboratory, and expert team input reduces volume status misclassification: secondary analysis of a large European cohort of hospitalized patients with hyponatremia

Laura Potasso[1], Julie Celine Refardt[2] and Mirjam Christ-Crain[1]

[1]Endocrinology, Diabetes and Metabolism, University Hospital of Basel, Basel, Switzerland; [2]Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

Introduction: Hyponatremia affects up to 30% of hospitalized patients and represents a frequent clinical challenge. Proper management requires accurate assessment of volume status, typically based on clinical evaluation and laboratory data. Despite its central role in both European and American guidelines, little is known about the effectiveness of volume status assessments. The aim of the present analysis was to evaluate the accuracy of a merely clinical vs a combined approach (clinical, laboratory, and team input) for volume status assessment hospitalized patients with hypotonic hyponatremia.

Methods: This preplanned secondary analysis of a multicentre, prospective, randomized-controlled European trial (NCT03557957) included hospitalized adults with plasma sodium <130 mmol/L from nine centers. Volume status at admission was classified as hypovolemic, euvolemic, or hypervolemic using either clinical assessment (patient history and physical examination) or a combined approach, which also included guideline-based laboratory indices, and team input if classification was uncertain. Treatment response served as the reference standard. Baseline characteristics of misclassified vs correctly classified patients were compared using chi-square or Mann–Whitney U tests, as appropriate.

Results: Among 2034 patients, misclassification was more frequent with clinical assessment than with a combined approach (333/2034, 16.4% vs 230/2034, 11.3%, $P < .001$). Clinical assessment showed high misclassification in hypovolemic (167/516, 32.4%) and hypervolemic patients (50/318, 15.7%), less in euvolemic (116/1033, 11.2%). Misclassified hypovolemic patients had higher body mass index (BMI, median 25.5 vs 23.6 kg/m^2, $P = .002$), misclassified hypervolemic patients more often chronic renal failure (+8.5%, $P = .03$), and misclassified euvolemic patients more often heart failure (+9.6%, $P < .001$) than correctly classified patients.

The combined approach as compared to clinical approach reduced misclassification across all volume states, most notably in hypovolemic (88/516, −14.6%), but also in euvolemic (108/1033, −1.2%) and hypervolemic patients (34/318, −5%). Misclassified euvolemic patients more frequently had liver cirrhosis (+4.1%, $P = .01$) or heart failure (+11.7%, $P < .001$) compared with correctly classified ones, in contrast to hypervolemic patients, where heart failure predominated in correctly classified patients (+34.9%, $P < .001$). Finally, liver cirrhosis was more prevalent in misclassified hypovolemic patients (+5.6%, $P = .01$) as compared to correctly classified ones.

Conclusions: In hospitalized patients with hyponatremia, combining clinical evaluation, laboratory data, and expert team input reduces misclassification of volume status. Special attention should be given to patients with comorbidities such as heart failure or liver disease, who are at higher risk of misclassification.

Abstract citation ID: lvag096.432

P274 - ECE_2789 - CAM2029 octreotide subcutaneous depot maintains biochemical and symptom control across a 4-week dosing interval and for intervals >28 days: data from the ACROINNOVA 2 trial

Mônica Gadelha[1], Diego Ferone[2], Maria Fleseriu[3], Pietro Maffei[4], Robert D Murray[5], Jochen Seufert[6], Julie M. Silverstein[7], Joanna L. Spencer-Segal[8], Jacob Råstam[9], Alberto M. Pedroncelli[9], Fredrik Tiberg[9] and Beverly M.K. Biller[10]

[1]Neuroendocrinology Research Center/Endocrinology Division, Medical School and Hospital Universitario Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil; [2]Endocrinology Unit, Department of Internal Medicine, IRCCS Ospedale Policlinico San Martino, Genova, Italy; [3]Pituitary Center, Departments of Medicine and Neurological Surgery, Oregon Health and Science University, Portland, OR, United States; [4]Department of Medicine, Padua University Hospital, Padua, Italy; [5]Department of Endocrinology, St James's University Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; [6]Division of Endocrinology and Diabetology, Department of Medicine II, Medical Centre—University of Freiburg, Freiburg, Germany; [7]Division of Endocrinology, Metabolism and Lipid Research, Department of Neurosurgery, Washington University School of Medicine, St. Louis, MO, United States; [8]Department of Internal Medicine and Michigan Neuroscience Institute, University of Michigan, Ann Arbor, MI, United States; [9]Camurus AB, Lund, Sweden; [10]Neuroendocrine and Pituitary Tumor Clinical Center, Massachusetts General Hospital, Boston, MA, United States

Background: Patients with acromegaly may experience waning biochemical and symptom control towards the end of dosing intervals with injectable somatostatin receptor ligands (SRLs). CAM2029, a long-acting octreotide subcutaneous depot, demonstrated stable insulin-like growth factor I (IGF-I) and symptom control across 4-week (W) and >28-day dosing intervals in ACROINNOVA 1 (NCT04076462). We report descriptive data for IGF-I and symptom stability over the final dosing interval for patients receiving long-term CAM2029 in ACROINNOVA 2 (NCT04125836).

Methods: Patients were directly-enrolled (baseline IGF-I ≤2× upper limit of normal [ULN]) or continued from ACROINNOVA 1 (baseline IGF-I ≤ULN; prior-CAM2029 or prior-placebo). CAM2029 20 mg was administered every 4W (±1W) for 52W (prior-placebo, W24-52). The final dose was received at W48, with IGF-I and Acromegaly Index of Severity (AIS) assessments at W48 (pre-CAM2029), W50 (IGF-I levels only) and W52/end of core phase (EOCP). Some patients had delayed W52/EOCP assessments; patients were grouped by on-time (≤28 days post-W48 dose) and later assessment (>28 days post-W48 dose).

Results: Of 135 patients enrolled, 122 completed W48 treatment and W52/EOCP IGF-I assessments and are included in the current analysis. Mean IGF-I levels (standard deviation [SD]) were stable across W48 (1.09 [0.46] × ULN), W50 (0.98 [0.36] × ULN) and W52/EOCP (1.06 [0.46] × ULN). Mean AIS overall scores (SD) were stable from W48 (3.2 [3.0]) to W52/EOCP (3.4 [3.1]). Eighty-six patients had on-time W52/EOCP assessments (mean interval 25.0 days) and 36 patients had later W52/EOCP assessments (mean interval 33.2 days). The table reports IGF-I × ULN values and AIS overall scores for patients with on-time or later assessments, overall and by subgroup.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

	Assessment							
	On-time				Later			
	Overall $n = 86$	Prior-CAM2029 $n = 22$	Prior-placebo $n = 13$	Directly-enrolled $n = 51$	Overall $n = 36$	Prior-CAM2029 $n = 11$	Prior-placebo $n = 4$	Directly-enrolled $n = 21$
Mean IGF-I × ULN (SD)								
W48	1.11 (0.48)	0.83 (0.20)	0.93 (0.72)	1.28 (0.43)	1.04 (0.40)	0.72 (0.24)	0.79 (0.31)	1.26 (0.34)
W50	0.97 (0.35)	0.74 (0.17)	0.69 (0.22)	1.13 (0.34)	1.02 (0.39)	0.73 (0.22)	0.68 (0.20)	1.25 (0.33)
W52/EOCP	1.02 (0.42)	0.75 (0.20)	0.67 (0.19)	1.23 (0.41)	1.16 (0.54)	0.92 (0.70)	0.76 (0.31)	1.37 (0.37)
Mean AIS overall score (SD)								
W48	3.1 (3.0)	3.1 (2.9)	2.6 (3.2)	3.3 (3.1)	3.6 (3.0)	4.8 (2.9)	3.5 (4.5)	2.9 (2.6)
W52/EOCP	3.2 (3.1)	3.5 (3.3)	1.8 (2.9)	3.5 (3.0)	3.7 (3.1)	5.0 (3.0)	3.5 (4.5)	3.0 (2.7)

Conclusions: Long-term CAM2029 provides stable biochemical and symptom control across the 4W dosing interval. CAM2029 can reduce waning disease control at the end of dosing intervals observed with other injectable SRLs.

Abstract citation ID: lvag096.433

P275 - ECE_3525 - Predictors for early response to fluid restriction in patients with SIAD—analysis of a randomized, controlled, parallel-group trial with blinded outcome assessment

Michelle Müller[1,2], Laura Potasso[1,2], Julie Celine Refardt[1,2,3] and Mirjam Christ-Crain[1,2]

[1]Department of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland; [2]Basel, Switzerland; [3]Department of Internal Medicine, Section of Endocrinology, Erasmus Medical Centre, Rotterdam, The Netherlands

Introduction: Fluid restriction is the current first-line therapy for hyponatremia induced by the syndrome of inappropriate antidiuresis (SIAD), but, up to 50% of patients do not achieve a sufficient sodium correction. Reported predictors of non-response are urine osmolality >500 mOsm/kg H_2O, a Furst Ratio >1 (UNa+UK/SNa) as well as a urine sodium (>130 mmol/L) and plasma urea (>5 mmol/L). This study aimed to validate current prognostic factors and potentially identify new predictors.

Materials and Methods: This predefined secondary analysis was based on an international, prospective study that included patients with moderate to severe hyponatremia (plasma sodium <130 mmol/L). Response to treatment with fluid restriction was defined as an increase in plasma sodium of >3 mmol/L within the first 24 hours, while non-response was defined as an increase of ≤3 mmol/L. Baseline laboratory parameters—particularly urine sodium, urine osmolality, and plasma urea—were analyzed using multivariate logistic regression.

Results: Of 853 patients with SIAD, 278 were treated with fluid restriction within the first 24 hours and had complete laboratory data. Among these patients, 103 (37%) were classified as responders and 175 (63%) as non-responders. We confirmed urine osmolality ($P = .001$) and urine sodium ($P = .028$) as predictors of non-response to fluid restriction in multivariate logistic regression analysis. In our cohort alternative cut-offs of urine osmolality >700 mOsm/kg H_2O (PPV 0.89, NPV 0.39, LR+ 4.71) and urine sodium >110 mmol/L (PPV 0.85, NPV 0.42, LR+ 3.24) showed better predictive performance than the previously proposed thresholds. In contrast, no other previously proposed markers were associated with treatment non-response in multivariate logistic regression analyses.

Conclusions: Our data confirm urine osmolality and urine sodium as a predictor of non-response to fluid restriction. We propose alternative cut-offs (urine osmolality >700 mOsm/kg H_2O and urine sodium >110 mmol/L) for better identification of non-responders.

Abstract citation ID: lvag096.434

P276 - ECE_3213 - Biomarkers for progression allowing individualized management of patients with non-functioning pituitary tumors

Medha Suman[1], Tobias Hallén[2], Thomas Skoglund[2], Linus Koster[2], Oskar Ragnarsson[2] and Gudmundur Johannsson[2]

[1]Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Gothenburg, Sweden; [2]Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska University Hospital, University of Gothenburg, Gothenburg, Sweden

Introduction: Post surgical tumor progression is observed in more than 50% of non-functioning pituitary tumors (NFPTs). There is no reliable method to predict individual tumor behaviour after surgery. Therefore, life-long surveillance with magnetic resonance imaging (MRI) is needed in all patients to monitor tumor growth. Biomarkers are needed to identify patients at risk of progression who may benefit from early re-operation, radiotherapy and/or medical treatment. In parallel, a deeper understanding of the biological mechanisms driving tumor progression is crucial for the development of novel therapeutic approaches.

Aims: In this project, we aim to investigate genome-wide DNA methylation and protein expression profiles in NFPTs to understand the interplay between the two molecular events and to potentially reveal driver events or pathways associated with tumor progression. Unravelling the underlying biology has potential for biomarker discovery and the development of novel therapeutic interventions.

Methods: We conducted an integrated analysis of DNA methylation and protein expression across 734 065 CpG sites and 457

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

differentially expressed proteins in NFPTs using hypernetwork models. We used our local retrospective cohort that included progressive ($n = 25$), and indolent ($n = 15$) NFPTs. The biomarkers identified in this study will be validated in another cohort that includes 88 NFPT cases.

Results: Of the 457 proteins, 101 proteins in progressive and 171 proteins in indolent NFPTs formed highly connected protein clusters that displayed coordinated epigenetic regulation. Some of the top hypernetwork proteins were encoded by genes *MCM6*, *SAFB*, *HDGFL2*, *PSMD6* and *LAMB2*. Several of these proteins were primarily involved in metabolic pathways and previously reported in other tumors with role in cell proliferation and migration. All these proteins were significantly upregulated in progressive NFPTs. Area under receiver curve analysis revealed that several of these proteins could predict the progressive tumor behaviour with over 80% accuracy.

Discussion: Hypernetwork analysis identified proteins involved in higher-order interactions between DNA methylation and protein expression that were not ranked high in conventional differential protein expression analysis. These proteins could potentially be functionally involved in driver events in tumor biology and warrant further investigation as candidate biomarkers for identifying individuals at risk of tumor progression after surgery.

Abstract citation ID: lvag096.435

P277 - ECE_1345 - Metabolic profiling of patients with active acromegaly and in remission by ultrahigh performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS): exploring pathophysiology and biomarkers

Amy Coulden[1,2], Catherine Winder[3], Wanchang Lin[3], Warwick Dunn[3], Gabriela Da Silva Xavier[1] and Niki Karavitaki[1,2]

[1]Department of Metabolism and System Science, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom; [2]Department of Endocrinology, Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [3]Centre of Metabolomics Research, Biochemistry, Cell and Systems Biology, Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool, United Kingdom

Background: Patients with acromegaly have multi-systemic co-morbidities (metabolic, cardio-/cerebrovascular, respiratory, musculo-skeletal) and increased mortality driven by metabolic and cardiovascular complications. Biochemical control is a main aim of treatment approaches and normalization of IGF-1 is considered indicative of biochemical remission. Nonetheless, acromegaly-related co-morbidities may persist even after apparent biochemical remission. Biomarkers reliably reflecting acromegaly activity and its sequelae in the body function are needed.

Aims: a) Explore global perturbations in the metabolism of patients with active acromegaly and acromegaly in biochemical remission, b) identify biomarkers discriminating patients from matched controls.

Methods: Non-targeted plasma metabolomic assessment was performed in plasma samples from 39 patients with active acromegaly, 39 with acromegaly in biochemical remission and 35 age-, sex- and BMI-matched controls by ultrahigh performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS)**;** assays were detecting more than 800 water-soluble metabolites (HILIC assay) and 1000 lipid metabolites (C_{18} reversed phase assay). No participants were on medical treatment for the acromegaly or on antidiabetic medications. Analyses were performed with the MetaboAnalyst platform.

Results: 257 and 309 metabolites were different between active acromegaly and controls and between remission and controls, respectively ($P < .01$, Benjamini-Hochberg corrected). 74 water-soluble and 97 lipid metabolites were different in both comparisons and were investigated further. Eight pathways were enriched using the water-soluble metabolites ($P < .05$, Benjamini-Hochberg corrected), including amino acid metabolism (branched chain amino acids and arginine metabolism), purine metabolism and the pentose phosphate pathway. 26 (lyso)glycerophospholipids, 21 acyl carnitines, 15 fatty acids and oxidised fatty acids, 12 sterol lipids and 8 ceramides/sphingolipids were enriched based on lipid classes. 11 of the metabolites which were significantly different in both comparisons had AUROC ≥ 0.95 providing a panel to discriminate between active disease and control samples. In patients with active disease, 109 metabolites were correlated with IGF-1 levels ($-0.4 <$ correlation coefficient > 0.4; $P < .01$); no water-soluble metabolic pathways were enriched, whereas 36 glycerophospholipids (including 8 glycerophosphoinositols), 11 phosphosphingolipids, 9 sterol lipids, and 3 glycosphingolipids were statistically significant. Only 20 metabolites were different between patients with active acromegaly and on remission.

Conclusions: The metabolic profile of patients with acromegaly but also of those in remission is distinct from that of matched controls challenging the value of IGF-1 as biochemical marker of successful treatment. Correlations of IGF-1 levels with specific metabolites propose pathways involved in the pathophysiology of acromegaly. A number of metabolites can reliably discriminate disease status. Larger scale studies are needed to further explore these findings.

Abstract citation ID: lvag096.436

P278 - ECE_2785 - Diagnostic usefulness of fractional uric acid excretion as a supplementary criterion for SIAD

Emanuele Ferrante[1], Alessandro Maria Berton[2], Roberta Mungari[1], Michela Sibilla[2], Emanuele Varaldo[2], Nunzia Prencipe[2], Valeria Lanzi[1], Arianna Cremaschi[1], Silvia Grottoli[2], Gianluca Aimaretti[2], Ezio Ghigo[2] and Giovanna Mantovani[3]

[1]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]Division of Endocrinology, Diabetology and Metabolism, Medical Sciences Department, University of Turin, Turin, Italy; [3]Department of Clinical Sciences and Community Health, Dipartimento di Eccellenza 2023-2027, University of Milan, Milan, Italy

Background: The syndrome of inappropriate antidiuresis (SIAD) is the most frequent cause of hypotonic euvolemic hyponatremia. However, the differentiation between extracellular hypovolemia and euvolemia can be difficult and SIAD remains a diagnosis of exclusion. Other than essential criteria, a fractional uric acid excretion (FE-UA) >12% has been proposed as supplementary diagnostic criterion, independently of diuretics use.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

This study aimed to evaluate the diagnostic performance of FE-UA in SIAD and to validate the guideline-proposed thresholds.

Methods: biochemical parameters (serum and urine), including FE-UA, were prospectively analyzed in consecutive hyponatremic patients at diagnosis who were referred to two different Endocrinology Divisions in Northern Italy from November 2020 to December 2025. Patients who had already received treatment for hyponatremia, receiving hypouricemic drugs, or with hyponatremia due to primary polydipsia were excluded.

Results: 101 patients [66 females (65.3%), 35 males (34.7%), median age: 73 (61-80)] were included in the study. 86 patients (85.1%) had a diagnosis of SIAD, and 15 (14.9%) were classified as non-SIAD. 23 patients (22.8%) were on diuretics (17 in the SIAD group, 6 in the non-SIAD group), while 6 patients (5.9%) were on SGLT2-inhibitors (3 in the SIAD group and 3 in the non-SIAD group). In the whole group, median sodium was 129 (126-132) mmol/L, p-Osm 268 (258-276) mOsm/Kg, u-Osm 421 (318-541) mOsm/Kg and FE-UA 10.9% (7.5-13.6).

FE-UA median levels were significantly different between the two groups of patients (11.1% (8.6-15.4) vs 0.2% (0.07-6.79) in SIAD and non-SIAD groups, respectively, $P < .001$). Logistic regression showed a strong association between diagnosis and FE-UA levels (OR: 1.49, 95%CI: 1.23-1.79, $P < .001$). ROC analysis showed good discriminative performance, with an area under the curve (AUC) of 0.857 (95%CI: 0.737-0.976). The empirical optimal cut-off, determined using Liu Method, was 6.8%, at which the sensitivity and specificity were 87% and 80%, respectively. A cut-off of 12.5% showed a specificity and a positive predictive value (PPV) of 100% (95%CI: 89.4-100%), while a value of 2.5% showed a sensitivity and a negative predictive value (NPV) of 100% (95%CI: 63.1-100%). The diagnostic performance remained unchanged after excluding patients receiving diuretics and/or SGLT2 inhibitors, and the empirical optimal cut-off remained unchanged.

Conclusions: FE-UA showed a good diagnostic performance for SIAD. Values ≥12.5% reliably confirmed, whereas values <2.5% excluded the diagnosis. Diagnostic accuracy and optimal cut-off values were not influenced by diuretic and/or SGLT2 inhibitor use, supporting FE-UA as a robust supplementary diagnostic criterion for SIAD.

Abstract citation ID: lvag096.437

P279 - ECE_1060 - Association between SUDOSCAN-derived cardiac autonom neuropathy score and cardiovascular risk scores in patients with acromegaly

Nijat Nasirov[1], Humeyra Rekalı Şahin[2], Onour Chasan[1], Melike Cevikdizici[2], Ümmü Mutlu[1], Fulya Calikoglu[2], Hulya Hacisahinogullari[2], Nurdan Gul[2], Ozlem Soyluk Selcukbiricik[2], Ayse Kubat Uzum[2] and Gulsah Yenidunya Yalin[1]

[1]Department of Internal Diseases Division of Endocrinology and Metabolism Disorders, Istanbul University Istanbul Faculty of Medicine, Istanbul, Türkiye; [2]Department of Internal Diseases Division of Endocrinology and Metabolism, Istanbul University Istanbul Faculty of Medicine, Istanbul, Türkiye

Background: Acromegaly is associated with increased cardiovascular risk due to excess growth hormone and insulin-like growth factor-1 secretion. Cardiac autonomic neuropathy (CAN) represents an early manifestation of the associated cardiometabolic alterations. SUDOSCAN, a non-invasive device, quantifies electrochemical skin conductance (ESC) and estimates autonomic dysfunction. However, its clinical utility in acromegaly has not been systematically evaluated. This study aimed to assess the relationship between the SUDOSCAN-derived CAN risk score and cardiovascular risk algorithms SCORE2 and Framingham in patients with acromegaly.

Methods: A total of 72 participants, acromegaly patients (n: 36) and age and sex matched healthy control group (n:36) were evaluated in a cross-sectional design. Autonomic function was assessed with the Ewing test battery and SUDOSCAN (Impeto Medical, Paris, France). Ewing protocol included five standard cardiovascular reflex tests; heart rate response to deep breathing, valsalva maneuver, heart rate response to standing (30:15 ratio), blood pressure response to standing, and sustained handgrip test. Each test was scored (normal: 0, borderline: 0.5, or abnormal: 1) generating a total Ewing score (range 0-5). SUDOSCAN measurements were performed under standardized conditions by the same trained investigator. ESC values were obtained for hands and feet, and the device generated CAN risk scores adjusted for age, sex, and BMI. Cardiovascular risk was estimated using SCORE2 and Framingham algorithms. Statistical analyses included Mann–Whitney U, Spearman correlation, multivariate linear regression, and ROC analysis.

Results: Baseline demographic features, metabolic parameters (glucose, HbA1c, non-HDL cholesterol, triglyceride) and Ewing scores were similar between groups. SUDOSCAN-derived CAN risk scores were significantly higher in acromegaly patients (median 22.5 [14-35.5] vs 17 [10-25.8], $P = .023$). CAN scores correlated strongly with SCORE2 ($r = 0.773$, $P < .001$) and moderately with Framingham ($r = 0.471$, $P = .007$) and Ewing ($r = 0.458$, $P = .005$) scores. In multivariate regression, SCORE2 remained an independent predictor of CAN score ($\beta = .376$, $P = .02$). ROC analysis demonstrated excellent discriminative ability of SCORE2 (AUC = 0.937, 95% CI: 0.859-1.000) and good performance for Framingham (AUC = 0.865, 95% CI: 0.694-0.960) in identifying abnormal CAN scores, no significant predictive value was observed in the control group.

Conclusions: SUDOSCAN-derived CAN scoring correlates strongly with established cardiovascular risk algorithms and Ewing test parameters in acromegaly patients. Incorporating sudomotor-based autonomic assessment into cardiovascular risk stratification may enhance early identification of autonomic dysfunction and provide a practical adjunct to conventional scoring systems in this population.

Abstract citation ID: lvag096.438

P280 - ECE_1603 - Ketoconazole ESTEVE in endogenous Cushing's syndrome: post-authorisation safety study in 132 patients

Anna Aulinas[1], Alicia Santos Vives[1], Frederic Castinetti[2], Filippo Ceccato[3], Jérôme Bertherat[4], Rogelio Garcia-Centeno[5], Karin Zibar Tomsic[6], Claudia Amaral[7], Richard Feelders[8], Emanuele Ferrante[9], Eleni Papakokkinou[10], Marta Zivanov[11],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Myriam Bou Nader[11], Mariano Sust[11], Jesus Cebrecos[11], Thierry Brue[2] and Susan Webb[1]
[1]Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [2]Department of Endocrinology, Hôpital de la Conception, Marseille, France; [3]Department of Endocrinology, University Hospital of Padova, Padova, Italy; [4]Department of Endocrinology, Hôpital COCHIN, Paris, France; [5]Hospital General Universitario Gregorio Marañón, Madrid, Spain; [6]Department of Endocrinology, University Hospital Zagreb, Zagreb, Croatia; [7]Department of Endocrinology, Centro Hospitalar Universitário do Santo António, Porto, Portugal; [8]Department of Endocrinology, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands; [9]Unit of Endocrinology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy; [10]Institute of Medicine at Sahlgrenska Academy, Department of Internal Medicine and Clinical Nutrition, University of Gothenburg, Gothenburg, Sweden; [11]ESTEVE Pharmaceuticals, S.A., Barcelona, Spain

Background: Ketoconazole ESTEVE is approved for the treatment of endogenous Cushing's syndrome (CS) with a requirement to collect safety data in this indication.

Methods: The primary objective of this prospective open-label Post-Authorisation Safety Study (PASS), using the European Registry on Cushing's Syndrome (ERCUSYN), is to document liver and cardiac safety in patients treated with Ketoconazole ESTEVE for CS. Overall safety, treatment pattern, and effectiveness are secondary objectives. Data from the last annual interim report are presented.

Results: At the cut-off date (31 August 2025), 134 patients were enrolled. One hundred and thirty-two patients were included in the full analysis set, 129 were evaluated for safety, and 130 for efficacy. Mean (SD) age of the patients was 46.9 (15.25) years. The majority of patients were female (78.8%) and were diagnosed with pituitary-dependent CS (73.6%). Ketoconazole ESTEVE was mainly used as monotherapy (87.1%), with a mean (SD) exposure of 1.4 (1.8) years and a median average daily dose of 400 mg.

Fifty-two cases (40.3%) of liver function test (LFT) abnormalities observed, occurred at the mean time of 1.7 months, with the median resolution time of 53.5 days. The proportion of patients with hepatotoxicity (ALT$\geq 5\times$ULN; ALP$\geq$2x ULN (without known bone fractures); or ALT$\geq$3x ULN and TB $>$ 2x ULN) decreased since the last report to 6.2% (8/129), with no new hepatotoxicity events being reported during this reporting period. Mean time to occurrence was 5.1 months, and the mean resolution time was 13.9 days. Co-administration of a known hepatotoxic drug was suspected in 6 of these patients. In all 8 patients, liver injury resolved after discontinuation of ketoconazole, 5 of these events were hepatocellular. No QTc prolongation cases were reported.

Effectiveness analysis suggests improved clinical outcomes in most patients treated with Ketoconazole ESTEVE, with 20.0% (26/130) of patients reaching remission and 60.0% (78/130) partial remission. Additionally, UFC or plasma cortisol levels were normal at the last visit in the majority of treated patients (72.2%, 65/90) with available data.

Conclusions: The results confirm the established safety and efficacy profile of Ketoconazole ESTEVE, with no new or unexpected safety signals detected.

Abstract citation ID: lvag096.439

P283 - ECE_3680 - Prevalence and risk factors for radiotherapy-induced hypopituitarism in survivors of primary, non-pituitary brain tumours treated with intensity-modulated radiotherapy

Darran Mc Donald[1,2], Liam O'connell[3], Maria Tomkins[1,2], Tara McDonnell[1,2], Niamh Mc Dermott[2], Jack Lee[2], Claire Carthy[2], Mary Moore[2], Amar Agha[1,2], Donncha O'brien[4], Kieron Sweeney[4], Stephen McNally[4], Mohsen Javadpour[4], Clare Faul[3], David Fitzpatrick[3], Michael W. O'reilly[1,2] and Mark Sherlock[1,2]
[1]Department of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland; [2]Department of Endocrinology, Beaumont Hospital, Dublin, Ireland; [3]St Luke's Radiation Oncology Network, Dublin, Ireland; [4]Department of Neurosurgery, Beaumont Hospital, Dublin, Ireland

Background: Hypopituitarism is a well-recognised late-effect of cranial radiotherapy. However, there is limited evidence quantifying the risk of hypopituitarism in adult survivors of primary, non-pituitary brain tumours, treated with modern radiotherapy techniques. Intensity-modulated radiotherapy (IMRT) is an advanced form of photon-based radiotherapy that precisely delivers radiation to brain tumours, with relative sparing of surrounding structures, including the hypothalamic-pituitary axis (HPA).

Methods: We evaluated the prevalence of, and risk factors for, radiotherapy-induced hypopituitarism in adult survivors of brain tumours that were distant from the HPA and treated with IMRT in Beaumont Hospital (the Irish National Neurosurgical Centre) between 2012-2022. Two patient cohorts were assessed (i) a retrospective cohort of survivors previously referred for endocrine surveillance; and (ii) a prospective cohort of consecutively treated survivors without prior surveillance. Prospectively recruited patients underwent a glucagon stimulation test and baseline pituitary assessment. Retrospectively recruited patients underwent annual synacthen testing and a pituitary profile, with growth hormone (GH) assessments performed in selected cases. Fischer's exact test compared prevalence rates between both cohorts. Multivariate logistic regression models evaluated the impact of independent variables on hypopituitarism risk.

Results: Pituitary function was assessed in 140 brain tumour survivors (prospective cohort $n=54$, retrospective cohort $n=86$). Median age at radiotherapy was 39.7 years (IQR 30.5-49.8) with a median post-radiotherapy interval of 60.5 months (IQR 36.0-83.0). The prevalence of hypopituitarism was 55% ($n=51/93$). GH deficiency was most common (54%; $n=50/93$), followed by adrenocorticotrophic hormone (ACTH) deficiency (12%; $n=17/138$), gonadotropin deficiency (11%; $n=15/138$) and thyroid-stimulating hormone (TSH) deficiency (9%; $n=12/137$). Hypopituitarism, ACTH, gonadotropin and TSH deficiency were more significantly prevalent in the retrospective compared to prospective cohort ($P<.05$). The composite endpoint of gonadotropin, ACTH or TSH deficiency occurred in 16% ($n=22/134$). The prevalence of this endpoint was significantly lower than a prior study in our institution using older 2 and 3-dimensional radiotherapy (16 vs 34%;$P<.01$). Multivariate logistic regression analysis revealed higher pituitary doses were independently associated with developing deficits across all hormone axes.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Longer follow-up interval was significantly associated with gonadotropin and TSH deficiency. Age, sex, tumour type and adjuvant chemotherapy were not associated with any hormone deficits.

Conclusions: This is the largest study evaluating the prevalence of radiotherapy-induced hypopituitarism in adult-onset-brain tumour survivors. The prevalence of the most clinically significant pituitary hormone deficits (ACTH, TSH and gonadotropin) is lower than previously reported, likely reflecting advances in modern radiotherapy techniques. Pituitary radiation dose exposure is an independent risk factor for radiotherapy-induced hypopituitarism.

Abstract citation ID: lvag096.440

P284 - ECE_3767 - [68Ga]DOTATOC PET/MRI guided stereotactic radiosurgery for residual pituitary adenomas

Linus Hesse[1,2,3], Larissa Kilian[4], Carolin Senger[4], Leonard Kozarzewski[1,2], Jawed Nawabi[5], Goda Kalinauskaite[4], Christian Furth[6], Vanessa Hubertus[2,7], Peter Vajkoczy[2,7], Daniel Zips[4], Dominik Soll[1,2], Lukas Maurer[1,2], Christian J. Strasburger[1,2], Knut Mai[1,2,8], Güliz Acker[2,4,7] and Linus Haberbosch[1,2,3]

[1]Department of Endocrinology and Metabolism, Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin Institute of Health, Berlin, Germany; [2]Pituitary Tumor Center of Excellence at Charité, Universitätsmedizin Berlin, Berlin, Germany; [3]Cambridge Endocrine Molecular Imaging Group, Institute of Metabolic Science, Cambridge, United Kingdom; [4]Department of Radiation Oncology, Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin Institute of Health, Charité CyberKnife Center, Berlin, Germany; [5]Department of Neuroradiology, Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany; [6]Department of Nuclear Medicine, Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin Institute of Health, Berlin, Germany; [7]Department of Neurosurgery, Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin Institute of Health, Berlin, Germany; [8]Department of Human Nutrition, German Institute of Human Nutrition Potsdam-Rehbrücke, Nuthetal, Germany

Background: Stereotactic radiosurgery (SRS) is an effective salvage therapy for progressive non-functioning and medically refractory hormone-secreting pituitary adenomas, albeit requiring precise and confident target delineation. This, however, can be difficult on often equivocal postoperative MRI scans. While functional imaging is gaining importance in the diagnostic workup of challenging pituitary tumours, its value for radiosurgical planning in pituitary adenomas is largely unknown.

Methods: In this single-centre retrospective study, we report clinical outcomes of [68Ga]DOTATOC PET/MRI-guided SRS at a tertiary pituitary centre. Furthermore, we assessed the impact of [68Ga]DOTATOC PET on radiosurgical target delineation by comparing MRI-only contours, generated by an experienced radiosurgeon blinded to PET data, with clinically used PET/MRI-based plans using overlap and dose metrics.

Results: Twenty-three patients (57% women, median age 40 years) received PET-guided SRS at our centre; 44% had functioning adenomas. Visual PET uptake was present in all suspected residual tumours. At a median follow-up of 20.5 months [IQR: 11.8-50] for 20 patients without previous sellar irradiation, local tumour control was 94%. In tumours treated for uncontrolled hypersecretion ($n = 7$), 86% achieved biochemical normalization or improvement ($n = 6$). Only two patients (10%) developed additional pituitary deficits after SRS. Overall toxicity was predominantly low grade; 40% reported at least one adverse event (mostly headache, exclusively grade 1 according to the Common Terminology Criteria for Adverse Events [CTCAE]). One patient (5%) developed an oculomotor nerve disorder (CTCAE grade 3).

In simulation contouring, MRI-only and PET/MRI gross tumour volume (GTV) sizes did not show significant differences (5.57 cm^3 [3.29-7.95] vs 4.97 [3.22-7.33], $P = .8$). Spatial agreement was moderate (median GTV Dice coefficient 0.795 [0.753-0.838]), with MRI-only contouring missing a median of 18.7% [12.6-25.6%] of the PET/MRI GTV. Applying the PET/MRI-based dose distribution to the MRI-only planning target volume reduced coverage from 98.7% to 88.4% ($P < .001$), illustrating that even minor target delineation differences can markedly affect radiosurgical planning.

Conclusions: [68Ga]DOTATOC PET/MRI appears to identify residual adenoma more precisely than MRI-defined targets, suggesting that functional imaging may enhance radiosurgical planning. While early clinical outcomes are encouraging, the clinical value of functional imaging in guiding stereotactic radiosurgery requires validation in larger prospective multicentre trials.

Abstract citation ID: lvag096.441

P285 - ECE_2115 - Genomic characterization of aggressiveness in pituitary neuroendocrine tumors (PitNETs)

Nesrine Benanteur[1], Chiara Villa[1,2], Fabio Bioletto[1,3], Maria Francesca Birtolo[1,4], Daniel de Murat[1], Julien Masliah-Planchon[5], Victor Gravrand[1], Inès Lebib[1], Mounia Benkhellat[1], Robin Boezennec[1], Stéphanie Allassonnière[6], Franck Letourneur[7], Yoann Martin[7], Fidéline Bonnet-Serrano[1,8], Julian Jacob[9], Valentin Calugaru[10], Maxime Barat[1,11], Anthony Dohan[1,11], Jennifer Arrondeau[12], Olivier Huillard[13], Marie-Laure Raffin-Sanson[14], Emile Jean Francois[15,16], Gerald Raverot[17,18], Rossella Libe[1,19], Laurence Guignat[19], Cyril Garcia[20], Lionel Groussin[1,19], Xavier Bertagna[1], Stephan Gaillard[1], Jérôme Berthera[1,19], Anne Jouinot[1], Bertrand Baussart[1,21] and Guillaume Assié[1,19]

[1]CNRS UMR8104, INSERM U1016, Institut Cochin, Université Paris Cité, Paris, France; [2]Department of Pathology, Hôpital Lariboisière, Assistance Publique-Hôpitaux de Paris, Paris, France; [3]Division of Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, Turin, Italy; [4]Department of Biomedical Sciences, Humanitas University, Milan, Italy; [5]Department of Diagnostic and Theranostic Medicine, Somatic Genetics Unit, Institut Curie, Paris-Science Lettres University, Paris, France; [6]Université Paris Cité, Unité Mixte de Recherche S1138, Institut national de recherche en sciences et technologies du numérique, Sorbonne University, Paris, France; [7]INSERM U1016, Institut Cochin, Plate-Forme Séquençage et Génomique (Genom'IC), Paris, France; [8]Hormonology Department, Cochin Hospital, Paris, France; [9]Department of Radiation Oncology, Hôpital La Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Paris, France; [10]Department of Radiation Oncology, Paris/

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Saint-Cloud/Orsay, Institut Curie, PSL Research University, Paris, France; [11]Department of Radiology, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Paris, France; [12]Department of Clinical Oncology, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Paris, France; [13]Medical Oncology Department, Université Paris Cité, Institut du Cancer Paris CARPEM, AP-HP, Hôpital Cochin-Port Royal, Paris, France; [14]Department of Endocrinology, Diabetology, and Nutrition, Ambroise Paré University Hospital, Assistance Publique-Hôpitaux de Paris, Boulogne Billancourt, France; [15]EA4340, University of Versailles Saint-Quentin-en-Yvelines, UFR of Health Sciences Simone Veil, Montigny-le-Bretonneux, France; [16]Department of Pathology, Hôpital Ambroise Paré, Assistance Publique-Hôpitaux de Paris, Boulogne Billancourt, France; [17]Cancer Research Center of Lyon, Inserm U1052, CNRS UMR5286, Lyon 1 University, Lyon, France; [18]Endocrinology Department, Reference Center for Rare Pituitary Diseases HYPO, "Groupement Hospitalier Est" Hospices Civils de Lyon, Bron, France; [19]Department of Endocrinology, Hôpital Cochin, Reference and Competence Center for Rare Adrenal Diseases and Rare Pituitary Diseases, Assistance Publique-Hôpitaux de Paris, Paris, France; [20]Service D'Endocrinologie, Hôpital National D'Instruction des Armées Bégin, Saint-Mandé, France; [21]Department of Neurosurgery, Hôpital Lariboisière, Assistance Publique-Hôpitaux de Paris, Paris, France

Aggressive evolution of PitNETs is uncommon and remains difficult to characterize. Defining aggressiveness and malignancy is challenging, and subsequently hard to predict, and to understand. The aim of this study was to provide a molecular definition of aggressiveness using genomic approaches.

Methods: Tumor samples from 206 patients with PitNETs were included. Associations between 9 clinical features of aggressiveness and PitNETs' omics were explored. Omics included transcriptome, DNA methylation, chromosomal alterations and mutations. Clonal tumor evolution was monitored in 7 patients.

Results: Among the 9 clinical features of aggressiveness evaluated, only rapid progression, progression after radiotherapy, Ki67/MIB1 proliferation index ≥10%, temozolomide treatment, metastases and specific death were associated with distinct molecular signatures. In contrast, tumor maximal diameter ≥40 mm, cavernous and sphenoid invasion were not linked to specific omic signatures. The omic signatures associated with these features of aggressiveness overlapped but remained distinct between corticotroph and mammo-somato-thyrotroph lineages. For each lineage, a common signature of aggressiveness emerged, associating proliferative transcriptome signature and DNA hypermethylation. Alterations in specific cancer-related genes were associated with aggressive features. *USP8* and *GNAS* alterations were associated with a better outcome. Integrative analysis of gene alteration, methylome, and transcriptome signatures identified a subset of molecularly aggressive PitNETs, enabling the development of a histomolecular risk stratification strategy. Molecular signatures remained globally stable during the course of the disease, despite evolution towards aggressiveness and potential clonal divergence.

Conclusions: This systematic analysis of clinical and histopathological features of aggressiveness using an integrated multiomic approach refines the concept of aggressiveness in PitNETs with a molecular definition. High risk PitNETs with pejorative outcome can be individualized according to a histomolecular risk assessment workflow. Prospective cohort studies are needed to validate this approach in clinical practice.

Abstract citation ID: lvag096.442

P286 - ECE_1919 - Tirzepatide in patients with hypothalamic obesity secondary to craniopharyngioma: a single-center case series

Elisa Sala[1], Giulia Carosi[1], Giulia Del Sindaco[1], Giacomo Noschese[1,2], Alessandra Mangone[1,2], Roberta Mungari[1], Arianna Cremaschi[1], Emanuele Ferrante[1] and Giovanna Mantovani[1,2]

[1]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

Background: hypothalamic obesity is a severe condition affecting patients with craniopharyngioma, resulting from hypothalamic damage and characterized by rapid weight gain, hyperphagia, and dysregulation of energy expenditure. Lifestyle interventions show limited efficacy, and pharmacological options remain scarce. Currently, setmelanotide can be prescribed in pediatric patients with hypothalamic obesity; however, no pharmacological therapy is specifically approved for adults. To date, only one published case report has suggested potential benefits of tirzepatide in a patient with surgically treated craniopharyngioma.

Methods and Results: we report a single-center case series including 3 adult patients (2 females, 1 male; mean age 45 ± 6.4 years) with hypothalamic obesity secondary to transsphenoidal surgery for adamantinomatous craniopharyngioma. Body mass index (BMI) at diagnosis was 25 (patient 1, F), 20 (patient 2, F), and 29 (patient 3, M) kg/m^2. Before starting tirzepatide, prescribed according to clinical practice 14, 24, and 5 months after surgery, BMI was increased to 30, 36, and 39 kg/m^2, respectively (median weight increase: 36 kgs (29-48 IQR); median percentage increase: 51% (34-80 IQR)). Changes in body weight, metabolic parameters, appetite-related symptoms, body image perception assessed by the Body Uneasiness Test (BUT-A), and safety outcomes were evaluated during follow-up.

Tirzepatide treatment was associated with a weight reduction in female patients, corresponding to a 10% of body weight loss after 4 months in patient 1 (final dose: 5 mg/w) and a 5% of body weight loss after 2 months in patient 2 (final dose: 5 mg/w). In the male patient, an initial weight gain of 5 kg was observed during the first month of therapy (2.5 mg/w), followed by weight stabilization over the subsequent 2 months (dose: 7.5 mg/w). All patients reported a reduction in hyperphagia and food-seeking behavior. Treatment was well tolerated, and no adverse events were reported. Weight changes were accompanied by improvements in metabolic parameters in patient 1, after 4 months follow-up: HOMA-IR decreased from 4.5 to 2.6, and glycated hemoglobin levels were reduced from 37 to 33 mmol/mol. Moreover, body image perception improved, with the Global Severity Index of the BUT-A decreasing from a pathological

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

value of 1.6 at baseline to 1.1 after four months, below the pathological threshold (>1.2).

Conclusions: In this single-center case series, tirzepatide was associated with clinically relevant weight improvements in patients with hypothalamic obesity secondary to craniopharyngioma surgery. Despite the small sample size, these findings suggest that tirzepatide may represent a promising therapeutic option for this challenging condition.

Abstract citation ID: lvag096.443

P288 - ECE_3351 - Pharmacological steroid secretion inhibition in Cushing's disease: the risk of acute kidney injury

Brian Randazzo[1], Giacomo Fabio Antonio Grifoni[1], Vittoria Favero[1,2], Andrea Saladino[3], Edoardo Porto[3], Renato Cesare Cozzi[2] and Iacopo Chiodini[1,2]
[1]Department of Biotechnology and Translational Medicine, University of Milan, Milano, Italy; [2]Endocrinology Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [3]Milan, Italy

Background: Medical therapy has an established role in treating Cushing's disease (CD) when surgery is delayed, contraindicated or unsuccessful, with the aim of normalizing 24-hour urinary free cortisol and/or late-night salivary cortisol. However, the normalization of these hormonal parameters may become excessive in some cases, such as cyclic disease or during stress conditions, leading to adrenal insufficiency (AI). Several studies have linked AI to acute kidney injury (AKI), but to date, AKI associated with medical therapy-induced AI has not been systematically described.

Cases Presentation: Case 1. A 54-year-old man with CD treated with Osilodrostat since May 2022 (2 mg/day). In July 2025, due to worsening metabolic control, the dose was up-titrated to 4 mg/day. Two weeks later, he developed asthenia, weight loss and hypotension. Biochemical evaluation showed low cortisol levels. At the same time, serum creatinine increased from a baseline of 1.34 mg/dL up to 3.57 mg/dL, and eGFR reached a nadir of 18 mL/min/1.73 m^2.

Osilodrostat was discontinued and the patient received intravenous hydrocortisone and isotonic saline, followed by a replacement therapy with oral hydrocortisone for few days. His clinical symptoms improved rapidly, and renal function progressively recovered, with serum creatinine decreasing to 1.58 mg/dL within a month.

Case 2. A 79-year-old woman with a long-term persisting CD, treated with Pasireotide since 2018. In April 2024 she underwent knee arthroplasty and block and replace treatment was prescribed for surgery. Surgery was uneventful and rehabilitation started. Three weeks later she developed nausea, vomiting, asthenia, hypotension; laboratory evaluation showed hyperkalaemia (6.4 mEq/L) and serum creatinine of 6.2 mg/dL. Pasireotide therapy was suspended, while intravenous steroids and supportive therapy were administered. Oral hydrocortisone was then started, with clinical benefit and gradual complete recovery of renal function.

Conclusions: These two cases highlight the need for close monitoring of CD patients on medical therapy. Although the primary goal of treatment is to normalize cortisol secretion, therapy-adjusted cortisol levels may not be sufficient in conditions that require increased physiological demand (eg stress and surgery). In this setting, patients may develop AKI as a sign of AI. Prompt discontinuation of the culprit agent, administration of intravenous hydrocortisone and fluid resuscitation, yielded full clinical and renal recovery in both patients, supporting a multimodal strategy over isolated measures.

These observations underscore the need for evidence-based, standardized protocols to guide the prevention and management of AI in Cushing patients medically treated.

Abstract citation ID: lvag096.444

P289 - ECE_1810 - Differential skeletal recovery after surgical vs medical remission in Cushing's disease: a 5-year observational study

Giacomo Voltan[1,2], Pierluigi Mazzeo[1,2], Irene Tizianel[1,2], Carlo Mogno[1,2], Giulia Bovo[1,2], Filippo Ceccato[1,2], Mattia Barbot[1,2] and Valentina Camozzi[1,2]
[1]Endocrinology Unit, University Hospital of Padova, Padova, Italy; [2]Department of medicine—DIMED, University of Padova, Padova, Italy

Background: Skeletal fragility is a major and often irreversible complication of Cushing's disease (CD). Although remission of hypercortisolism may allow partial bone recovery, long-term data comparing surgical and medical remission are scarce. In particular, whether sustained eucortisolism achieved through medical therapy results in skeletal recovery comparable to surgical cure remains unresolved.

Methods: We conducted a 5-year retro-prospective observational study including 58 patients with CD and sustained normalization of 24-h urinary free cortisol (UFC), achieved after transsphenoidal surgery (surgical remission, $n = 36$) or during long-term medical therapy (medical remission, $n = 22$). Baseline assessment was performed during active disease. Endocrine, metabolic and skeletal evaluations, including DXA-derived bone mineral density (BMD) and fragility fracture assessment, were performed at 2 and 5 years after first UFC normalization. A complete 5-year follow-up was available in 33 patients (22 surgical, 11 medical).

Results: At baseline, patients were comparable for age and biochemical severity, whereas disease duration before UFC normalization was significantly longer in medically treated patients (12 vs 1 months, $P = .001$). Lumbar spine BMD significantly increased in the overall cohort at 2 years (0.863 vs 0.830 g/cm^2, $P = .018$) and further at 5 years (0.960 vs 0.830 g/cm^2, $P = .001$). This improvement was robust and consistent in surgically cured patients at both 2 ($P = .039$) and 5 years ($P = .002$), while only a non-significant trend was observed in the medical remission group. No significant changes were detected at femoral neck or total hip in either group.

The prevalence of densitometric osteoporosis decreased from 68% at baseline to 57% at 5 years. Despite biochemical remission, incident fragility fractures occurred during follow-up (3 at 2 years and 3 at 5 years). In multivariate regression analysis adjusted for age, sex, disease duration and baseline UFC, baseline

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

lumbar spine BMD emerged as the only independent predictor of 5-year lumbar spine BMD (β = .573, $P = .002$).

Conclusions: In Cushing's disease, long-term skeletal recovery remains incomplete and strongly site-specific, predominantly affecting trabecular bone. Surgical remission is associated with a significantly greater lumbar spine BMD recovery compared with medical remission, despite sustained UFC normalization in both groups. Persistent fracture occurrence indicates that biochemical control alone does not fully restore skeletal integrity. Early diagnosis and baseline bone status critically determine long-term bone outcomes, supporting the need for prolonged skeletal surveillance and targeted bone-protective strategies, particularly in patients managed with long-term medical therapy.

Abstract citation ID: lvag096.445

P290 - ECE_2273 - Continuing imbalance in sex distribution among pediatric patients with growth hormone deficiency in Poland

Katarzyna Majewska[1], Magdalena Tchorzewska-Skrobich[1], Paulina Wais[2], Monika Naskręcka[3] and Andrzej Kędzia[1]

[1]Department of Pediatric Diabetes, Auxology and Obesity, Poznan University of Medical Sciences, Poznan, Poland; [2]Poznan, Poland; [3]Department of Applied Mathematics, Poznan University of Economics and Business, Poznan, Poland

Introduction: Short stature, by statistical definition, affects nearly 2.5% of children and therefore represents a substantial pediatric problem. Both boys and girls are diagnosed with short stature when their height falls below −2 SD appropriate for their age and sex. Consequently, similar proportions of both sexes meet these criteria. A specific group of children with short stature are those with growth hormone deficiency (GHD), as they require long-term therapy with recombinant human growth hormone (rhGH) to achieve growth improvement. Reports indicating sex disparity, with more males than females diagnosed with GHD, date back over three decades and were confirmed by numerous studies worldwide. This study aimed to investigate the current gender distribution among Polish pediatric patients with GHD compared to all children undergoing diagnostic procedures due to short stature in a single specialist center.

Methods: The study used a retrospective analysis of medical records collected between 2014 and 2024. The cohort comprised 336 children with short stature from central and western Poland, aged 3 to 17 years, who were admitted to a single specialist center for diagnostic procedures. Sex distribution was analyzed among all short stature patients, and within subgroups based on growth hormone (GH) peak levels: ≥10 ng/mL, <10 ng/mL, and <5 ng/mL.

Results: There were significantly more boys than girls among all children with short stature who underwent diagnostic procedures (66.1% vs 33.9%, respectively; $P < .001$). Similar findings, with significant male prevalence, also applied to all subgroups based on GH status: ≥10 ng/mL, <10 ng/mL, and <5 ng/mL ($P < .001$ in each subgroup). The sex distribution did not significantly differ across all analyzed subgroups. No significant differences were observed in hSDS or peak GH levels between girls and boys.

Conclusions: The prevalence of males in our study was similar across all analyzed groups, regardless of GH results, and including all patients with short stature analyzed together. Apparently, the number of boys referred for diagnostic procedures is significantly higher than the number of girls, and in consequence, proportionally more boys are diagnosed with GHD. Our observation supports the thesis that girls with short stature are generally underinvestigated, likely because of the social acceptance of girls and women being short, in contrast to boys and men. This disparity has persisted for decades, even though, according to current guidelines, girls should have the same diagnostic and treatment options as boys.

Abstract citation ID: lvag096.446

P291 - ECE_1177 - Effect of carbohydrate quality index on plasma IGF-1 levels in acromegaly patients receiving somatostatin analogue therapy

Sena Nur Demirtas[1], Fulya Calikoglu[2], Humeyra Rekalı Şahin[2], Ümmü Mutlu[2], Hulya Hacisahinogullari[2], Cemile İdiz[2], Nurdan Gul[2], Ozlem Soyluk Selcukbiricik[2], Ayse Kubat Uzum[2] and Gulsah Yenidunya Yalin[2]

[1]Department of Internal Medicine, Nutrition and Dİetetics Program, Istanbul University, Institute of Graduate Studies in Health Sciences, Istanbul, Türkiye; [2]Department of Internal Diseases Division of Endocrinology and Metabolism Disorders, Istanbul University Istanbul Faculty of Medicine, Istanbul, Türkiye

Background: Acromegaly is characterized by chronic excess secretion of growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Somatostatin analogues (SSAs) constitute the mainstay of medical treatment. Emerging evidence suggests that nutritional factors may influence IGF-1 regulation. However, studies evaluating this relationship are limited.

Objective: To investigate the effect of improving dietary carbohydrate quality, quantified by the Carbohydrate Quality Index (CQI), on serum IGF-1/upper-limit ratio (IGF-1/ULR) and metabolic parameters in acromegaly patients on stable-dose SSA treatment.

Methods: Acromegaly patients who had been receiving a stable dose of long-acting SSA treatment for at least six months were enrolled in this study (*n*: 24; M: 15, F:9). Dietary intake was assessed using a validated food frequency questionnaire, and CQI was calculated based on dietary fiber intake, glycemic index, whole-grain ratio, and solid-to-total carbohydrate ratio. Patients received a structured nutrition education program and were followed up for three months by weekly schedules regarding their nutritional intake. A total of 20 patients completed the study protocol (M:13,F:7). At the end of the nutritional intervention period CQI was recalculated. Patients were divided in two groups by median split based on final CQI (CQI ≥ 12 vs CQI <12). The change in baseline and final results of anthropometric measurements, biochemical parameters and IGF-1/ULR were compared. ΔIGF-1/ULR was defined as the change in IGF-1/ULR levels before and after the nutritional intervention. Statistical analyses included paired t-tests, Pearson correlations, and multivariable regression.

Results: CQI was improved significantly in all of the patients ($P <$ .001); characterised by higher fibre intake, lower glycaemic index, and increased whole-grain ratio ($P = .005$, $P = .007$, $P < .001$,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

respectively). Significant reductions were observed in fasting glucose, LDL and triglyceride levels ($P = .02$, $P = .03$ and $P = .01$). No significant changes were detected in IGF-1/ULR levels and ΔIGF-1/ULR levels were similar between CQI groups ($P > .05$). Total energy intake correlated positively with baseline IGF-1/ULR ($r = 0.48$, $P = .031$), and negatively with ΔIGF-1/ULR ($r = -0.53$, $P = .017$). Multiple regression analysis did not reveal independent predictors of IGF-1 change.

Conclusions: A three-month CQI-oriented dietary intervention improved carbohydrate quality and metabolic parameters; however did not produce significant effects on the change in IGF-1/ULR levels in SSA-treated acromegaly patients. Role of high CQI diets in modulating the IGF-1 axis should be investigated in larger cohorts with longer-term studies.

Abstract citation ID: lvag096.447

P292 - ECE_1639 - Volume status of patients with hyponatremia across the age span—a secondary analysis of a large prospective international study

Emanuele Varaldo[1,2,3], Laura Potasso[1,2], Julie Celine Refardt[1,2,4] and Mirjam Christ-Crain[1,2]

[1]Department of Endocrinology, Diabetology and Metabolism, University of Basel, Basel, Switzerland; [2]Department of Clinical Research, University of Basel, Basel, Switzerland; [3]Division of Endocrinology, Diabetology and Metabolism, Department of Medical Sciences, University of Turin, Torino, Italy; [4]Department of Internal Medicine, Section of Endocrinology, Erasmus Medical Center, Rotterdam, The Netherlands

Introduction: Hypotonic hyponatremia is the most common electrolyte disorder observed in hospitalized patients, with its prevalence increasing with age. It is generally classified into hypovolemic, euvolemic, and hypervolemic forms based on extracellular fluid volume status. The aim of our study was to evaluate the characteristics of volume status and the etiologies of different forms of hypotonic hyponatremia across the age span in adult patients hospitalized with hyponatremia.

Methods: This secondary analysis of a prospective, randomized, controlled, international trial (NCT03557957) included hospitalized adult patients with plasma sodium <130 mmol/L from nine European centers. Participants were classified into three age groups (<65, 65-79, and ≥80 years). At study inclusion, physicians assessed volume status as hypervolemic, euvolemic, or hypovolemic. A reassessment at the end of hospitalization provided a definitive classification based on the patient's full clinical course and hospital management. For this analysis, only patients with a documented volume status reassessment before discharge or death were included.

Results: A total of 1992 patients (F/M 1050/942, median age 73 [63-81] years) were included. Plasma sodium levels and the prevalence of profound hyponatremia did not differ across age groups ($P = .198$ and $P = .774$, respectively). Euvolemic hyponatremia ($n = 1073$) was the most prevalent across all age groups and sexes, primarily due to SIAD ($n = 853$). However, a significant difference in the distribution of volume status subtypes was observed ($P = .007$), mainly driven by a higher prevalence of hypervolemic forms in both males and females aged ≥80 years. Moreover, a higher prevalence of SIAD was observed in patients aged 65 years or older compared to younger patients ($P = .033$). In the hypovolemic subgroup ($n = 613$), the leading causes differed by age: among patients <65 years, gastrointestinal sodium losses accounted for 41.3% of cases, whereas in patients aged ≥80 years, diuretic use was the cause in nearly 50% of cases. In the hypervolemic subgroup ($n = 306$), heart failure was the leading cause, accounting for 70.3% of patients, followed by liver insufficiency (11.8%), with heart failure increasing and liver insufficiency decreasing across age groups.

Conclusions: Euvolemic hyponatremia is the most prevalent form in hospitalized patients of all age groups. It is commonly due to SIAD, which is more frequent in individuals aged 65 years or older. Moreover, the underlying causes of both hypervolemic and hypovolemic hyponatremia varies across different age groups.

Abstract citation ID: lvag096.448

P293 - ECE_2003 - Recognising the burden of acquired hypothalamic obesity in craniopharyngioma: cross-country insights from lived experiences to support integrated care across all life stages

Hanneke van Santen[1,2], Nienke Biermasz[3,4], Petra Brügmann[5,6], Michael Doelle[7,8], Hoong-Wei Gan[9,10], Cathrin E. Hansen[11], Teun Schutte[11], Tom Rouwette[12], Johan De Graaf[3,4,13], Zainaba Mohamed[14,15], Helen A. Spoudeas[16] and Hermann L Müller[17]

[1]Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands; [2]Department of Pediatric Endocrinology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands; [3]Leiden University Medical Center, Leiden, The Netherlands; [4]European Reference Network on Rare Endocrine Conditions (Endo-ERN), Amsterdam, The Netherlands; [5]Netzwerk Hypophysen- und Nebennierenerkrankungen, Fürth, Germany; [6]Endo-ERN European Patient Advocacy Group (ePAG), Amsterdam, The Netherlands; [7]Praxis Vahrenwald, Hannover, Germany; [8]MVZ Labor Krone GmBH, Bad Salzuflen, Germany; [9]Department of Paediatric Endocrinology, Great Ormond Street Hospital for Children, London, United Kingdom; [10]Genetics and Genomic Medicine Research and Teaching Department, University College London, Great Ormond Street Institute of Child Health, London, United Kingdom; [11]@teunschutte, Amsterdam, The Netherlands; [12]Rhythm Pharmaceuticals, Inc, Boston, United States; [13]Dutch Pituitary Foundation, Nijkerk, The Netherlands; [14]Department of Paediatric Endocrinology and Diabetes, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom; [15]School of Medical Sciences, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom; [16]Success Charity Life After Cure, London, United Kingdom; [17]Department of Pediatrics and Pediatric Hematology/Oncology, Carl Von Ossietzky Universität Oldenburg, Klinikum Oldenburg AöR, Oldenburg, Germany

Background: Acquired hypothalamic obesity (aHO) represents a rare, complex disease, manifesting as loss of satiety and reduced energy expenditure due to disrupted hypothalamic signalling within the melanocortin-4 receptor pathway. Clinically, aHO presents as hyperphagia, accelerated and sustained weight gain, and profound metabolic dysregulation. Childhood-onset craniopharyngioma (CO-CP), a slow growing tumour of the pituitary region, is a leading cause of aHO, with hypothalamic injury from the tumour and/or treatment causing a secondary chronic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

disease burden. Despite high survival, transition to adult care often limits access to multidisciplinary support, further reducing quality of life and increasing premature mortality. This qualitative study aimed to highlight the persistent, under-recognised health burden of aHO across life stages, drawing on the experiences of individuals with CO-CP from the Netherlands, Germany, and the UK.

Methods: Individuals with CO-CP diagnosed between 3-14 years, now aged 6-68 years, were recruited from charities/medical centres in the Netherlands ($n = 12$), Germany ($n = 11$), and the UK ($n = 10$). A mixed-methods approach combined online and in-person interviews with individuals ($n = 33$) and family members ($n = 11$), with insights from healthcare professionals ($n = 9$).

Results: Across all three countries, aHO emerged as a dominant and persistent consequence of CO-CP and/or its treatment. Reported core symptoms for aHO included weight gain (79%), fatigue and reduced stamina (76%), extreme hunger [hyperphagia] (36%), as well as other symptoms of hypothalamic dysfunction such as pituitary hormone dysfunction (100%), and visual impairment (76%). Furthermore, fear of Addisonian crises (91%), social stigma (88%), relationship struggles (82%), challenges at work/school (88%) and emotional dysregulation (64%) were reported as the most frequent daily struggles. Furthermore, despite centralised, structured paediatric care with early tertiary referral pathways across all three countries, the transition to adult care was reported as abrupt, inconsistent and fragmented with significant needs and gaps in adult follow-up.

Conclusions: The findings of this study highlight the critical importance of recognising aHO and secondary metabolic syndrome as life-limiting fundamental, long-term neuroendocrine consequences of CO-CP with a substantial impact on patients' ability to engage fully in daily life. aHO should be a primary component of CO-CP management, research, care planning, clinical guidelines, and healthcare resource allocation. Cost-effective long-term management requires bespoke pituitary-specialist care in expert centres, targeted pharmacotherapy and patient-empowered transition from paediatric to adult neuroendocrine/metabolic care, fully supported by multidisciplinary care including endocrinologists, specialised dietitians and psychologists, and neurorehabilitation specialists, essential to address the diverse physical and mental health needs of patients with aHO across the life-span.

Abstract citation ID: lvag096.449

P294 - ECE_2059 - Oral semaglutide—a novel stimulant for the hypothalamic-pituitary-adrenal axis?

Inge Nobbenhuis[1,2], Martin Bidlingmaier[3], Kevin Cj Yuen[4] and Sandrine A. Urwyler[1,2]

[1]*Endocrinology, Diabetology & Metabolism, University Hospital Basel, Basel, Switzerland;* [2]*University of Basel, Department of Clinical Research, Basel, Switzerland;* [3]*Medizinische Klinik und Poliklinik IV, Ludwig Maximilians University Munich, Munich, Germany;* [4]*Saint Joseph's Hospital & Medical Center, Barrow Pituitary Center, Phoenix, United States*

Background: Symptoms of adrenal insufficiency (AI) are often nonspecific, hence can complicate or delay its diagnosis. The insulin tolerance test (ITT) remains the gold standard for diagnosing secondary and tertiary AI, but is elaborate, uncomfortable and carries risks for patients due to insulin-induced hypoglycemia. Consequently, there is need for a safe, feasible oral test capable of accurately assessing the entire hypothalamic–pituitary–adrenal (HPA) axis. Limited evidence indicates that glucagon-like peptide-1 receptor agonists (GLP-1 RAs) can activate the HPA axis in rodents and humans. However, the effects of orally administered GLP-1 RAs, such as semaglutide, on the HPA axis have not yet been investigated.

Patients and Methods: In this randomized, placebo-controlled, double-blind, cross-over study we investigated the acute effect of a single dose 14mg oral semaglutide vs placebo on the HPA axis. During both study visits, blood and saliva samples were drawn every 15-30 minutes until 210 minutes for measurements of serum cortisol, adrenocorticotropic hormone (ACTH) and salivary cortisol levels. Delta values for each time point were calculated (eg delta serum cortisolΔ_{30min} = serum cortisol$_{30min}$—serum cortisol$_{baseline}$).

Results: Twenty male healthy volunteers were included. Median age was 27 years (IQR 24, 31) and mean body mass index 24.5 kg/m^2 (SD ±2.3). Mean baseline serum cortisol values were similar in the semaglutide group with 394 nmol/L (± 81) and the placebo group with 371 nmol/L (±75), $P = .17$. Mean delta serum cortisol levels were significantly higher at 75 min after oral semaglutide (delta serum cortisol −34.6 nmol/L (±120)) vs placebo (−103.5 nmol/L (±76)), $P = .02$, and this effect was even more pronounced at 90 min and 120 min. Delta salivary cortisol was higher at 120 min after semaglutide (0.2 nmol/L (±9.8)) vs placebo (−5.6 nmol/L (±4.7), $P = .04$). In parallel, delta median ACTH was higher after semaglutide at 75 min and 90 min with a maximal effect at 90 min (6.95 pmol/L (IQR) (−0.98; 12.15) vs placebo −3.65 pmol/L (−6.35; 0.08), $P = .01$.

Conclusions: Oral semaglutide can stimulate serum cortisol, salivary cortisol and ACTH in healthy men, and may therefore be evaluated as a novel oral stimulation test for the entire HPA axis in assessing for AI. Possible mechanisms could include co-stimulation due to the anatomical proximity of hypothalamic GLP-1 receptors to corticotropin releasing hormone producing neurons and a relative blood glucose-lowering effect of oral semaglutide.

Abstract citation ID: lvag096.450

P295 - ECE_3019 - Wolfram syndrome in adult clinical practice: a retrospective, single-center case series

Mustafa Berkay Tastekin[1], Selin Tekin[2], Nergis Basmacı[2], Suleyman Nahit Sendur[2], Selcuk Dagdelen[2] and Tomris Erbaş[2]

[1]*Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Türkiye;* [2]*Department of Internal Medicine, Division of Endocrinology & Metabolism, Hacettepe University School of Medicine, Ankara, Türkiye*

Background: Wolfram syndrome (WS) is a rare, progressive, fatal syndrome characterized by endocrinological and neurological degeneration. WS mainly caused by pathogenic variants in WFS1 gene chromosome 4p16.1. AVP deficiency, diabetes mellitus, optic atrophy, and deafness are major components. Also, many neurological, endocrinological, and systemic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

complications can occur. Although they are diagnosed in the pediatric age, they spend almost half of their lives in adulthood. In this study, we examined the clinical characteristics and real-life data of seven patients who applied to our center. Thus, we aimed to contribute to the management of the syndrome in the adult period of life.

Methods: In this single-center retrospective study, we described the clinical characteristics of seven patients diagnosed with Wolfram (DIDMOAD) syndrome who presented to our center between January 2000 and 2025.

Results: Four patients (51.7%) were female. The median age was 4 (IQR 4-5) at diagnosis and 30 (IQR 27-36) at the time of the study. Diabetes mellitus was the first component of the syndrome to appear and was present in all patients. At the time of diagnosis, three of the patients (42.9%) were diagnosed with diabetes mellitus with ketoacidosis. The median of the latest HbA1c values was 8.1% (7.6%-11.3%) and insulin doses were 1.44 (1.00-1.46) IU/kg/day. Statistical analysis of the difference between the HbA1c values at the time of diagnosis and the final HbA1c values showed no significant difference ($P = .67$). Arginine vasopressin (AVP) deficiency occurred in all patients, with a median age of 10 (IQR 4-13). The median age for the onset of visual impairment was 11 (IQR 9.5-22) and was observed in all seven patients. Hearing loss was observed in two patients; it emerged during infancy in one, and at the age of 22 in the other. Similarly, urological complications (neurogenic bladder, hydroureteronephrosis) were present in two patients developing at the ages of 19 and 28, respectively. Three of the patients (42.9%) showed widespread atrophy on brain MRI. In terms of hypopituitarism, isolated GH deficiency was found in one patient, gonadotropin deficiency in another, and a combination of both in a third patient.

Conclusions: More clinical trials in adult settings are essential for improving treatment and complication management; this will help patients lead productive lives in society once curative genetic therapies become available in the future.

Abstract citation ID: lvag096.451

P296 - ECE_3232 - The third phenotype: high preoperative serum IGF-1 imprints post-surgical discordant trajectory in acromegaly

Anna Pennlund[1], Thomas Olsson Bontell[1,2], Thomas Skoglund[3], Helena Carén[3], Gudmundur Johannsson[3], Daniel S Olsson[3] and Daniela Esposito[2]

[1]Gothenburg, Sweden; [2]Department of Endocrinology, Sahlgrenska University Hospital, Gothenburg, Sweden; [3]University of Gothenburg, Gothenburg, Sweden

Introduction: The 2024 consensus on acromegaly remission relies on biochemical concordance, yet a gray zone of discordant growth hormone (GH) and Insulin-like Growth Factor-1 (IGF-1) levels still exists. We postulate this represents a distinct "Third Phenotype"—neither cured nor classically active—and investigated the characteristics of this discordant group and biological predictors in a large single-center surgical cohort.

Methods: We performed a longitudinal analysis of 103 patients (1994-2019) treated at a dedicated Pituitary Center of Excellence. The final cohort ($n = 82$) had complete postoperative Oral Glucose Tolerance Test and IGF-1 data. Discordance was rigorously defined as one parameter (GH nadir or IGF-1) indicating remission while the other remained elevated. Phenotypic stability was tracked across three assay eras (RIA/Immulite/iSYS).

Results: Biochemical discordance manifested in 20% (16/82) of patients, predominantly as the High-IGF1/Normal-GH pattern (88%). The median age of discordant patients was 44 (range:30-75 years), 75% of discordant patients were men. Most patient (81%) presented with a macroadenoma at diagnosis of acromegaly and 47% had an invasive tumour. Hypertension was observed in 38%, and diabetes mellitus in 19% of patients. The phenotype demonstrated remarkable stability (94% retention of discordance type over a decade), arguing against transient assay variability. While tumor size and invasiveness were non-predictive, high preoperative IGF-1 was the defining predictor: median IGF-1 at diagnosis was significantly higher in discordant vs concordant-controlled patients (3.1 vs 2.5 × ULN, $P = .01$).

Conclusions: Biochemical discordance represents a stable biological entity rather than a methodological artifact. Approximately one fifth of patients exhibited postoperative discordance, most commonly elevated IGF-1 with a normal GH nadir. The majority of discordant patients had macroadenomas. Higher IGF-1 levels at diagnosis predicted postoperative discordance. These patients remain in a gray zone between remission and active disease, requiring careful and individualized follow-up.

Abstract citation ID: lvag096.452

P297 - ECE_1848 - Sellar metastases from solid tumors and hematological malignancies: a 20-year single-centre experience

Sandra Pekic Djurdjevic[1,2], Marko Stojanovic[1,2], Mirjana Doknic[1,2], Dragana Miljic[1,2], Emilija Manojlovic Gacic[1,3], Zvezdana Jemuovic[2], Ivana Cekic[2], Ivan Jevtic[2], Boris Kurcubic[2], Jelena Bajic[2], Aleksandar Stanimirovic[1,4], Vuk Scepanovic[1,4], Mihailo Milicevic[1,4], Marina Nikolic Djurovic[1,2] and Vera Popovic[1]

[1]Medical Faculty, University of Belgrade, Belgrade, Serbia; [2]Department of Neuroendocrinology, Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Center of Serbia, Belgrade, Serbia; [3]Belgrade, Serbia; [4]Clinic for Neurosurgery, University Clinical Center of Serbia, Belgrade, Serbia

Introduction: Malignant or metastatic origin of sellar–suprasellar lesions is comparatively rare. This often leads to diagnostic delays or misdiagnosis. Highly vascularised pituitary is however the most attractive intracranial site for hematogenic neoplastic dissemination.

Aims: Analysis of clinical, biochemical, hormonal and neuroradiological characteristics of sellar/suprasellar lesions representing solid tumor metastases and hematological malignancies in a large single-centre cohort.

Patients and Methods: We retrospectively analysed 1867 patients with sellar or suprasellar lesions diagnosed and treated at Department of Neuroendocrinology over a 20-year period (2005-2025).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: Twenty patients (1.07%) were identified (12 females), diagnosed at mean age of 55.7 ± 2.1years (range, 32-69). Twelve of those (60%) had solid tumor metastases, with lung cancer as predominating origin ($n = 7$; six males). Breast cancer, renal cell carcinoma, papillary thyroid carcinoma, melanoma, and cancer of unknown primary origin were each observed in one patient. Hematological malignancies accounted for 8 cases (40%), including lymphoma ($n = 4$: intravascular large B-cell lymphoma, $n = 1$; high-grade B-cell non-Hodgkin lymphoma, $n = 3$), multiple myeloma ($n = 2$), and acute leukaemia ($n = 2$). Mean age did not differ between hematological malignancies and solid tumor metastases (54.3 ± 4.0 vs 56.7 ± 2.4 years, $P > .05$). Female sex strongly predominated in hematological malignancies, (75%) while gender distribution was neutral (50:50%) in solid tumor metastases. Predominant presenting symptoms were headache (70%), visual impairment (50%), and cranial nerve palsies due to cavernous sinus infiltration (50%). Most patients (90%) had multiple anterior pituitary hormone deficiencies. AVP-deficiency was present in 35% and was isolated in one (acute myeloid leukaemia). Symptom duration was short (15-180 days). Patients with hematological malignancies commonly exhibited elevated ESR and abnormal blood counts; elevated LDH was observed in lymphoma patients. In majority (85%) of affected patients sellar/suprasellar lesion was the presenting manifestation of underlying malignancy. In three patients, primary cancer was diagnosed 3-20 years earlier. Imaging most commonly showed intrasellar mass with suprasellar extension (55%). Exclusive intrasellar or suprasellar localisation were observed in 20% each. Pituitary stalk infiltration was present in four patients, empty sella in one, and absent posterior pituitary T1-weighted hyperintensity in one patient. Surgery was performed in 35%, while 50% of patients received immunochemotherapy and/or stereotactic radiotherapy.

Conclusions: Metastatic involvement of sellar–suprasellar region should be suspected in patients with rapid symptom onset, neurological signs, pituitary dysfunction, and atypical imaging features. Surgical decompression may provide rapid symptom relief and enable diagnosis. Lung cancer metastases and hematological malignancies were the most frequent non-pituitary sellar lesions in this 20-year single-centre cohort.

Abstract citation ID: lvag096.453

P298 - ECE_2816 - Craniopharyngiomas, Clinical And Surgical Outcomes: Results Of A Single-Center Retrospective Study

Simone Antonio De Sanctis[1], Federico Valeri[2], Gianluca Trevisi[3], Antonella Giampietro[1], Rosalinda Calandrelli[4], Marco Gessi[4], Antonio D'amati[4], Ciro Mazzarella[5], Simona Gaudino[4], Mario Rigante[6], Pier Paolo Mattogno[2], Liverana Lauretti[7], Laura De Marinis[1], Francesco Doglietto[2], Antonio Bianchi[1], Sabrina Chiloiro[1] and Alfredo Pontecorvi[1]

[1]Endocrinology, Policlinico Agostino Gemelli, Roma Capitale, Italy; [2]Neurosurgery, Policlinico Agostino Gemelli, Roma, Italy; [3]Neurosurgery, Ospedale Santo Spirito, Pescara, Italy; [4]Radiology, Policlinico Agostino Gemelli, Roma, Italy; [5]Radiotherapy, Policlinico Agostino Gemelli, Roma Capitale, Italy; [6]ORL, Policlinico Agostino Gemelli, Roma, Italy; [7]Mater Olbiae, Olbia, Italy

Background: Craniopharyngioma is a rare tumor of the sellar region that causes significant clinical effects due to its proximity to critical structures such as the hypothalamus.

Patients and Methods: Data of 68 patients, followed at our center between 2003 and 2025, were retrospectively reviewed. Endocrine, cognitive, and metabolic outcomes were assessed pre- and postoperatively. The extent of resection and tumor location were evaluated by a dedicated neuroradiologist. Univariable and multivariable logistic regression identified predictors of residual tumor and recurrence/progression. Survival was assessed via Kaplan–Meier analysis.

Results: We included 22 papillary craniopharyngiomas (CPs) (13 females; 9 males) with a mean age of 52.3 years (18-82) and 46 adamantinomatous craniopharyngiomas (CAs) (18 females; 28 males) with a mean age of 46.3 years (5-74). Preoperatively, hypopituitarism, diabetes insipidus (DI), obesity, and cognitive deficits were present in 31.8%, 12.1%, 24.2% and 39.4% of patients, respectively. Surgery mostly required a transsphenoidal endoscopic approach (EEA) (45.5% CPs; 50% CAs). Gross total resection (GTR) was achieved in 47% of cases. Residual tumor occurred in 53% of patients and was strongly associated with hypothalamic infiltration (71.9% vs 33.3%, $P = .007$), pituitary stalk resection (92.9% vs 42.2%, $P = .004$), and surgical approach ($P = .039$), with EEA showing the strongest association with GTR. Papillary histotype was the only independent predictor of lower residual tumor risk (OR 0.205, $P = .019$). Surgical complications were rare, mainly hydrocephalus (CPs 2; CAs 3). Postoperatively, hypopituitarism affected 79.6%, permanent DI 54.7%, and obesity 42.2% of patients; cognitive deficits were present in 10.6%. During a mean follow-up of 62 months, recurrence/progression occurred in 40% of patients. Residual tumor ($P = .026$), surgical approach ($P = .013$), and tumor location ($P = .014$) significantly predicted progression/recurrence. Recurrence after GTR occurred earlier (mean 6.5 months), whereas progression of residuals occurred later (16.5 months) but required reoperation more frequently (72%). No variable independently predicted recurrence/progression. Seven patients (10.8%) died during follow-up, including three perioperative deaths. Mortality was strongly associated with hypothalamic infiltration ($P = .018$), postoperative cognitive deficits ($P = .003$), complications ($P < .001$), and surgical approach ($P = .002$). Survival analysis showed significantly reduced survival with non-total resection ($P < .001$), pituitary stalk preservation ($P < .001$), and non-EEA approaches ($P < .001$).

Conclusions: Tumor–hypothalamus relationship is the strongest determinant of surgical radicality, postoperative morbidity, and long-term survival. EEA offers superior resection rates and lower complication rates.

Abstract citation ID: lvag096.454

P299 - ECE_3842 - Comparative analysis of macroprolactinomas and giant prolactinomas

Monica Livia Gheorghiu[1,2], Ana-Iolanda Badita[1], Maria Anghel[1], Viorica Nicuta[1], Anda Dumitrașcu[1], Carmen Iordachescu[1], Dana Manda[1], Daniel Mihai[1], Simona Georgeta Jercalau[1] and Corin Badiu[1,2]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]CI Parhon National Institute of Endocrinology, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Introduction: Giant prolactinomas are pituitary adenomas with ≥ 4 cm in at least one diameter, usually associated with very high prolactin (PRL) levels, extrasellar extension and lower response rate to treatment.

Objective: To compare the clinical characteristics and treatment response in patients with giant prolactinomas (gPRM) vs those with macroprolactinomas (mPRM) with a maximal diameter of 1- 3.9 cm from a single center of Endocrinology.

Patients and Methods: A retrospective file review identified 66 patients, of which 33 patients with gPRM M:F = 2.3:1, median age at diagnosis 37 years (16-67) and 33 patients with mPRM M:F = 1.2:1 ($P = .04$), median age at diagnosis 38 years (13-82), P = NS.

Results: In gPRM median PRL level at diagnosis was 2509.7 ng/mL (>200 up to 31 398 ng/mL) compared to , 418.74 ng/mL (133.6 up to 11430 ng/mL), $P < .01$ in mPRM, while median of the largest tumor diameter was 5 cm (4-8.6 cm) compared to 2.1 cm (1-3.7 cm), $P < .001$. Neuro-optic abnormalities were recorded in 87.9% of gPRM and 30.3% of mPRM ($P < .001$). Pituitary insufficiency affecting at least one hormonal axis (TSH, ACTH or GH) at diagnosis was found in 72.7% of gPRM and 30.3% of mPRM ($P = .001$), global pituitary insufficiency was 21.2% in gPRM and 3% in mPRM ($P = .05$). All patients received Cabergoline (CBG) treatment. Mean initial dose of CBG was 2.1 mg/week in gPRM and 1.6 mg/week in mPRM ($P = .03$), mean maximal CBG dose was 3.5 mg/week in gPRM and 2.7 mg/week in mPRM ($P = .01$). Surgery was used in 54.5% gPRM and 18.2% mPRM ($P = .002$) (none cured after surgery), radiotherapy (RT) was used in 30.3% gPRM vs 9.1% mPRM ($P = .03$), prior Bromocriptine treatment was administered in 33.3% patients in each group. Initial PRL resistance to DA was noted in 6 gPRM (18.1%) and 7 mPRM (21.2%). RT improved the response to CAB in resistant patients in 4 gPRM and in 1 mPRM. At the last evaluation, 2 gPRM (6%) and 4 mPRM are cured (12%). From gPRM only 1 patient was not controlled after complex treatment.

Conclusions: Giant prolactinomas had higher levels of PRL and increased prevalence of hypopituitarism compared to mPRM; however, gPRM demonstrated good response to first-line dopamine agonists even in patients with optic chiasm syndrome, in a similar proportion with mPRM. Radiotherapy improved the response to dopamin agonists in resistant cases in both gPRM and mPRM. Extremely large and invasive tumors are more difficult to control overall.

Abstract citation ID: lvag096.455

P301 - ECE_2849 - "Head-to-head" lncRNAs and non-canonical DNA structures in the regulation of lineage-determining transcription factors, Foxl2 and Nr5a1

Philippa Melamed[1], Hadas Gruber[1], Gil Golan[1], Lilach Pnueli[1] and Sally Camper[2]

[1]Haifa, Israel; [2]Department of Human Genetics at the University of Michigan Medical School, Ann Arbor, United States

The gonadotrope lineage-determining transcription factors (TFs) FOXL2 and NR5A1 are essential for pituitary development and reproductive function. Pathways reported to govern their transcription in the gonads are not active in the pituitary gonadotropes, and their regulation in these cells remains poorly understood. Both protein-coding genes are located "head-to-head" with sequences transcribed divergently to long non-coding RNAs (lncRNAs). This organization is highly conserved across species for *FOXL2*, but less so for *NR5A1*. The *FOXL2*-associated lncRNAs, *FOXL2NB* in human and *Foxl2os* in mouse, are expressed in a cell-type-specific manner and show correlated expression with *FOXL2* mRNA in the human fetal pituitary and during murine postnatal gonadotrope differentiation, as well as in gonadotrope cells under various experimental conditions. Although the *Nr5a1*-associated *Nr5a1os* lacks a clear human orthologue, its expression in mouse gonadotropes is similarly coordinated with *Nr5a1* during postnatal pituitary development and in experimental cells. We therefore hypothesized that these lncRNAs might play a role in regulating their adjacent protein-coding gene or, perhaps, arise merely as by-products of divergent RNA polymerase II activity.

We examined first the polyA-tailing and subcellular localization of these lncRNAs. *Foxl2os*, but not *Nr5a1os*, was found to be chromatin-associated and not-polyadenylated, consistent with a possible *cis*-regulatory function. Moreover, functional depletion of *Foxl2os*, using RNase H-dependent antisense oligonucleotides, reduced *Foxl2* mRNA levels significantly. In contrast, knockdown of *Nr5a1os* resulted in a slower response, with reduction in *Nr5a1* expression as well as H3K4me3 at the promoter, suggesting a role in maintaining an active chromatin state. To explore further the role of *Foxl2os*, we performed **T**argeted **R**NA-directed **E**xtraction of crosslinked proteins (TREX) coupled with mass spectrometry, which identified 18 proteins associated significantly with this lncRNA, including factors involved in chromatin remodeling, transcriptional elongation, and mRNA processing.

The divergent promoter regions at both *loci* contain sequences predicted to form non-canonical G-quadruplex (G4) structures. Pharmacological stabilization of G4s with pyridostatin or their targeted resolution by DHX36, a G4-specific helicase targeted by dCas9 and gRNAs, shifted the balance between the two divergent transcripts. Most notably, G4-stabilization increased *Foxl2os* while reducing *Foxl2* mRNA levels, and its unwinding favored transcription of *Foxl2* mRNA.

These findings reveal that promoter G4 structures can affect transcriptional direction, and demonstrate that, although these lncRNA facilitate expression of their neighboring genes, their expression is not inevitably linked. Our study thus exposes novel components of the regulatory organization of the *Foxl2* and *Nr5a1* genomic loci relevant for other similarly organized lncRNA-gene pairs.

Abstract citation ID: lvag096.456

P303 - ECE_3193 - Cardiac safety of long-term cabergoline therapy in men with macroprolactinomas: a retrospective, longitudinal, echocardiographic study

Dario De Alcubierre[1,2], Tiziana Feola[1,2], Antonella Notte[3], Francesca Di Giulio[4], Luca Spagnuolo[4], Sara Palazzi[4],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Giuseppe Lembo[3], Andrea Isidori[2,5], Alessandro Landolfi[3] and Marie-Lise Jaffrain-Rea[1,4]
[1]Neuroendocrinology, Neuromed IRCCS, Pozzilli, Italy; [2]Department of Experimental Medicine, Sapienza University, Rome, Italy; [3]Cardiology, Neuromed IRCCS, Pozzilli, Italy; [4]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [5]Policlinico Umberto I, Centre for Rare Diseases, Rome, Italy

Background: Concerns about cabergoline (CAB)–associated valvular disease in prolactinoma patients have generally been mitigated by reassuring data. However, most studies included a majority of young women with microprolactinomas. Men are generally older, more frequently affected by macroprolactinomas and often requiring higher weekly CAB dose, potentially increasing cardiovascular risk, but this issue has been poorly addressed.

Objective: To assess the cardiac safety of long-term CAB therapy in men with macroprolactinomas.

Methods: A real-life, longitudinal, single-center observational study including 35 male patients referred for treatment of macroprolactinoma between January 2005 and July 2021. Clinical, biochemical, and echocardiographic data were prospectively collected for up to 18 years. Quantitative cardiac parameters were retrieved from ecochardiography performed by a single observer (AN). Cumulative CAB exposure was calculated over time and cardiac findings were analyzed according to CAB dose, treatment duration, and additional risk factors.

Results: Median age at diagnosis was 43 (IQR 30-54) and median follow-up was 122 months (87-170). Median baseline PRL and maximal tumor diameter were 2347 ng/mL (159-82 300) and 25.0 mm (13.8-58.4), respectively. CAB was the first-line treatment in 94.3% of cases, only two patients undergoing first-line surgery. At diagnosis, no patient had relevant valvular disease, but 4 (all over 60 years old) had mild mitral or aortic sclerosis. The weekly CAB dose (CABw) was titrated according to PRL response, seven patients (20%) showing partial resistance (CABw >2 mg). In responsive patients, PRL normalization was achieved with a median CABw of 1.0 mg (0.5-1.5), after a median time of 8.5 months and an overall median CAB exposure of 27.7 mg (12-67). At last follow-up, median CABw was 0.75 mg (0.5-1.0) and overall CAB exposure was 390 mg (279-713). Clinically relevant valvular regurgitation was found at last follow-up in 3 patients (8.6%) (2 aortic, 1 mitral), regardless of CABw, cumulative CAB exposure and treatment duration. In contrast, an increase in the prevalence of aortic ($n = 8$) and/or mitral ($n = 3$) sclerosis was observed, age at diagnosis being the only independent predictor (OR 1.137 per year; $P = .005$). All cases of clinically relevant regurgitation occurred in patients with valvular sclerosis at baseline or during follow-up.

Conclusions: These data suggest that long-term CAB therapy is not significantly associated with clinically relevant valve regurgitations in men with macroproactinoma. Valvular sclerosis may develop in relation with age rather than CAB regimen. Thus, regular echocardiographic monitoring remains indicated, especially in older patients or in the presence of preexisting valvular alterations.

Abstract citation ID: lvag096.457

P304 - ECE_3632 - Distinguishing primary hyperparathyroidism from IGF-I–induced changes in calcium and phosphate metabolism in acromegaly using routine biochemical markers

Cécilia Laure[1], Marie Verdoux[2], Margot Dupeux[3], Maureen Lopez[4], Anne-Lise Lecoq[1], Sylvie Salenave[1,5], Luigi Maione[1,5], Fanny Chasseloup[1,5], Pauline Romanet[6], Severine Trabado[7], Jacques Young[1,5], Isabelle Raingeard[8], Philippe Chanson[1,5] and Peter Kamenicky[1,5]
[1]AP-HP, Hôpital de Bicêtre, Service Endocrinologie et des Maladies Rares de l'Hypophyse (CRMR HYPO), Le Kremlin Bicêtre, France; [2]AP-HP, Hôpital Bicêtre, Unité de recherche clinique Paris Saclay, Le Kremlin Bicêtre, France; [3]AP-HP, Hôpital Bicêtre, Service d'anatomopathologie, Le Kremlin Bicêtre, France; [4]AP-HP, Hôpital Bicêtre, Service de Génétique Moléculaire, Pharmacogénétique et Hormonologie, Le Kremlin Bicêtre, France; [5]Université Paris-Saclay, Inserm, Physiologie et physiopathologies endocriniennes, Le Kremlin Bicêtre, France; [6]Aix Marseille Univ, APHM, INSERM, MMG, La Timone University Hospital, Laboratory of Molecular Biology GEnOPé, BIOGENOPOLE, Marseille, France; [7]AP-HP, Hôpital de Bicêtre, Service de Biochimie, Hormonologie, Pharmacotoxicologie, Le Kremlin Bicêtre, France; [8]Hôpital Lapeyronie, Service Endocrinologie-Diabétologie, Centre Hospitalier Universitaire, Montpellier, France

Background: Acromegaly is frequently associated with disturbances in calcium–phosphate metabolism, including mild hypercalcemia. These biochemical changes complicate the assessment of parathyroid function in a clinical context where the prevalence of primary hyperparathyroidism (PHPT) is increased among patients with acromegaly (approximately 6·0%). Although the coexistence of acromegaly and PHPT may occur as part of multiple endocrine neoplasia, most reported cases arise in individuals without identifiable pathogenic variants in *MEN1* or other predisposing genes. We aimed to refine the diagnosis of PHPT in acromegaly by integrating serum calcium, phosphate, and PTH concentrations into a classification model.

Methods: We conducted a retrospective diagnostic study (CEEI/IRB00003888) at two university hospitals in France. Adult patients with acromegaly evaluated between January 2013 and December 2024 were included. Eligible patients had at least one serum calcium measurement obtained while acromegaly was biochemically uncontrolled. Patients with isolated acromegaly were compared cross-sectionally with those diagnosed with PHPT. Diagnostic models were developed using support vector machine (SVM) algorithms.

Findings: A total of 396 patients with acromegaly were included, of whom 212 (54%) were women. Median age at evaluation was 43.5 years [IQR 33-55], and median IGF-I concentration was 467 ng/mL [IQR 322-655]. Isolated acromegaly was present in 372 patients (93·9%); among these, hyperphosphatemia occurred in 138 (37·1%) and mild hypercalcemia in 12 (3·2%), all of which resolved following effective treatment of acromegaly. Twenty-four patients (6·1%) had acromegaly with PHPT. All but one exhibited mild hypercalcemia (median serum calcium 2·72 mmol/L [IQR 2.66-2.86]) with elevated PTH concentrations, and low-to-normal serum phosphate. No pathogenic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

variants in *MEN1* or other tested genes were identified. Eleven patients underwent less-than-subtotal or subtotal parathyroidectomy, with normalization of serum calcium concentrations in all cases. A SVM-derived model incorporating serum calcium, phosphate, and PTH correctly classified 220 of 221 patients with complete data (99·5%; 95% CI 98.7-100). A simplified model including calcium and phosphate correctly classified 384 of 386 patients with available measurements (99·5%; 95% CI 98.8-100), with no difference in diagnostic performance between models.

Interpretation: These findings offer a practical and readily applicable diagnostic tool to refine the biochemical evaluation of hypercalcemia in acromegaly. By distinguishing IGF-I–mediated alterations in mineral metabolism from true PHPT, this approach may help avoid unnecessary parathyroid surgery and inappropriate genetic testing in patients with isolated acromegaly, while ensuring timely and appropriate referral for specialized surgical management in patients with PHPT, in whom multiglandular involvement is frequent.

Abstract citation ID: lvag096.458

P305 - ECE_1719 - High prevalence of deleterious germline variants in cancer risk genes among subjects with young-onset, sporadic pituitary macroadenomas

Adrian Daly[1], Kalyani Sridharan[2], Marie-Lise Jaffrain-Rea[3,4], Giampaolo Trivellin[5], Francesca Carbonara[4], Wouter Willem de Herder[6], Ismene Bilbao Garay[7], Reut Halperin[8], Yair Schwartz[8], Maria Segni[9], Margaret Zacharin[10], Mariana Solovey[11,12,13,14], Arancha Escribano[16], Kavita Kadian[2], Ulrich Paetow[17], Nalini Shah[18], Tushar Bandgar[18], Liliya Rostomyan[1], Amit Tirosh[8], Sebastian Neggers[6], Albert Beckers[1] and Patrick Petrossians[1]

[1]Department of Endocrinology, CHU Liège, Liège, Belgium; [2]All India Institute of Medical Sciences-Rishikesh, Rishikesh, India; [3]Neuromed Institute, Istituto di Ricovero e Cura a Carattere Scientifico, Pozzilli, Italy; [4]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [5]Department of Biomedical Sciences, Humanitas University, Milan, Italy; [6]Erasmus University Medical Center, Erasmus MC Cancer Center, Rotterdam, The Netherlands; [7]Department of Endocrinology and Nutrition, Hospital Universitario Donostia, San Sebastián-Donostia, Spain; [8]Division of Endocrinology, Diabetes and Metabolism, ENTIRE Center, Tel Aviv University, Tel Aviv, Israel; [9]Department of Maternal Infantile and Urological Sciences, University of Rome "Sapienza", Rome, Italy; [10]Royal Children's Hospital, Melbourne, Australia; [11]Instytut endokrynolohii ta obminu rechovyn im. V.P.Komisarenka NAMN Ukrainy, Kyiv, Ukraine; [12]Romodanov Neurosurgery Institute of National Academy of Sciencee, Kyiv, Ukraine; [13]Kyiv, Ukraine; [14]Romodanov Neurosurgery Institute, Kyiv, Ukraine; [15]Komisarenko Endocrinology and Metabolism Institute, Kyiv, Ukraine; [16]Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain; [17]Pediatric Endocrinology-Diabetology, Klinik für Kinder- und Jugendmedizin, University Clinic of Frankfurt, Frankfurt am Main, Germany; [18]Seth GS Medical College and KEM Hospital, Mumbai, India

Introduction: Pituitary adenomas are common intracranial tumors, clinically affecting 1:1000 individuals and most cases remain genetically unexplained. Emerging research has highlighted the major contribution of germline pathogenic variants to tumorigenesis across many tissue types in young subjects. We investigated whether young-onset (<30 years old) pituitary macroadenomas that were negative for known genetic causes harbor pathogenic or likely pathogenic (P/LP) variants in a panel of >200 cancer-risk genes.

Methods: We retrospectively analyzed 60 subjects (36 males; 95% GH- or PRL-secreting) with sporadic pituitary macroadenomas that were negative for known germline variants (*AIP, MEN1, CDKN1B*) or duplications (*GPR101*). Whole-exome sequencing (WES) was performed on germline DNA. Bioinformatics analysis including variant calling (for small variants and CNVs), annotation and variant prioritization were performed, using secondary analysis pipelines for WES data and a certified diagnostics predictor platform (AION) for tertiary analysis. Variants in established cancer-risk genes were prioritized.

Results: P/LP germline variants in 22 different cancer-risk genes were identified in 16.7% of subjects on ClinVar/ACMG criteria. This rose to 35.0% of subject with deleterious variants when additional *in silico* and AION predictor criteria were included.

Conclusions: Our findings expand the spectrum of genes potentially associated with young-onset pituitary macroadenomas. The identification of a high rate of deleterious germline variants in cancer-risk genes in pituitary adenomas echoes similar findings in young patients across a wide range of tumors affecting other organs. These results may have relevance for genetic counseling and potentially could expand targeted management strategies in young patients with large pituitary tumors.

Abstract citation ID: lvag096.459

P306 - ECE_1924 - Impact of osilodrostat on health-related quality of life in Cushing's disease: analysis of patient-reported outcomes from the Phase III LINC 3 and LINC 4 studies

John Newell-Price[1], Beverly M.K. Biller[2], Maria Fleseriu[3], Beatrice Gueron[4], Grzegorz Binowski[5], Anna Packowska[5] and Mônica Gadelha[6]

[1]The School of Medicine and Population Health, University of Sheffield, Sheffield, United Kingdom; [2]Massachusetts General Hospital, Neuroendocrine and Pituitary Tumor Clinical Center, Boston, MA, United States; [3]Pituitary Center, Departments of Medicine and Neurological Surgery, Oregon Health & Science University, Portland, OR, United States; [4]Recordati Rare Diseases, Puteaux, France; [5]MAHTA Intl Sp z o o, Warsaw, Poland; [6]Neuroendocrinology Research Center, Endocrinology Section, Medical School and Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

Introduction: Cushing's disease (CD) is a rare disorder of cortisol excess with increased morbidity and mortality risk, impacting health-related quality of life (HRQoL). Osilodrostat, an 11β-hydroxylase inhibitor, was well tolerated and effective in CD patients in the LINC 3 (NCT02180217) and LINC 4 (NCT02697734) trials. We report HRQoL outcomes in an exploratory pooled analysis of these two trials.

Methods: LINC 3: 26-week (W) open-label osilodrostat, 8W randomised-withdrawal phase, 14W open-label osilodrostat; LINC 4: 12W double-blind, placebo-controlled period, 36W open-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

label osilodrostat. Both studies included an optional extension. Mixed-effect models and paired t-tests assessed changes from baseline in Cushing's Quality of Life (CushingQoL), Beck Depression Inventory II (BDI-II) and EuroQol Five Dimensions Five Levels (EQ-5D-5L) total and domain/item scores. Minimal clinically important differences (MCIDs) were changes of: CushingQoL, 10.1 points; BDI-II, 17.5%; ED-5D-5L, 0.037-0.069. Patient data from baseline to W72 were pooled, excluding LINC 4 placebo-arm data. Data are reported as mean change from baseline unless otherwise stated.

Results: 185 patients were included (mean baseline total scores: CushingQoL, 44.0; BDI-II, 15.6; EQ-5D-5L, 0.7). CushingQoL total score significantly increased over time by: W12: 7.72, $n = 154$; W26: 11.45, $n = 160$; W48: 13.36, $n = 152$; W72: 15.32, $n = 128$ (all $P \leq .001$), reaching MCID at W26. All CushingQoL item scores significantly improved from baseline to W72 ($P \leq .05$), with largest changes in bruising, body image and irritability (W72: 0.93, 0.74 and 0.72, respectively; all $P \leq .001$); future worry, bruising and body image were most impaired at baseline. BDI-II total score significantly improved from baseline by: W12: −19.0%, $n = 154$; W26: −34.2%, $n = 160$; W48: −36.0%, $n = 153$; W72: −41.2%, $n = 128$ (all $P \leq .001$), reaching MCID at W12. All BDI-II item scores but one improved over time, with largest absolute changes at W72 in items with greatest burden at baseline (loss of energy, −0.46; sleep changes, −0.59; fatigue, −0.49; all $P \leq .001$). EQ-5D-5L utility score significantly improved from baseline after W26 by: W12: 0.02, $n = 154$; W26: 0.04, $n = 160$; W48: 0.06, $n = 153$; W72: 0.08, $n = 128$ ($P \leq .01$ for W26-72), reaching MCID at W26. Most-improved EQ-5D-5L domains at W72 were pain/discomfort (−0.42), anxiety/depression (−0.35) and mobility (−0.35; all $P \leq .001$); pain/discomfort and anxiety/depression were most impaired at baseline.

Conclusions: Osilodrostat significantly improved HRQoL, with consistent clinically meaningful, long-term improvements across all reported HRQoL instruments. Including LINC 3 placebo data may underestimate treatment effect.

Abstract citation ID: lvag096.460

P307 - ECE_1146 - Recurrent pituitary apoplexy: experience from a national registry

Betina Biagetti[1], Esteban Cordero[1], Pedro Iglesias[2], Rosa Camara-Gómez[3], Queralt Asla[4], Almudena Vicente[5], Elena Martinez-Saez[1], Silvana Isabel Sarria Estrada[1], Manel Puig-Domingo[6] and Marta Araujo Castro[7]
[1]Hospital Universitario Vall d'Hebron, Barcelona, Spain; [2]Hospital Puerta de Hierro, Madrid, Spain; [3]Hospital la Fé de Valencia, Valencia, Spain; [4]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [5]Hospital UNiversitario de Toledo, Toledo, Spain; [6]Hospital Germans Trias i Pujol, Badalona, Spain; [7]Hospital Universitario Ramón y Cajal., Madrid, Spain

Background and Objective: Pituitary apoplexy (PA) is a neuroendocrine emergency characterized by acute hemorrhage or infarction of a pituitary adenoma. While initial presentation and management are well-documented, data on recurrent PA remain scarce.

Methods: We analyzed 274 patients from the Spanish Pituitary Apoplexy Registry (2010-2023) with complete follow-up data. Recurrent PA was defined as a new acute episode with radiological evidence of new hemorrhage or infarction in a previously affected lesion. A systematic literature review complemented registry findings.

Results: Recurrent PA was identified in 9 patients (3.3%), of which 6 of 214 had non-functioning adenomas (2.8%) and 3 of 60 with functioning adenomas (5.0%). Patients with recurrence had significantly larger tumors (median 35 vs 25 mm, $P = .006$), higher rates of cavernous sinus invasion (77.9% vs 37.3%, $P = .006$), and more frequent prior cabergoline treatment (33.3% vs 6.3%, $P = .020$) compared to non-recurrent cases. Median time to recurrence was 18 months (range 2-108). Literature review identified 11 studies reporting recurrence rates of 2.6-16.7%, with larger series ($n \geq 50$) showing rates of 4-9.6%. All of them had favorable clinical course and recovery.

Conclusions: Recurrent PA is uncommon, affecting only 3% of patients with prior PA. It is associated with larger tumor size, cavernous sinus invasion, and dopamine agonist therapy. The second episodes were not more severe than the initial event, and overall prognosis was favorable. The association between dopamine agonist therapy and recurrence, observed in both prolactinomas and nonfunctioning adenomas, warrants further investigation.

Abstract citation ID: lvag096.461

P309 - ECE_2276 - Pituitary metastases: a case series

Jowita Fiszer[1,2], Magdalena Guzek[1,2], Barbara Buchalska[3], Sonia Kaniuka-Jakubowska[1,2], Wiesława Grajkowska[3], Maria Maksymowicz[4], Anna Lewczuk[1,2], Jacek Kunicki[3] and Renata Świątkowska-Stodulska[1,2]
[1]Department of Endocrinology and Internal Medicine, Medical University of Gdansk, Gdańsk, Poland; [2]Department of Endocrinology and Internal Medicine, University Clinical Centre (UCK), Gdańsk, Poland; [3]Department of Neurosurgery, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [4]Department of Cancer Pathomorphology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background: Pituitary metastases are rare lesions in this region; their exact incidence has not been clearly determined, although it is estimated at approximately 0.5%. However, given the increasing incidence of neoplastic diseases, a gradual rise in the number of diagnoses can be expected.

Purpose: The aim of this study is to present a series of cases of pituitary metastases, with particular emphasis on their clinical manifestations and their relevance in the differential diagnosis of lesions in the pituitary region.

Methodology: The presented case series includes 18 patients: 12 patients were hospitalized in Maria Sklodowska-Curie National Research Institute of Oncology and 6 were hospitalized at the University Clinical Center in Gdańsk between 2008 and 2025. In 4 patients from the University Clinical Center in Gdańsk, the diagnosis was based on clinical and radiological findings, and radiotherapy targeting the pituitary gland and brain was administered; however, no histopathological confirmation of the lesion was obtained.

Results: In 9 patients, the primary malignancy had been previously diagnosed and treated prior to admission, whereas in the remaining cases, the metastasis manifested for the first time as

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

a parasellarmass. The mean age at metastasis diagnosis was 61. The primary origin of pituitary metastases included lung cancer ($n = 7$), breast cancer ($n = 6$), renal cell carcinoma ($n = 1$), prostate carcinoma ($n = 1$), and hepatocellular carcinoma ($n = 1$). In three patients the primary of metastases was not identified. The main clinical symptoms were neurological and visual disturbances. Three patients presented symptoms of diabetes insipidus prior to neurosurgical intervention.

Conclusions: Although pituitary metastases are rare, they should be considered in the differential diagnosis of lesions in this region, particularly in patients with a history of malignancy. Importantly, a pituitary metastases are not a manifestation of end-stage disease—it may also be the first clinical presentation. The analyzed case series only suggest that diabetes insipidus is not an obligatory symptom, and nonspecific neurological complaints often predominate. It should be emphasized that the actual incidence of pituitary metastases may be underestimated, as biopsies in this region are not always performed and therefore the definitive diagnosis is not always established.

Keywords metastasis, pituitary gland, pituitary metastases

Abstract citation ID: lvag096.462

P311 - ECE_3667 - Proteomic analysis of GH-secreting and non functioning pituitary adenomas

Francesco Ferraù[1], Francesca Polito[2], Laura Licitri[2], Luca Bini[3], Laura Bianchi[3], Elena Sofia Blanca[4], Giordana Siracusano[4], Carla Paola Costa[4], Rossana De Salvo[3], Alfonso Carleo[5], Lorenza Vantaggiato[6], Enxhi Shaba[3], Filippo Flavio Angileri[7], Marta Ragonese[8], Oana Ruxandra Cotta[4], M'hammed Aguennouz[2] and Salvatore Cannavò[9]

[1]Department of Human Pathology of Adulthood and Childhood, University of Messina, Messina, Italy; [2]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; [3]Department of Life Science, University of Siena, Siena, Italy; [4]Endocrine Unit, University of Messina, Messina, Italy; [5]University of Siena, Siena, Italy; [6]Department of Life Science, University of Siena, Messina, Italy; [7]Department of Biomedical and Dental Sciences, and Morpho-Functional Imaging, University of Messina, Messina, Italy; [8]Department of Human Pathology of Adulthood and Childhood DETEV, University of Messina, Messina, Italy; [9]Department of Human Pathology, University of Messina, Messina, Italy

Pituitary neuroendocrine tumors (PitNETs), are generally benign neoplasms and encompasse both hormone-secreting and non-functioning lesions. Their marked clinical and biological heterogeneity, together with the limited availability of validated biomarkers, complicates early diagnosis, prognostic evaluation, follow-up strategies, and therapeutic management.

In this study, we performed a comparative proteomic analysis of growth hormone–secreting pituitary adenomas (GH-Pnets), non-functioning pituitary adenomas (NFPnets), and normal pituitary tissue.

Despite inter-patient variability, distinct proteomic differences were consistently observed between GH-Pnets, NFPnets, and controls. Functional annotation of differentially expressed proteins highlighted alterations in pathways related to cell adhesion, glycolytic metabolism, and oxidative stress responses. Notably, a substantial proportion of the identified proteins were associated with mitochondrial function, suggesting dysregulation of cellular energy metabolism and impaired protection against oxidative stress. In detail, SOD enzymes were overexpressed in GH-Pnets as compared to NFPnets.

Overall, our findings provide insight into subtype-specific proteomic features of PitNETs and support the relevance of metabolic and mitochondrial pathways in pituitary tumor biology, potentially offering a basis for the identification of clinically meaningful biomarkers and novel therapeutic targets.

Abstract citation ID: lvag096.463

P312 - ECE_3726 - Arginine vasopressin deficiency, is that all?

Emma Capparelli[1], Elisabetta Sciarroni[1], Silvia Canovetti[2], Giulia Marconcini[1], Maurizio Carbonari[1], Alessio Basolo[1], Claudio Urbani[1], Mirco Cosottini[2], Antonio Tavoni[3], Luca Manetti[1], Ferruccio Santini[1] and Isabella Lupi[1]

[1]Department of Clinical and Experimental Medicine, Unit of Endocrinology 1, Pisa University Hospital, Pisa, Italy; [2]Neurordiology Unit, Universitary Hospital of Pisa, Pisa, Italy; [3]Clinical Immunology Unit, Pisa, Italy

Background: Hypophysitis includes a broad range of chronic inflammatory disorders involving the anterior and/or the posterior lobe of the pituitary gland. Neuro-hypophysitis (NH) can manifest clinically with arginin-vasopressin defect (AVP-d) and radiologically with pituitary stalk thickening at MRI. There are primary (autoimmune) forms of NH, where the cause is unknown, and secondary forms, where an initiating event is identifiable. However, MRI or serological findings are not specific and pathology from a stalk lesion is rarely obtained, thus etiology is often not immediately apparent. AVP-d can indeed precede for years diagnosis of systemic infiltrative disease.

Aim of the Study: Determine the prevalence of secondary NH in a cohort of patients with AVP-d.

Patients and Methods: A retrospective review of patients diagnosed with AVP-d and MRI pituitary stalk thickening, from 2008 to 2024, at Pisa Endocrinology Unit, was conducted. Mean follow-up was 8 years (range 1-20). Results Twenty-eight patients were included: 19 females (F), 9 males (M), age at diagnosis 45 + 17 and 38 + 19 years, respectively. Duration of polyuria/polydipsia was less than 12 months in 20 patients (68%) and up to 48 months in 3 (10%). Secondary NH was found in 15 (53%). Five (33%), were diagnosed simultaneously with AVP-d and a systemic disease: 3 IgG4-related disease (mean age 32 years, 2F, 1 M), 2 Erdheim Chester disease (mean age 70 years, 1M, 1F). Ten (67%), were diagnosed during follow-up: 2 F (mean age 70 years) manifested Erdheim-Chester disease, and 7 (5 F, 2 M, mean age 37 years) manifested Langerhans cells histiocytosis. Partial hypopituitarism, mainly hypogonadism, was found in 10 (66%). Overtime, pituitary stalk thickening disappeared in 8 (53%), AVP-d persisted in all. The remaining 13 patients (46%; 8 F, 5 M mean age 43 + 16) did not develop other clinical manifestations thus were diagnosed as primary NH. Partial hypopituitarism, mainly hypogonadism, was found in 5 (38%). Pituitary stalk thickening spontaneously reduced in 8 (62%), AVP-d persisting in all patients except one.

Conclusions: Careful clinical evaluation and prolonged follow-up are needed to establish the etiology of NH. AVP-d is persistent

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

in both primary and secondary NH even when pituitary stalk thickening regresses.

Abstract citation ID: lvag096.464

P314 - ECE_2051 - Crooke's cell corticotroph adenoma or metastatic carcinoma? A different perspective of pitNETs: a case report

Ece Seçgin Demir[1], Nevra Karademir[2], Serhat Özçelik[1], Hande Erman[2], Naile Gokkaya[1], Ziya Mithat Bıyıklı[1], Meryem Özoğlu[1], Müge Yılmaz[1], Senem Boz Aksoy[1], Sevinç Keser[3], Mehmet Tiryaki[4], Özcan Keskin[2] and Kadriye Aydin[1]

[1]Department of Endocrinology and Metabolism, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye; [2]Department of Internal Medicine, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye; [3]Department of Pathology, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye; [4]Department of Neurosurgery, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye

Objective: Crooke's cell adenomas (CCA)/pitNETs (pituitary neuroendocrine tumours) are very rare and aggressive forms of corticotroph pitNETs causing Cushing's disease. They are associated with a low response to surgery and/or radiotherapy, but they rarely metastasize. Given the rarity of Crooke cell pitNETs, we aimed to present a case with a crooke cell pathology in pituitary surgery, who was observed to have a devastating clinical features and distant organ metastasis.

Results: A 60-year-old female patient with a history of pituitary surgery and a Cushingoid appearance was found to have a pitNET and laborotary results consistent with Cushing's disease. There is no evidence for distant organ metastasis in FDG PET-CT imaging. The patient, whose initial surgical pathology was a Crooke's cell adenoma/pitNET, underwent a second transsphenoidal surgery. As remission could not be achieved, another surgery was recommended, but the patient declined. The patient underwent stereotactic radiotherapy with a CyberKnife device at 30 Gy in 5 fractions. As remission was still not achieved, cabergoline, ketoconazole, and metyrapone treatments were initiated, but due to side effects, all treatments except metyrapone were discontinued. A decision was made to perform bilateral adrenalectomy. Preoperative CT and FDG PET-CT images revealed lesions consistent with metastasis in the liver, the biopsy result from the suspected metastatic lesions in the liver was consistent with tumor infiltration containing ACTH-positive neuroendocrine features. The patient declined further investigation and discontinued follow-up at our center.

Conclusions: Although Crooke's cell pitNETs are rare, they are aggressive. Treatment response may not be achieved after repeated surgeries and/or radiotherapy, or the disease may recur. As far as we know, less than 10 cases of CCA with distant organ metastasis have been described in the literature. The time to metastasis has been observed to be defined in years. In our case, liver metastases was observed 18 months after the first operation, and two FDG PET-CT scans taken 9 months apart revealed that a lesion that could be described as an adenoma 9 months earlier had transformed into metastatic carcinoma. We are introducing our case of aggressive Crooke's cell pitNET, which metastasized quite rapidly, to the literature.

Keywords Crooke's cell pitNET, Cushing disease, liver metastasis

Abstract citation ID: lvag096.465

P315 - ECE_2127 - Hypertonic saline test induces significant electrolytic alterations

Michela Sibilla[1], Nunzia Prencipe[1], Emanuele Varaldo[1], Iulia Petria[2], Gianluca Aimaretti[1], Silvia Grottoli[1], Giovanna Mantovani[2], Emanuele Ferrante[3], Valentina Gasco[1] and Alessandro Maria Berton[1]

[1]Division of Endocrinology, Diabetology and Metabolism, Medical Sciences Department, University of Turin, Turin, Italy; [2]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico; Department of Clinical Sciences and Community Health, Dipartimento di Eccellenza 2023-2027, University of Milan, Milan, Italy; [3]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Background: The hypertonic saline test (HST) is the new gold standard for the differential diagnosis of polyuria–polydipsia syndrome (PPS), strongly stimulating AVP secretion by increasing plasma osmolality (p-Osm). Transient hyperkalemia has been reported during HST, possibly due to an osmotic drive ("solvent drag") in Na/K balance or to hypertonic saline-induced hypercloremic metabolic acidosis that causes a shift of K from the *intra* to the *extra* cellular fluid. Other electrolytic alterations, however, have not been assessed. The aim of this study was therefore to describe possible electrolytic alterations occurring during HST.

Methods: Thirty-nine patients (28 F; age 38 [31-53] years; BMI 23.4 [21.8-26.1] Kg/m^2) with PPS ($n = 24$) or a previous diagnosis of AVP-deficiency (AVP-D, $n = 15$) underwent HST between 12/2023 and 12/2025 at two tertiary centers in Northern-Italy. Serum Na, K, Ca, glucose, copeptin, p-Osm and pH levels were measured at baseline and upon achieving hypernatremia (Na >149 mmol/L) via 3% saline bolus (250 mL at 500 mL/h) followed by continuous infusion (9 mL/Kg/h).

Results: As expected, HST induced significant increases in Na (140 [138-143] vs 150 [150-152] mmol/L, $P < .0001$), p-Osm (284 [281-289] vs 305 [298-318] mOsm/Kg, $P < .0001$) and copeptin concentrations (2.2 [1.7-2.9] vs 9.9 [2.8-26.4] pmol/L, $P < .001$). Glucose levels remained unchanged. K levels significantly increased (3.9 [3.8-4.0] vs 4.4 [4.1-4.6] mmol/L, $P < .001$) and two cases of hyperkalemia were observed (K = 6.1 and 5.7 mmol/L). Ca levels decreased significantly, both by blood gas analysis (1.22 [1.16-1.24] vs 1.14 [1.11-1.16] mmol/L, $P < .001$) and in the subset with total serum Ca measured (2.31 [2.22-2.33] vs 1.95 [1.92-2.01] mmol/L, $P = .028$), all developing mild to moderate hypocalcemia by the end of the test. Notably, pH levels remained stable (7.38 [7.34-7.39] vs 7.35 [7.33-7.36], $P = .127$).

Conclusions: This study demonstrates, in addition to the expected increase in K, also a significant decrease in Ca. This likely reflects increased urinary Ca excretion, as hypercalciuria commonly follows NaCl-induced natriuresis. Although modest, these changes underscore the importance of assessing baseline electrolyte status before HST. Additionally, ECG monitoring should be considered following the procedure in cases where significant electrolyte disturbances occur in response to HST.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.466

P316 - ECE_2696 - Elevated risk of hip fractures in patients with Cushing's syndrome

Hiba Masri Iraqi[1], Yaron Rudman[1], Tzipora Shochat[2], Shiri Kushnir[3], Keren Kaminer[1], Idit Dotan[1], Gloria Tsvetov[1], Ilan Shimon[1], Maria Fleseriu[4] and Amit Akirov[1]

[1]Institute of Endocrinology, Beilinson Hospital, Rabin Medical Center, Petah Tiqva, Israel; [2]Biostatistics Unit, Rabin Medical Center, Beilinson Hospital, Petah-Tiqva, Israel; [3]Research Authority, Rabin Medical Center, Beilinson Hospital, Petah-Tiqva, Israel; [4]Pituitary Center, Departments of Medicine and Neurological Surgery, Oregon Health & Science University, Portland, OR, United States

Background: Glucocorticoid-induced osteoporosis is a common complication of Cushing's syndrome (CS). While the increased risk for vertebral fractures is well-established, evidence regarding hip fracture risk are limited. This study investigates the association between endogenous CS and hip fracture risk and examines the effect of remission on this risk.

Methods: A nationwide retrospective matched-cohort study was conducted using the Clalit Health Services database in Israel, including patients diagnosed with endogenous CS between 2000 and 2023. Patients with CS were matched 1:5 with controls based on age, sex, socioeconomic status, and body mass index. The primary outcome was the first diagnosis of hip fractures following the diagnosis of CS. Patients with a history of hip fractures prior to CS diagnosis were excluded.

Results: The study included 606 patients with CS and 2988 matched controls, with a mean age at diagnosis of 47.8 ± 17.14 years; 65.3% were female. Follow-up durations were 13.2 ± 6.1 years for patients with CS and 13.1 ± 6.2 years for controls. The risk of hip fracture was significantly higher in patients with CS compared to controls (3.9% vs 2.5%, HR 1.54, 95% CI 1.0-2.5). The risk was significantly elevated among patients with a pituitary source of CS (HR 2.2, 95% CI 1.0-4.7) but not in those with an adrenal source (HR 1.3, 95% CI 0.6-2.8). Analysis by remission status showed that hip fractures occurred in 4.4% of patients without remission and 3.6% of those in remission, with no significant difference between groups (HR 1.1, 95% CI 0.4-3.0).

Conclusions: Patients with CS, especially those with Cushing's disease, have an increased risk of hip fractures.

Abstract citation ID: lvag096.467

P317 - ECE_2868 - Arginine vasopressin deficiency—a single center retrospective analysis from the endocrinological perspective

Mustafa Berkay Tastekin[1], Burcin Gonul Iremli[2], Selin Tekin[2], Suleyman Nahit Sendur[2], Seda Hanife Oguz[2], E. Nazlı Gönç[3], Rahşan Göçmen[4], Figen Söylemezoğlu[5], Selcuk Dagdelen[2] and Tomris Erbaş[2]

[1]Internal Medicine, Hacettepe University School of Medicine, Ankara, Türkiye; [2]Department of Internal Medicine, Division of Endocrinology & Metabolism, Hacettepe University School of Medicine, Ankara, Türkiye; [3]Department of Pediatrics, Division of Pediatric Endocrinology, Hacettepe University School of Medicine, Ankara, Türkiye; [4]Department of Radiology, Hacettepe University School of Medicine, Ankara, Türkiye; [5]Department of Pathology, Hacettepe University School of Medicine, Ankara, Türkiye

Background: Arginine vasopressin deficiency (AVP-D) is a rare hypothalamus and/or posterior pituitary disorder due to deficient AVP secretion, causing hypotonic polyuria and polydipsia. The aim of this study is to describe the distinctive characteristics of the various etiologies of AVP-D from a single center.

Methods: We retrospectively reviewed 181 patients with confirmed AVP-D who followed up at the Hacettepe Medical School, between 1980 and 2024. Demographic data, symptoms, hormonal profile, imaging findings, treatment response and prognosis were retrieved. The study was approved by Ethics Committee.

Results: The cohort included 181 patients (104 F/ 77 M) with a median age at diagnosis of 22 (12.0-37.5) years and a median follow-up of 9 years (3-18). The average duration from the onset of symptoms to diagnosis was one year (79%). In 8.8% of the patients, the diagnostic delay was longer than 4 years. In the cohort, 36 diseases causing AVP-D were divided into 7 etiological groups. The most common etiologies were CNS neoplasia (24.3%, $n = 44$), consequence of neurosurgery (19.9%, $n = 36$) and histiocytosis—Langerhans cell histiocytosis and Erdheim Chester disease—(18.8%, $n = 34$). Other causes of AVP-D included idiopathic (16.0%, $n = 29$), hereditary (8.3%, $n = 15$) and autoimmune (7.2%, $n = 13$). Head trauma, radiotherapy and apoplexy was observed in 5.5% ($n = 10$) of cases. Hypopituitarism were identified in 71.3% ($n = 129$) of patients; 55.2% had GH deficiency, 49.2% secondary hypothyroidism, 45.9% hypogonadotropic hypogonadism, 39.8% secondary hypocortisolism and 12.2% hypoprolactinemia. At the time of diagnosis, 37.1% of the patients had hypernatremia, there was no significant difference between the groups. Thirteen patients had sodium levels above 150 meq/L. Diabetes mellitus was initially considered in 11 patients (6.1%) due to symptoms of polyuria and polydipsia. Significant differences were found between etiology groups in terms of pituitary gland size, infundibulum thickening, and optic tract involvement ($P < .001$, $<.001$ and $<.02$, respectively). In MRI, bright spots, which are not expected to be seen in AVP-D, were found in 17% in patients. Forty one patients who underwent water restriction testing, 7 (17%) of them had bright spots. There was no significant difference in the presence of bright spots between the first and last MRI during the follow-up. No difference in desmopressin dose was observed between the groups.

In summary, maintaining a wide differential diagnosis is critical when assessing AVP-D to avoid overlooking rare causes. Our study highlights that identifying the underlying cause and assessing for concurrent pituitary deficiencies are essential when managing patients with AVP-D.

Abstract citation ID: lvag096.468

P320 - ECE_1295 - Limited utility of cluster analysis in polycystic ovary syndrome for defining clinically meaningful subtypes and case–control discrimination in unselected populations

Asmamaw Bizuneh[1], Chau Thien Tay[1,2], Arul Earnest[3], Raja Ram[1], Sylvia Kiconco[1], Ricardo Azziz[4], Larisa Suturina[5], Xiaomiao Zhao[6], Alessandra Gambineri[7], Fahimeh Tehrani[8], Bulent Yildiz[9], Jin Ju Kim[10], Liangzhi Xu[11], Christian Makwe[12], Anju Joham[1,2] and Helena Teede[1,2]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Monash Centre for Health Research and Implementation, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Australia; [2]Department of Endocrinology and Diabetes, Monash Health, Clayton, Melbourne, Australia; [3]School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia; [4]Departments of Obstetrics and Gynecology, and Medicine, University of Alabama at Birmingham, Birmingham, AL, United States; [5]Department of Reproductive Health Protection, Scientific Center for Family Health and Human Reproduction Problems, Irkutsk, Russia; [6]Department of Reproductive Medicine, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China; [7]Department of Medical and Surgical Science-DIMEC, Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [8]Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [9]Division of Endocrinology and Metabolism, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Türkiye; [10]Division of Reproductive Endocrinology, Department of Obstetrics and Gynecology, Healthcare System Gangnam Center, Seoul National University Hospital, Seoul, South Korea; [11]Department of Obstetrics and Gynecology, West China Second University Hospital, Sichuan University, Chengdu, China; [12]Department of Obstetrics and Gynaecology, College of Medicine, University of Lagos, Lagos, Nigeria

Background: The diagnosis of polycystic ovary syndrome (PCOS) is controversial, historically based on common features in selected populations. Advanced analytics offers opportunities to cluster features to better define PCOS. The main objective of this study was to explore what features clearly differentiated PCOS from controls and clustering criteria thresholds using the PCOS Phenotype in Unselected Populations (P-PUP) dataset.

Methods: The study was conducted in an internationally diverse, well-characterized, and harmonized cohort from unselected populations. Unsupervised k-means cluster analysis (k = 3) was conducted using robustly selected clinical features, including body mass index (BMI), modified Ferriman-Gallwey (mFG) score, androgen measures (total testosterone [TT], free androgen index [FAI], and dehydroepiandrosterone sulfate [DHEAS]), menstrual characteristics (menstrual cycle length in days and menstrual cycle per year), antral follicle counts, lipid profiles (total cholesterol, high density lipoprotein, and triglyceride), and systolic and diastolic blood pressure. We characterized the distribution of clinical features within the clusters to differentiate groups.

Results: This analysis included 1651 reproductive-aged women. Considering the entire population together, we were able to generate three distinct clusters: the hyperandrogenic cluster (34.2%), including women with higher mFG score, TT, FAI, androstenedione, and ovarian volume, the metabolic cluster (32.1%) with higher age, BMI, waist circumference, insulin, and blood pressure, and the healthier cluster (33.7%) having higher SHBG levels coupled with lower BMI and waist circumference. The hyperandrogenic and metabolic clusters encompassed 87.2% of PCOS women diagnosed with PCOS, but did not clearly distinguish cases from controls in population-based analysis.

Conclusions: The P-PUP study, utilizing an ethnically diverse unselected population, identified three clusters in the general population, but did not clearly distinguish cases from controls. These findings highlight the challenge of clustering on clinical and biochemical features alone in PCOS and more broadly, such as in type 2 diabetes mellitus. This indicates the need to integrate clustering with genetic markers, undertake predictive and longitudinal modelling, and consider alternative personalised medicine approaches, such as risk prediction, to advance clinical utility.

Abstract citation ID: lvag096.469

P321- ECE_1361 - Reduced circulating and skeletal muscle MOTS-c expression in women with polycystic ovary syndrome: evidence for disrupted mitochondrial-derived peptide regulation

Irem Sonmezoglu Kutuk[1], Senay Akın[2], Ali Haydar Demirel[3], Sezcan Mumusoglu[4], Turkmen Turan Ciftci[5] and Bulent Yildiz[6]

[1]Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Türkiye; [2]Division of Exercise and Sport Physiology, Hacettepe University Faculty of Sport Sciences, Ankara, Türkiye; [3]Center for Sport Sciences, Near East University, Nikosia, Cyprus; [4]Department of Obstetrics and Gynecology, Hacettepe University Faculty of Medicine, Ankara, Türkiye; [5]Department of Radiology, Hacettepe University Faculty of Medicine, Ankara, Türkiye; [6]Division of Endocrinology and Metabolism, Hacettepe University Faculty of Medicine, Ankara, Türkiye

Background: Polycystic ovary syndrome (PCOS) is characterized by insulin resistance and metabolic dysfunction, Mitochondrial-derived peptides (MDPs), specifically MOTS-c, have recently been identified as potent regulators of glucose homeostasis and skeletal muscle metabolism. Whether MOTS-c expression is altered in PCOS across different physiological compartments is unknown.

Objective: To assess circulating and skeletal muscle MOTS-c levels in women with PCOS and to examine their associations with metabolic and hormonal parameters.

Methods: Forty women with PCOS and 40 age- and BMI-matched healthy controls underwent detailed clinical, biochemical, and hormonal phenotyping. Serum MOTS-c concentrations were quantified by ELISA. In a representative subgroup, skeletal muscle MOTS-c expression was determined from vastus lateralis biopsy specimens using Western blotting.

Results: Women with PCOS exhibited lower circulating MOTS-c concentrations compared with controls (220.2 ± 147.6 pg/mL vs 498.3 ± 224.4 pg/mL, $P < .001$). Skeletal muscle MOTS-c expression was also reduced in the PCOS group (74.2 ± 15.2 vs 100.0 ± 8.5 arbitrary units; $P = .005$). Serum MOTS-c levels were inversely associated with total testosterone ($r = -0.224$, $P = .046$) and total cholesterol ($r = -0.228$, $P = .044$), with additional inverse trends observed for 2-hour insulin during oral glucose tolerance testing, triglycerides, and LDL cholesterol.

Conclusions: Women with PCOS display reduced MOTS-c expression in both the circulation and skeletal muscle, indicating impaired availability of this mitochondrial-derived peptide. The associations with hyperandrogenism and lipid profiles suggest a link between altered mitochondrial peptide biology and the endocrine–metabolic phenotype of PCOS. These findings identify MOTS-c as a novel marker of tissue-specific mitochondrial involvement in PCOS and warrant further mechanistic and therapeutic exploration.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.470

P322 - ECE_3313 - The gonadotrophin response to kisspeptin administration reveals hypothalamic dysfunction in obesity-related hypogonadism in men

Kanyada Koysombat[1,2], Patrick McGown[1,2], Arthur Yeung[1], Agathoklis Efthymiadis[1,2], Sandhi Nyunt[1,2], Maria Phylactou[1,2], Megan Young[1], Bijal Patel[1,2], Elisabeth Daniels[1,2], Aureliane Pierret[1,2], Aaran Patel[1,2], Jovanna Tsoutsouki[1,2], Margarita Solodovnikoff[1], Folakemi Olujimi[1], Edouard G Mills[1,2], Anna Kowalka[1], Chioma Izzi-Engbeaya[1,2], Tricia Tan[1,2], Alexander Comninos[1,2], Ali Abbara[1,2] and Waljit Dhillo[1,2]
[1]*London, United Kingdom;* [2]*Department of Endocrinology, Imperial College Healthcare NHS Trust, London, United Kingdom*

Background: Male obesity-related secondary hypogonadism (MOSH) affects over half of men with BMI ≥ 40 kg/m^2, exacerbating morbidity and mortality. Animal models suggest decreased hypothalamic function in obesity-related hypogonadism. Kisspeptin enables direct examination of hypothalamic dysfunction in men with obesity.

Methods: We enrolled men with obesity (BMI ≥ 30 kg/m^2, $n = 35$), and healthy eugonadal men without obesity ($n = 97$). Men with obesity with symptoms of hypogonadism and fasting free testosterone ≤0.22 nmol/L were subcategorised as MOSH ($n = 7$). Endocrine profiling included LH-pulsatility assessment (10-minutely sampling for 8 hrs), responses to intravenous bolus of kisspeptin and GnRH to interrogate hypothalamic and pituitary function, respectively. Hormone concentrations were compared using Kruskal-Wallis test, and temporal endocrine profiles using mixed-effects models.

Results: Men with MOSH had higher BMI than age-matched eugonadal men with obesity (BMI 49.0 vs 34.1 kg/m^2). In addition to lower total (5.55 vs 12.93 nmol/L; $P < .0001$) and free testosterone (0.15 vs 0.31 nmol/L; $P < .0001$), men with MOSH had lower DHT 0.43 vs 0.90 nmol/L, AMH 15.0 vs 37.9 pmol/L, inhibin B 81.53 vs 156.30 ng/L (all $P < .0001$); whilst oestradiol was higher 147.3 vs 116.7 pmol/L ($P = .0038$). Total testosterone ($\beta = -.48$), free testosterone ($\beta = -.01$), and dihydrotestosterone ($\beta = -.04$) were inversely associated with BMI ($P < .0001$). Median LH pulse-frequency was increased with obesity: (BMI < 25.0 kg/m^2: 3.00 vs >40 kg/m^2: 5.00) pulses per 8 h ($P = .0004$). LH pulse-amplitude and GnRH responses did not differ. Men with obesity had augmented gonadotrophin response to kisspeptin than controls ($P < .0001$). The maximum LH-response to kisspeptin was delayed in MOSH compared to controls 315 vs 270 mins ($P = .0055$). Whilst the total area-under-the-curve (AUC) of LH rise over 6 hrs after kisspeptin did not differ, the early-phase LH rise over 1 hr was blunted in MOSH (median AUC at 60 mins: MOSH 28.4 vs lean controls 126.4 IU·h/L ($P < .0001$) vs eugonadal men with obesity 89.9 IU·h/L ($P = .0076$).

Conclusions: In contrast to existing reports, our data demonstrated an increase in LH pulse-frequency with obesity rather than a reduction in pulse-amplitude. Men with obesity had an increased response to kisspeptin consistent with decreased endogenous hypothalamic function. Notably, the LH rise after kisspeptin was delayed in men with MOSH resulting in a decreased early phase response. Pituitary responses to GnRH were preserved. Our data provides first evidence that hypothalamic dysfunction plays a key role in the pathophysiology of obesity-related hypogonadism in men.

Abstract citation ID: lvag096.471

P323 - ECE_3289 - Comparing dual-energy X-ray absorptiometry and radiofrequency echographic multi-spectrometry for bone mineral density assessment in patients with Turner syndrome: preliminary results of a pilot study

Laura Rotolo[1,2], Matteo Malagrinò[1,2], Carolina Cecchetti[2,3], Paola Dionese[1,2], Elisabetta Belardinelli[1,2], Beatrice Solmi[1,2], Guido Zavatta[1,2], Uberto Pagotto[1,2] and Alessandra Gambineri[1,2]
[1]*Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy;* [2]*Bologna, Italy;* [3]*Endocrinology Unit, Ospedale Morgagni-Pierantoni, Forlì, Italy*

Background: Turner syndrome (TS) is often characterized by reduced bone mineral density (BMD). Dual-energy X-ray absorptiometry (DXA) is the gold standard method for monitoring BMD in these patients. Nonetheless, its BMD measurement is affected by radiological artefacts and altered bone geometry, frequently found in TS patients. Radiofrequency Ecographic Multi-Spectrometry (REMS) is a new, validated tool to measure BMD without the interference from such radiological artefacts. However, it has not yet been applied to measure BMD in TS patients.

Aim: To compare the diagnostic classification between DXA and REMS in a cohort of TS patients.

Methods: We conducted an exploratory comparison on 34 consecutive adult TS patients (median age: 41 yo; min-max: 24, 5-71,7 yo). All patients underwent lumbar spine and femoral BMD assessment with both DXA and REMS. We classified all patients according to T-score (osteoporosis: T-score ≤ −2,5/osteopenia: T-score −2,5 − −1/normal BMD: T-score ≥ −1), Z-score (low BMD: Z-score ≤ −2/normal BMD: Z-score > −2) and using the appropriate score as per general population guidelines according to age/current hormonal replacement treatment (T-score if considered post-menopausal).

Results: We found a significant correlation between DXA and REMS for T-score at lumbar and total hip sites (R = 0.489; $P = .005$ and R = 0.464; $P = .015$, respectively), while no significant correlation was found for femoral neck T-score or Z-scores of all three sites. According to DXA BMD value, 8 patients (25.8%) were classified as osteoporotic, 13 (41.9%) as osteopenic, 10 (32.3%) with normal BMD. On the other hand, according to REMS 11 (32.4%) patients were classified as osteoporotic, 15 (44.1%) as osteopenic and 8 (23.5%) as normal BMD. Using Z-score, 7 patients (22.6%) had low BMD and 24 (77.4%) patients had normal BMD according to DXA. Using REMS, 6 (17.6%) patients showed low BMD and 28 (82.4%) patients had normal BMD. Using T- or Z-score where appropriate, the overall concordance of their diagnostic classification was 72.7% ($\kappa = 0.372$, $P = 1.000$ between discordant cases). When analysing T-score categories separately,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

the concordance was lower (61.3%,κ = 0.576), with REMS identifying a higher prevalence of osteopenia or osteoporosis compared to DXA ($P = .010$ between discordant cases).

Conclusions: These preliminary data suggest REMS could be a promising tool for monitoring bone health in patients with TS, potentially overcoming known radiological artefacts affecting BMD measurement by DXA. While REMS showed a tendency towards identifying more cases of reduced BMD, further studies on larger cohorts are needed to validate its accuracy and to identify which patients could benefit from this method.

Abstract citation ID: lvag096.472

P324 - ECE_2476 - The impact of waist to height ratio in the assessment of women with polycystic ovary syndrome. Evidence from a large European cohort

Sarantis Livadas[1], Nicholas Angelopoulos[1], Jelica Bjekic MacUt[2], Justyna Kuliczkowska-Płaksej[3], Ralitsa Robeva[4], Rodis Paparodis[1], Uglješa Barać[5], Andromahi Vryonidou[6], Tamara Baltić[2], Vaia Lambadiari[7], Andrzej Milewicz[3], George Mastorakos[8] and Djuro MacUt[5]
[1]Hellenic Endocrine Network, Athens, Greece; [2]Department of Endocrinology, KBC Bežanijska kosa, belgrade; [3]Department of Endocrinology, Diabetology and Isotope Therapy, University of Medicine, Wroclaw, Poland; [4]Ushate 'acad. IV. Penchev', Department of Endocrinology, Faculty of Medicine, Medical University, Sofia, Bulgaria; [5]Clinic for Endocrinology, Diabetes and Metabolic Diseases, belgrade; [6]Department of Endocrinology and Diabetes, Hellenic Red Cross Hospital, Athens, Greece; [7]2nd Propaedeutic Department of Internal Medicine, Research Unit and Diabetes Center, Attikon University Hospital, Athens, Greece; [8]Division of Endocrinology, Diabetes and Metabolism, Aretaieion University Hospital, Athens, Greece

Background: Women suffering from PCOS display a variety of metabolic and hormonal abnormalities. Waist to height ratio (WHtR,), is considered as a valuable predictor of cardiovascular risk and central obesity.

Aim of the Study: To assess the association of WHtR with metabolic/hormonal profile in PCOS.

Methods: Data from 2201 PCOS women, mean age 25.0 years (21-29), BMI 24.7 kg/m^2 (21.3-30.80) were analyzed. Participants were classified into three WHtR categories according to the established cut-offs (A: <0.50, B: 0.50-0.59, C: ≥0.60). Findings are presented before and after adjustment for age and BMI.

Results: A gradual statistically significant increase was observed among subgroups regarding HOMA-IR [A: 1.5 (0.9-2.3), B: 2.7 (1.6-4.0), C: 4.2 (2.6-6.3)] and the existence of impaired glucose tolerance (IGT) [A: 7.3%, B: 12.4%, C: 24.0%], (P for trend <.001). The relationship of HOMA-IR with WHtR remained statistically significant ($P < .001$) even after adjustment for age and BMI. These subgroups were also associated with a progressively adverse lipid profile, characterized by higher triglyceride [A: 78 (58-102), B: 89 (67-111), C: 96 (75-142)mg/dl] and LDL cholesterol levels [A: 108 (86-133), B: 114 (94-139), C: 118.0 (98-133)mg/dl] and lower HDL cholesterol concentrations [A: 51(43-61), B: 51 (42-57), C: 45 (40-54)mg/dl], with strong linear trends across WHtR strata. Notably, the associations with triglycerides and HDL cholesterol persisted after adjustment for age and BMI ($P < .001$). Considering, hormonal profile, subgroups based on WHtR categories were associated with a progressive increase in free androgen index (FAI) [A: 4.97 (3.07-7.66), B: 7.49 (4.54-11.11), C: 9.38 (6.00-13.90)] and the prevalence of hirsutism [A: 55.5%, B: 61.8%, C: 69.3%] (P for trend <.001). Total testosterone levels showed a modest, but significant increase across WHtR strata, whereas DHEAS, D4 and 17OP concentrations did not differ significantly. Gonadotropins exhibited an inverse association with WHtR, with lower LH and FSH levels observed in higher WHtR categories, while TSH showed only a weak trend. In multivariate analyses, sugbroups were strongly associated with increased FAI values in a graded manner, and these associations remained statistically significant after adjustment for age and BMI ($P < .001$).

Conclusions: Multivariate analysis showed that WHtR constitutes a solid denominator of insulin resistance, dyslipidemia and hyperandrogenemia even after adjustment of age and BMI. These findings suggest that WHtR captures a distinct aspect of PCOS pathophysiology as it integrates both metabolic and androgenic interaction in PCOS and emerges as a pragmatic anthropometric marker for early metabolic risk stratification in PCOS.

Abstract citation ID: lvag096.473

P325 - ECE_3527 - Metabolomic profiling reveals distinct metabolic signatures in women with functional hypothalamic amenorrhoea (FHA) and polycystic ovary syndrome (PCOS)

Sandhi Nyunt[1,2], Thomas Hopkins[3], Adrien Le Guennec[3], Arthur Yeung[1,2], Kanyada Koysombat[1,2], Jovanna Tsoutsouki[1,2], Bijal Patel[1,2], Megan Young[1], Agathoklis Efthymiadis[1,2], Aaran Patel[1,2], Tricia Tan[1,2], Alexander Comninos[1,2], Kim Jonas[3], Ali Abbara[1,2] and Waljit Dhillo[1,2]
[1]Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom; [2]Department of Endocrinology, Imperial College Healthcare NHS Trust, London, United Kingdom; [3]Department of Women and Children's Health, Kings College London, School of Life Course and Population Health Sciences, London, United Kingdom; [4]Women and Children's Health, King's College London, London, United Kingdom

Background: Reproductive endocrine disorders are tightly linked to alterations in energy balance and metabolism, with functional hypothalamic amenorrhoea (FHA) associated with reduced energy availability, and polycystic ovary syndrome (PCOS) with metabolic dysfunction and insulin resistance, further exacerbated by obesity. Metabolomics provides comprehensive analysis of small-molecule metabolites offering an integrated assessment of systemic metabolic activity. Herein, we describe the first direct comparison of metabolomic signatures in these two common causes of menstrual disturbance.

Methods: Metabolomic evaluation was conducted in healthy controls ($n = 32$), women with FHA ($n = 37$) and women with PCOS ($n = 54$). PCOS was further stratified into lean PCOS (BMI < 25 kg/m^2; $n = 30$) and obese PCOS (BMI ≥30 kg/m^2; $n = 24$). Serum was analysed using nuclear magnetic resonance (NMR) spectroscopy,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

with metabolites categorised into amino acid, carbohydrate, and lipid pathways. Metabolites are presented as normalised expression values and compared by Kruskal-Wallis test.

Results: *Amino acid profiles:* Branched-chain amino acids (BCAA) were increased in PCOS, with higher leucine and isoleucine than healthy controls ($P < .0015$) and FHA ($P < .0099$), whilst valine was higher in PCOS than in healthy controls ($P = .0034$). Glycine was lower in PCOS than other groups ($P < .0001$), whereas tyrosine was higher in PCOS than FHA ($P = .0076$). Aromatic amino acids (AAA) including phenylalanine and tyrosine were higher in obese PCOS ($P < .036$). Carbohydrate metabolites were also altered, with lower lactate in FHA than healthy controls ($P = .01$) and lower citrate in PCOS than FHA ($P < .0001$) and healthy controls ($P = .048$). Lipid profiling demonstrated higher triglycerides in PCOS than healthy controls ($P = .001$), while total cholesterol ($P = .008$) and polyunsaturated fatty acids ($P = .009$) were higher in FHA than PCOS. Citrate concentrations were lower in obese PCOS than healthy controls ($P = .02$) and FHA ($P < .0001$) and triglyceride levels were higher than in healthy controls ($P = .003$) and FHA ($P = .02$).

Conclusions: PCOS is characterised by a distinct metabolomic signature consistent with insulin resistance, demonstrated here by elevated BCAA and AAA, reduced glycine, altered carbohydrate metabolism, and triglyceride enrichment. By contrast, FHA exhibits a metabolic profile consistent with energy conservation, reduced glycolytic activity and preserved lipid composition. Collectively, these findings indicate that PCOS and FHA represent fundamentally divergent metabolic states, with obesity acting as a key modifier of metabolic dysfunction in PCOS.

Abstract citation ID: lvag096.474

P327 - ECE_1893 - Prospective short and long-term changes in cardio-metabolic risk markers following gender affirming hormone therapy

Louise Lehmann Christensen[1], Camilla Viola Palm[2], Marianne Andersen[1], Guy T'sjoen[3], Jan Frystyk[1], Tine Taulbjerg Kristensen[1], Rikke Hjortebjerg[1] and Dorte Glintborg[1]

[1]Endocrinology, Odense University Hospital, Odense, Denmark; [2]Gynecology and Obstetrics, Odense University Hospital, Odense, Denmark; [3]Endocrinology, Ghent University Hospital, Ghent, Belgium

Introduction: Gender affirming hormone treatment (GAHT) may associate with increased cardiometabolic disease (CMD) risk. Prospective CMD risk screening is recommended, but long-term data are needed regarding changes in CMD markers.

Objectives: To evaluate prospective changes in CMD risk markers during GAHT.

Methods: Transgender persons initiating (GAHT naïve) or on current GAHT (GAHT ongoing) were included in a 36 month prospective study at a Danish center of gender identity. Participants were categorized as transmasculine (TransM, $N = 245$: GAHT naïve, $N = 129$; ongoing, $N = 116$) and transfeminine (TransF, $N = 250$: GAHT naïve, $N = 157$; ongoing, $n = 93$) persons. BMI, waist-hip-ratio, lipids, blood pressure (BP), and HbA1c were measured annually.

Results: In transM, the baseline age was median (interquartile range) 23 (20-28) years in GAHT naïve and 25 (21-29) years in GAHT ongoing with median GAHT duration of 3.1 (1.8-4.8) years. Masculinizing GAHT until 36 months in GAHT naïve and ongoing transM ($N = 84$) was followed by increased LDL and triglycerides, whereas GAHT naïve transM ($N = 53$) in addition had significantly increased waist, and HbA1c and decreased HDL. In TransF, the median age at baseline was 25 (22-30) years) in GAHT naïve and 27 (23-36) years in GAHT ongoing with median GAHT duration of 2.2 (1.3-3.7) years. In GAHT naïve, 36 months of feminizing GAHT ($N = 38$) was followed by increased weight, BMI, waist and hip and decreased t-cholesterol and triglycerides, whereas CMD risk markers were stable in transF GAHT ongoing.

Conclusions: Masculinizing GAHT was associated with long-term adverse changes in lipid status, whereas initializing feminizing GAHT was associated with metabolically unfavorable body composition changes.

Abstract citation ID: lvag096.475

P328 - ECE_1888 - Morphometric and transcriptomic profiles in porcine testicular maturation

Petra Ferjan[1], Nina Batorek Lukač[1], Mette Rosenkilde[2] and Milka Vrecl Fazarinc[1]

[1]University of Ljubljana, Veterinary faculty, Institute of Preclinical Sciences, Ljubljana, Slovenia; [2]Faculty of Health and Medical Sciences, Department of Biomedical Sciences, Laboratory for Molecular Pharmacology, University of Copenhagen, Copenhagen, Denmark

Pigs offer a unique model for studying testicular development because of their large interstitial compartment, three-stage Leydig cell differentiation akin to humans, and a functional gonadotropin-releasing hormone receptor 2 (GnRHR2), which induces luteinizing hormone –independent testosterone secretion by Leydig cells. This study aims to connect age-dependent morphometric and transcriptomic changes in porcine testis to enhance our understanding of testicular maturation and its translational relevance.

Testis samples were collected at 0, 1, 3, 6, 12, 19, 22, and 27 weeks of age (6-10 animals/group) and processed for histomorphometric, qPCR[1,2] and LC–MS/MS analyses. Preselected qPCR target genes were cell markers SOX9 (Sertoli cells), ACTA2 (peritubular myoid cells), CD68 (macrophages), UCHL1 (pre-meiotic germ cells) and SYCP1 (meiotic/post-meiotic germ cells), Leydig cell development and function markers (STAR, HSD3B1, HSD17B7, HSD17B3, PDGFRA, BHMT) and genes involved in regulation of testicular function (FSHR, LHCGR, GnRHR2). Kruskal–Wallis test with Bonferroni correction was used for statistical analysis.

Histomorphometric analysis revealed a significant increase in seminiferous tubule diameter and their luminisation from week 19, accompanied by a decreased proportion of Leydig cells and other interstitial components. Leydig cells showed a distinct developmental pattern, with the N:C index lowest at 3 weeks during mini puberty, peaking at 12 weeks, and declining after week 19, reflecting the transition from perinatal to adult Leydig cells. Transcriptome analysis showed that LHCGR, FSHR, HSD3B1, and SOX9 peaked at week 12, marking the transition toward mature testicular function. PDGFRA, marker for stem and progenitor Leydig cells, showed a marked decline in expression from week 19, while HSD17B3, a marker of immature Leydig cells, peaked at week 12. BHMT, a marker of adult Leydig cells,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

increased significantly from week 19 onward, paralleled by an upregulation of GnRHR2. Increased expression of UCHL1, SYCP1, and ACTA2 from weeks 12 and 19 onward indicated the initiation and progression of seminiferous tubule development. Expressions of STAR and CD68 and testosterone concentrations in testicular tissue declined throughout development, reflecting the reduced proportion of Leydig cells and other interstitial components. HSD17B7 expression remained stable throughout development.

Observed changes align with the three-phase Leydig cell developmental pattern and the onset of puberty at week 19, coinciding with activation of the GnRH-II/GnRHR-II system. Collectively, these findings highlight the coordinated interplay between structural remodeling and transcriptional regulation underlying testicular development in pigs.

References

1. Ferjan P, Fazarinc G, Škrlep M, Vrecl M. Histology and mRNA expression of unilateral testicular atrophy in three immunocastrated boars: a case report. *BMC Vet Res*. 2026;22(1):67
2. Lukač NB, Škrlep M, Poklukar K, Ferjan P, Stefanski V, Fazarinc G, Vrecl M. INSL3 Expression in Leydig Cells is a Biomarker for Immunocastration in Boars: Transcriptional Evidence. *Andrology*. 2026;14(3):782-795

Abstract citation ID: lvag096.476

P329 - ECE_1941 - Role of the FGF signaling pathway in the etiopathogenesis of congenital hypogonadotropic hypogonadism

Rosa García Moreno[1], Patricia Martín Rojas-Marcos[1], Cristina Álvarez Escolá[1], Paula Muñiz Sevilla[2], Isabel González Casado[3] and Angel Campos Barros[4]

[1]*Endocrinology and Nutrition, Hospital Universitario La Paz, Madrid, Spain;* [2]*Instituto de Genética Médica y Molecular (INGEMM), IdiPAZ., Hospital Universitario La Paz, Madrid, Spain;* [3]*Pediatric Endocrinology, Hospital Universitario La Paz, Madrid, Spain;* [4]*Instituto de Genética Médica y Molecular (INGEMM), IdiPAZ. CIBER de Enfermedades Raras (CIBERER; U 753), ISCIII, Madrid., Hospital Universitario La Paz, Madrid, Spain*

Introduction: The Fibroblast Growth Factor (FGF) signaling pathway is essential for the development and migration of GnRH neurons. Besides genes encoding ligands and receptors (*FGF8, FGF17*, *FGFR1)*, several modulatory genes (*IL17RD, SPRY4, DUSP6, FLRT3)* regulate this pathway. Deleterious variants may cause normosmic congenital hypogonadotropic hypogonadism (nCHH) or Kallmann syndrome (KS).

Objectives: To characterize the phenotype and inheritance patterns of patients with CHH harboring deleterious variants in FGF-pathway genes.

Methods: Targeted NGS analysis of 84 CHH patients with custom panels including up to 482 genes implicated in CHH and hypothalamic-pituitary development.

Results: Heterozygous deleterious variants in FGF-pathway genes were identified in 19% of patients. Four familial cases showed probable autosomal dominant (AD) inheritance due to pathogenic *FGFR1* variants: 1) Mother and daughter with nCHH, presented the nonsense p.(Arg609*) variant; the mother also presented a missense *DUSP6* VUS. 2) Father and daughter with KS, presented a frameshift variant p.(Val102Profs*2). 3) Mother and son with nCHH presented a missense p.(His621Asn) variant; the son also inherited a *SOX2* VUS from his father, suggesting digenic contribution. 4) A woman with nCHH, and her brother with KS, whose mother had hyposmia and pubertal delay, presented a frameshift p.(Asn568LysfsTer67) variant. In three additional cases without family history of CHH, parental genetic studies revealed: 1) a *de novo* pathogenic *FGFR1* variant, p.(Trp691*) in a nCHH case (probably monogenic); 2) a probable digenic KS case due to a pathogenic *FGF8* variant inherited from the mother (unaffected) and a *PROKR2* VUS inherited from the father (delayed puberty); 3) a probable oligogenic CHH case, involving 2x VUS in *SPRY4* and *SMAD6* (inherited from his mother), and predicted deleterious variants in *NPFFR1*, *CHD7,* and *PLEKHA5* (from his father). Among the remaining cases, isolated variants in *FGFR1* or *FGF8* were identified in two, while five cases had VUS in *FGFR1, FLRT3,* or *ILR17D*, combined with variants in other CHH candidate genes.

Conclusions: FGF-signaling pathway genes are implicated in nCHH and KS. *FGFR1* variants may follow AD or oligogenic inheritance, whereas other pathway genes likely contribute to CHH predominantly through oligogenic mechanisms.

Gene	Variant	Classification (ACMG)
FGFR1 (NM_023110)	c.1825C>T; p.(Arg609*)	Pathogenic
	c.303_304insCC; p.(Val102Profs*2)	Pathogenic
	c.1861C>A; p.(His621Asn)	Likely pathogenic
	c.1703_1704ins GGGCAAGG; p.(Asn568 LysfsTer67)	Pathogenic
	c.2072G>A; p.(Trp691*)	Pathogenic
	c.1078G>T; p.(Glu360*)	Pathogenic
	c.266A>G; p.(Gln89Arg)	VUS
	c.2366C>T; p.(Ser789Phe)	VUS
FGF8 (NM_033163)	c.157-2A>G; p.(?)	Pathogenic
	c.77C>T; p.(Pro26Leu)	VUS
ILR17D (NM_017563)	c.665C>T; p.(Pro222Leu)	VUS
FLRT3 (NM_013281)	c.47G>A; p.(Gly16Glu)	VUS
	c.1382G>A; p.(Arg461His)	VUS
DUSP6 (NM_001946.3)	c.35C>T; p.(Ser12Leu)	VUS
SPRY4 (NM_030964)	c.313G>A; p.(Asp105Asn)	VUS

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.477

P330 - ECE_3180 - The role of insulin-like growth factor-I in predicting growth response during GnRH-agonists treatment for central precocious puberty

Valeria Citterio[1], Giulia Rodari[1], Eriselda Profka[1,2], Valentina Collini[2], Aurora Pedroli[2], Giovanna Mantovani[1,2] and Claudia Giavoli[1,2]

[1]*Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy;* [2]*Department of Clinical Sciences and Community Health, Dipartimento di Eccellenza 2023-2027, University of Milan, Milan, Italy*

Introduction: Central precocious puberty (CPP) is characterized by early activation of hypothalamic-pituitary-gonadal axis and is often associated with elevated insulin-like growth factor-I (IGF-I) levels and accelerated growth and bone maturation, leading to reduced adult height (HT). Treatment with GnRH-agonists (GnRHa) slows growth and bone maturation, though not always restores prepubertal growth velocity (GV). The causes of different growth response to GnRHa treatment remain unclear and although several studies have examined the role of IGF-I on GV during CPP-treatment, results are still debated.

Aims: To investigate the IGF-I response to GnRHa therapy and its potential role in growth outcomes in girls with CPP.

Methods: 69 girls with CPP (Tanner stage B2 before 8 years of age and LH peak response to GnRH test >5 mU/L) treated with GnRHa for at least 12 months were included. Auxological (HT-SDS, BMI-SDS, GV-SDS, Tanner stage), biochemical (LH, FSH, oestradiol, IGF-I-SDS) and radiological (pelvic ultrasonography and bone age) data were collected at diagnosis and during treatment.

Results: At diagnosis, median age was 7.8 years (IQR 7.2-8), mean HT was 0.4 ± 1 SDS and mean BMI 0.6 ± 1.2 SDS. Median estradiol was 5.7 pg/mL (IQR 5-16), mean basal and stimulated LH levels were 0.9 ± 1.1 mU/L and 16.2 ± 16.1 mU/L, respectively. Median IGF-I SDS was 1.8 (IQR 0.6-2.6), with 42% patients showing IGF-I levels >2 SDS. Baseline IGF-I SDS correlated positively with chronological age ($P = .0012$), bone age advancement ($P = .014$), LH peak ($P = .0056$) and HT expressed as distance to mid-parental height (deltaMPH) SDS ($P = .033$). During treatment, IGF-I levels did not show significant overall changes, though decreased in 57% and 56% patients after 6 and 12 months, respectively, and increased in the remainder. IGF-I levels at 6 months significantly correlated with deltaMPH both at 6 and 12 months of therapy ($P = .012$, $P = .004$, respectively), and with GV after 18 months ($P = .03$). Furthermore, girls with IGF-I levels ≥2 SDS at 6 months had higher GV not only at 6, but also at 12 and 18 months compared with those with IGF-I within the normal range ($P = .029$, $P = .034$, $P = .01$, respectively).

Conclusions: Present results confirm the importance of pretreatment IGF-I in supporting CPP diagnosis and firstly highlight the potential role of short-term IGF-I changes in predicting growth response to GnRHa to treatment, even in the long-term. This finding supports the role of IGF I as an early marker of treatment effectiveness, reflecting individual variability in growth response during GnRHa therapy.

Abstract citation ID: lvag096.478

P332 - ECE_2573 - Mechanistic insights into the effects of intranasal insulin in increasing postprandial energy expenditure in obese women with polycystic ovary syndrome

Colin Duncan[1], Yuan Wang[1], Riada McCredie[1], Stephen Franks[2], Paul Fowler[3], Roland Stimson[1], Mick Rae[4] and Katarzyna Siemienowicz[4]

[1]*The University of Edinburgh, Edinburgh, United Kingdom;* [2]*Imperial College London, London, United Kingdom;* [3]*University of Aberdeen, Aberdeen, United Kingdom;* [4]*Edinburgh Napier University, Edinburgh, United Kingdom*

Polycystic ovary syndrome (PCOS) is a lifelong condition associated with reproductive and metabolic consequences. Obesity worsens PCOS and women with PCOS are more likely to be obese and find weight loss difficult. Women with PCOS have a reduced adaptive thermogenesis response to food meaning they burn off fewer calories after eating. Previous studies conducted in a clinically realistic ovine model of PCOS suggested that this is due to a reduced insulin signalling in the brain resulting in less sympathetic-mediated activation of thermogenesis in subcutaneous adipose tissue (SAT). In the ovine PCOS model intranasal insulin (INI) improved the thermic response to food. We have now shown that INI improves postprandial energy expenditure (PPEE) in dose dependent manner in obese women with PCOS. To discover molecular mechanistic insight, we examined the effects of INI using microdialysis and transcriptome analysis of SAT combined with plasma proteomics.

Obese women with PCOS ($n = 12$) were fed a standard meal on two occasions with either intranasal saline placebo or 40iu INI in a random and blinded manner. The effect of INI on PPEE was assessed by indirect calorimetry over the next 150 minutes. Microdialysis fluid from anterior abdominal wall SAT was collected throughout. Sixty minutes after INI or saline placebo, a SAT biopsy was taken from the lower abdominal wall. Noradrenaline (NA) concentrations were measured by ELISA and mass spectroscopy and the proteome and transcriptome were analysed by Ingenuity Pathway analysis.

SAT NA concentrations from 30 to 60 mins in the microdialysate were at the lower limit of detection. There was a trend (mean 50% rise and 30% more samples with detectable NA) to higher NA after INI in PCOS but this was not significant. There were 439 genes nominally differentially expressed in SAT after INI with activation of 10 canonical pathways (including RHO and Sirtuin signalling) and inhibition of one (mitochondrial protein degradation). There were 423 differentially expressed plasma proteins in PCOS after INI (420 were elevated) with activation of 36 canonical pathways (including FGF signalling). Interestingly of the differentially expressed genes and proteins, only 14 were common to both. Analysis of the source of the top ten differentially expressed proteins showed that the liver was a more common source of synthesis than SAT.

These results give additional insight into the molecular effect on metabolism of INI and highlight that INI has likely effects on the liver as well as SAT.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.479

P333 - ECE_3172 - Endocrine rhythm integrity: a novel AI-derived metric of menstrual cycle health of the cycle length

Tinatin Kutchukhidze[1,2]
[1]New Vision University, Tbilisi, Georgia; [2]University of Oxford, Oxford, United Kingdom

Background: Clinical assessments of the menstrual cycle remain largely focused on cycle length and bleeding regularity, although these measures account for less than 30% of inter-individual variability in reproductive endocrine functions. 30-40% of women with regular menstrual cycles experience unexplained infertility, indicating subclinical dysfunction not detected by standard evaluations. We introduce Endocrine Rhythm Integrity (ERI), a novel quantitative metric capturing the temporal coherence, phase synchrony, and feedback stability of Hypothalamic-Pituitary-Ovarian hormone dynamics across the menstrual cycle. ERI reframes menstrual health as a property of endocrine rhythm organisation rather than static hormone levels or cycle duration, enabling identification of clinically relevant dysfunction with hormonal "normal" cycles.

Methods: A prospective, observational clinical trial enrolled 312 reproductive-aged women (18-22 years) with self-reported regular menstrual cycles (24-35 days). Participants were stratified into fertility controls ($n+162$) and women with unexplained infertility ($n=150$). Over two consecutive cycles, participants underwent dense longitudinal hormonal profiling with serum LH, FSH, estradiol, and progesterone sampling during the luteal phase. Continuous physiological data (basal body temperature, heart rate, sleep metrics) were collected using wearable devices. An AI- based model integrating hormonal dynamics and physiological signals was developed to compute the ERI score, incorporating metrics of phase alignment signal entropy and feedback loop stability. Primary outcomes included between-group differences in ERI and its predictive performance for infertility status. Secondary outcomes assess correlations between ERI and implantation failure history.

Results: Mean cycle length did not significantly differ between fertile and infertile groups (28.9 ± 2.3 vs 28.9 ± 2.5 days, $P=.42$). In contrast, ERI scores were lower in the infertility group (0.61 ± 0.12 vs 0.78 ± 0.10; $P<.001$). Disrupted endocrine rhythm integrity was observed in 64% of infertile participants despite hormonally" normal" mid-luteal progesterone levels. ERI independently predicted infertility status after adjustment of age, BMI, and AMH (OR 2.84, 95% CL1.96-4.1; $P<.001$). Receiver operating characteristic analysis demonstrates superior discrimination of infertility by ERI (AUC 0.86) compared with cycle length (AUC 0.52) and single-time point progesterone assessment (AUC 0.64). Lower ERI scores were also associated with a higher incidence of implantation failure ($r=-0.48$, $P<.001$)

Conclusions: Endocrine rhythm integrity is an AI-Dirven mechanism that captures subtle but clinically relevant endocrine dysregulation and outperforms traditional metrics in identifying subclinical infertility.It represents a previously unmeasured dimension of menstrual cycle health that is independent of cycle regularity. These findings support a paradigm shift from static cycle assessment to dynamic endocrine rhythm evaluation in reproductive endocrinology

Abstract citation ID: lvag096.480

P334 - ECE_3358 - Comparison between Radiofrequency Echographic Multi-Spectrometry (REMS) and Dual-energy X-ray Absorptiometry (DXA) for the assessment of bone status in Klinefelter Syndrome—preliminary data

Francesca Allosso[1], Lucia Digitale Selvaggio[2], Raffaele Navarra[2], Raffaela Carotenuto[2], Giammarco Valentino[2], Claudia Cocchini[2] and Daniela Pasquali[2]
[1]Department of Advanced Medical and Surgical Sciences, University of Campania L. Vanvitelli, Naples, Italy; [2]Advanced Medical and Surgical Sciences, University of Campania L. Vanvitelli, Naples, Italy

Introduction: Klinefelter Syndrome (KS), the most frequent sex chromosome aneuploidy in males, is usually characterized by an increased risk of fragility fractures. Reduced bone mineral density (BMD) in KS has a multifactorial pathogenesis, including hypogonadism, vitamin D deficiency and alterated body composition. Dual energy X-ray Absorptiometry (DXA) is the gold standard for BMD assessment, but a new ultrasound-based technique, Radiofrequency Echographic Multi-Spectrometry (REMS), has recently emerged, showing several advantages like the absence of ionizing radiation and high reproducibility.

Aims: We conducted a cross-sectional study at the "Rare Endocrine Diseases" Unit, University of Campania L. Vanvitelli, Naples. The primary aim of our study was to compare DXA and REMS densitometric parameters in a population of KS patients. The secondary aim was to compare REMS results of KS patients with a healthy control group to evaluate potential differences in BMD, bone fragility and body composition.

Methods: We enrolled 29 patients with KS (aged $\geq$21 years) with a recent DXA scan. Anthropometric (age, weight, height, BMI, waist circumference), biochemical parameters (glycolipid profile, bone metabolism, hormonal profile), information regarding testosterone replacement therapy (TRT) were collected and densitometric parameters were obtained through DXA and REMS. Results were compared with 23 healthy male controls.

Results: All KS patients had normal testosterone levels (naturally or via TRT). Mean BMI was 27.47 ± 5.41 kg/m^2. Lumbar spine results were comparable between DXA and REMS. However, DXA showed significantly higher femoral BMD values (1.012 ± 0.149 g/cm^2 vs 0.842 ± 0.141 g/cm^2; $P<.001$) and T-score (-0.3 ± 0.9 vs -0.7 ± 0.8; $P=.047$) compared to REMS. Despite similar femoral BMD values between groups, KS patients exhibited a significantly lower REMS T-score (-0.09 ± 0.9; $P=.027$) and a higher Fragility Score (13.8 ± 3.73 vs 11.7 ± 1.43; $P=.017$) than controls, suggesting increased bone fragility. Additionally, KS patients had significantly higher body fat percentage (25.5 ± 5.19% vs 21.5 ± 3.84%; $P=.004$) and BMI (27.5 ± 5.38 kg/m^2 vs 24.8 ± 2.42 kg/m^2; $P=.021$).

Conclusions: REMS appears to be a reliable method for the early diagnosis of impaired mineral density in KS, overcoming

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

several DXA limitations as shown by the discrepancies in femoral evaluation.

Abstract citation ID: lvag096.481

P336 - ECE_3234 - Umasking hidden androgen rhythms with a real-time AI- enhanced testosterone patch

Tinatin Kutchukhidze[1,2]
[1]New Vision University, Tbilisi, Georgia; [2]New Anglia University, London, United Kingdom

Background: Hypogonadism and infertility evaluation relies on single morning serum testosterone measurements, which fail to capture the dynamic nature of androgen secretion. Up to 25-30% of men with normal testosterone levels present with symptoms of hypogonadism or unexplained infertility, suggesting the presence of subclinical androgen rhythm disorders undetectable by testing. Continuous hormonal monitoring has never been implemented in males, which is a critical gap in male reproductive endocrinology. This study introduces continues transdermal testosterone monitoring system combined with an AI- driven analysis platform as a novel method to detect previously unrecognised androgen rhythm disorders and provide real-time hormonal analysis.

Methods: A Prospective, observational study with 102 men aged 22-38 years with normal morning total testosterone (12-35 nmol/L) was conducted, including 54 men presenting with infertility or hypogonadal symptoms and 48 age-matched health controls. Participants wore a non-invasive transdermal biosensor patch cable of continuously captured testosterone every 15 minutes for 96 hours. Data were analysed in a real-time dedicated mobile application with integrated AI algorithms, which automatically quantified diurnal amplitude, peaking time, and rhythm stability using the coefficient of variation, phase delay, and AI-derived rhythmicality indices. The app provided clinicals immediate visualisation and analysis of variability of sleep, basal body temperature, and correlated endocrine fluctuations.

Results: Mean morning serum testosterone did not differ between symptomatic and control groups (22.4 ± 3.1 vs 23.1 ± 3.5 nmol/L; p+0.38). Continuous AI-assisted monitoring revealed significant differences in androgen dynamics. Men with symptoms exhibited lower diurnal amplitude(5.2 ± 1.1 vs 8.7 ± 1.4 nmol/L; $P < .001$)compared to controls. Disrupted androgen rhythmicity correlated with reduced sperm concentration ($r = 0.047$;$P = .002$). Rhythm indices, computed in real time by an AI platform, predicted subclinical dysfunction with superior accuracy(AUC 0.87) compared with static serum testosterone (AUC0.61)

Conclusions: Ai-driven Continues transdermal testosterone monitoring patches uncover hidden androgen rhythm disorders in men with normal morning testosterone levels, redefining male hypogonadism and subclinical reproductive dysfunction as disorders of dynamic endocrine regulation rather than absolute deficiency. AI-integrated system enables real- time analysis and clinical decision support, offering a foundation for rhythm-based diagnostic approaches, for transgender medicine, personalized interventions, and timing-optimized testosterone therapy.

Abstract citation ID: lvag096.482

P338 - ECE_2708 - Automated AI-assisted preantral ovarian follicle staging in a mouse model of chemotherapy-induced primary ovarian insufficiency (POI)

Malene Lundgaard Riis, David Ari Ostenfeldt, Susanne Pors, Annika Runegaard Thomsen, Jacob Lercke Skytte, Allison Butt and Line Zachariassen
Gubra A/S, Hørsholm, Denmark

Rationale: Classification and counting of ovarian follicles is a widely used as a key endpoint in evaluation of preclinical models of reproductive disorders. This has traditionally been done using manual histopathological scoring systems that are prone to inter- and intra-observer variability which can influence robustness and reproducibility of study results. The present study aimed to validate an automated deep learning-assisted digital imaging analysis pipeline, termed GHOST (Gubra Histopathological Objective Scoring Technology) for objective assessment of preantral follicle staging in a mouse model of chemotherapy-induced primary ovarian insufficiency (POI).

Methods: Female C57BL/6JRj mice, 11 weeks of age, were given an intraperitoneal injection with cyclophosphamide (10 mL/kg, 100-200 mg/mL) on day 1 and 8. At day 11, 18 and 30, the ovaries were dissected and fixed in formalin for 24 hours. The ovarian tissue was then paraffin embedded, sectioned at 5 μm with every 10^{th} section collected, and immunohistochemically stained for p63 (Abcam, Ab124762) and digitally scanned. Firstly, an oocyte segmentation model was established by sampling image tiles of 512×512 pixels (at 20x) throughout the entire study. Within each tile, p63-positive oocytes were annotated using manually drawn bounding boxes and the Segment-Anything-Model (SAM). Based on these annotation images, a U-Net was trained to segment oocytes at pixel-level. Secondly, to create data for a follicle staging model, follicle tiles of 299×299 pixels (at 40x) were extracted around each segmented oocyte and scored by histopathologist into four categories: primordial, transitional, primary and secondary follicles. A fifth category was added to contain false positives detections typically due to unspecific staining. The follicle staging model was created by using scored tiles to train InceptionV3 classification model.

Results: In total 500 tiles containing p63-positive oocytes were used to train the oocyte segmentation model, and 1000 tiles were used to train the follicle staging model. On the held-out test set, automated follicle staging into four categories (primordial, transitional, primary and secondary) showed good agreement with expert manual scoring (Cohen's kappa = 0.61), with the best agreement observed for follicles stages primary and secondary.

Conclusions: The GHOST pipeline shows high agreement with manual scoring of follicle stage by expert histopathologists. GHOST provides unbiased, fast, accurate, and reproducible histopathological scoring. This establishes GHOST as an accurate AI-based method for unbiased and automated preantral follicle staging in mouse ovaries and highlights its valuable application in preclinical studies for reproductive disorders as well as for assessing reproductive toxicology.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.483

P339 - ECE_3904 - The BRIDGE initiative: empowering university societies through evidence-based workshops co-created with patient support groups to support women with PCOS

Sumaya Osman[1], Maiar Elhariry[2], Alaee Ziani[3], Akshat Sinha[2], Esha Kaur[4], Zalanda Shinwarie[5], Halimah Salami[1], Sumayyah Amin[1], Karin Nassar[6] and Punith Kempegowda[1,7]

[1]College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom; [2]Midland Metropolitan University Hospital, Birmingham, United Kingdom; [3]Aston Medical School, Birmingham, United Kingdom; [4]Imperial College London, London, United Kingdom; [5]Birmingham, United Kingdom; [6]Keele University, Keele, United Kingdom; [7]Queen Elizabeth Hospital, Birmingham, United Kingdom

Background: Polycystic Ovary Syndrome (PCOS) affects up to 10% of individuals assigned female at birth, yet many often lack access to accurate information and appropriate support. Misinformation on social media and limited awareness contribute to stigma, confusion, and delayed help-seeking. University societies, often perceived as approachable sources of peer support, are seldom equipped with the training required to address PCOS-related concerns. The BRIDGE (Bridging Resources to Inform and Develop Groups for Effective Support) initiative was developed to address this gap by positioning student societies as informed, community-centred health hubs.

Aims: To deliver accurate, evidence-based information, practical resources, and structured training that address both the clinical and psychosocial dimensions of the condition.

Methods: RIDGE employed a multimodal educational programme grounded in Kolb's experiential learning model, delivered through two workshops (formative and summative) held four months apart. The team consisted of healthcare university students nationwide, doctors, and a patient support group. Each workshop combined simulation-based learning with anonymised real-patient PCOS scenarios, facilitated case discussions, focus groups, and input from Verity PCOS UK. Between workshops, participants designed and implemented community-based "PCOS interventions" within their student societies. Mixed-methods evaluation included pre- and post-session confidence surveys analysed using Wilcoxon signed-rank tests, and thematic analysis of focus group transcripts, with intercoder reliability assessed using Cohen's kappa (κ).

Results: Across both workshops ($n = 25$ completing all surveys), self-reported confidence in supporting peers with PCOS increased significantly from 14.7% to 76.0% ($P < .0001$). All participants reported improved knowledge of PCOS, holistic care principles, signposting skills, and the ability to challenge misinformation. Simulation cases were rated as effective by 94-100% of participants. Thematic analysis ($\kappa = 0.66–0.84$) identified key themes: enhanced PCOS awareness, the value of experiential and collaborative learning, the development of culturally sensitive and patient-centred approaches, and the recognition of logistical challenges in sustaining initiatives. Between the formative and summative sessions, participants produced diverse community interventions including peer-support programmes, podcast storytelling, awareness events, and partnerships with community leaders.

Conclusions: BRIDGE is the first initiative to equip university societies with structured, evidence-based training to support students living with PCOS. The programme significantly improved confidence, knowledge, and culturally sensitive support skills, demonstrating that simulation-based, co-produced, peer-led education can effectively counter misinformation and empower student communities. The BRIDGE model offers a scalable blueprint for addressing other stigmatised or poorly understood health conditions in higher education settings.

Abstract citation ID: lvag096.484

P340 - ECE_1053 - Research priorities for polycystic ovary syndrome: results of a priority setting partnership

Sue Channon[1], Elinor Coulman[1], Rachel Morman[2], Caroline Andrews[2], Fiona Morgan[2], Juliet Hounsome[1], Jo Watson[3] and Aled Rees[1]

[1]Cardiff University, Cardiff, United Kingdom; [2]Verity, Oxted, United Kingdom; [3]James Lind Alliance, Southampton, United Kingdom

Background: Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder associated with significant metabolic, reproductive and psychological manifestations. Co-production of research priorities is vital in ensuring that research addresses questions that matter most to individuals with lived experience of PCOS and to healthcare professionals (HCPs). We sought to identify the most important areas for research for people with PCOS by establishing a James Lind Alliance (JLA) Priority Setting Partnership.

Methods: Using standard JLA methodology, we launched an online survey to collect research questions from a diverse group of stakeholders. These were synthesised into summary questions and cross-referenced with existing evidence to identify gaps in the literature. Unanswered questions were included in a second survey for shortlisting by stakeholders. A final prioritisation workshop was held to reach consensus on the top 10 research priorities.

Results: The first survey yielded 1339 questions from 523 respondents (434 people with lived experience [3% 16-20 years, 35% 21-30 years, 39% 31-40 years, 15% 41-50 years, 8% >50 years; 79.6% White, 8.9% Asian, 3.5% Mixed or Multiple, 3.5% Black], 84 HCPs, 78 others). We formed 55 summary questions, of which 51 were unanswered and included in the second prioritisation survey. We heard from 374 respondents (286 people with lived experience) in this survey, with 3452 unanswered questions selected and ranked (2.0% 16-19 years, 28.1% 20-29 years, 46.2% 30-39 years, 14.4% 40-49 years, 7.0% 50-59 years: 7.0%, 2.0% 60-69 years: 2.0%; 78.3% White, 10.2% Asian, 4.0% Mixed or Multiple, 2.7% Black). The 27 highest-ranked questions were taken forward to the final consensus workshop, where individuals with lived experience of PCOS ($n = 13$) and HCPs ($n = 12$) collaboratively determined the top 10 research priorities. The most important question identified was '*What are the optimal care pathways for women and people living with PCOS in the UK, and how can they be adequately resourced and delivered so they are all accessible to everyone with PCOS?*'. Other important areas for research included association with other health

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

conditions, healthcare practitioner knowledge, ethnicity, non-pharmacological therapies, mental health needs, subtypes, anti-obesity and anti-androgen therapies, and fertility.

Conclusions: The study identified the top research priorities for PCOS, as determined jointly by people with lived experience and healthcare professionals. These findings should inform the PCOS research agenda for researchers, funders and policymakers, with the goal of improving outcomes that are meaningful to those affected by this common disorder.

Abstract citation ID: lvag096.485

P341 - ECE_1190 - The impact of pre-IVF day 2 TSH levels on treatment outcomes and obstetric results: a retrospective single-center study utilizing machine learning for data analysis

Bernadett Nádasdi[1], Viktor Vedelek[2], Kristóf Bereczki[3], Mátyás Bukva[4,5,6], Zoltán Kozinszky[3,7], Rita Sinka[2], János Zádori[3,8] and Anna Vágvölgyi[1]
[1]*Department of Medicine, Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary;* [2]*Department of Genetics, Faculty of Science and Informatics, University of Szeged, Szeged, Hungary;* [3]*Department of Obstetrics and Gynecology, Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary;* [4]*Department of Immunology, Albert Szent-Györgyi Medical School, Faculty of Science and Informatics, University of Szeged, Szeged, Hungary;* [5]*Department of Pediatrics and Pediatric Health Center, University of Szeged Albert Szent-Györgyi Health Center, Szeged, Hungary;* [6]*Laboratory of Microscopic Image Analysis and Machine Learning, Institute of Biochemistry, Biological Research Centre, Hungarian Research Network (HUN-REN), Szeged, Hungary;* [7]*Capio Specialized Center for Gynecology, Solna, Sweden;* [8]*Albert Szent-Gyorgyi Medical School, University of Szeged, Institute of Reproductive Medicine, Szeged, Hungary*

Introduction: Thyroid disorders, especially thyroid autoimmunity, are becoming more common in women of reproductive age and have been associated with fertility outcomes. Although endocrinology guidelines specify target thyroid-stimulating hormone (TSH) levels for women undergoing assisted reproductive technology, the ideal preconception TSH range for successful *in vitro* fertilization (IVF) remains uncertain.

Material and Methods: This study aimed to evaluate how baseline TSH levels within the recommended normal range affect IVF outcomes, focusing on clinical pregnancy and live birth rates. Additionally, machine learning models were used to analyze the predictive roles of factors such as maternal body mass index (BMI) and TSH levels. A retrospective cohort study was performed at the Institute of Reproductive Medicine, University of Szeged, including 996 women undergoing IVF with or without intracytoplasmic sperm injection. Data on biometric, medical history, laboratory, and procedural variables were evaluated. Pregnancy and live birth predictions were modeled using support vector machine (SVM), random forest (RF), and extreme gradient boosting (XGBoost) algorithms, with feature importance assessed for RF and XGBoost.

Results: The SVM models predicted pregnancy with an average accuracy of 72.26% but were less effective for live birth prediction. RF and XGBoost models showed an area under the curve (AUC) of 0.76 and 0.74 for pregnancy, and 0.67 and 0.61 for live birth, respectively. Significant predictors included embryo quality score, maternal age, BMI, and hormone levels, with paternal factors also influencing outcomes. Importantly, variations in maternal TSH within the normal 0.3-4.0 mIU/L range did not significantly affect IVF success.

Conclusions: The findings suggest that preconception TSH levels within the reference range do not have a substantial impact on IVF success, supporting current clinical recommendations on TSH management in this context.

Abstract citation ID: lvag096.486

P342 - ECE_2334 - Pro-inflammatory cytokine profiling in polycystic ovary syndrome phenotypes: excess abdominal adiposity vs hyperandrogenism

Martina Curcio[1,2], Fannie Lajeunesse-Trempe[3,4], Georgios K. Dimitriadis[1,5,6] and Royce Vincent[1,5]
[1]*King's College Hospital NHS Foundation Trust, London, United Kingdom;* [2]*Università Cattolica del Sacro Cuore, UCSC, Rome, Italy;* [3]*Quebec Heart and Lung Institute, Laval University, Quebec, Canada;* [4]*Nutrition Faculty, Laval University, Quebec, Canada;* [5]*Faculty of Life Sciences and Medicine, King's College, London, United Kingdom;* [6]*Eli Lilly and Company, Indianapolis, United States*

Background: Polycystic Ovary Syndrome (PCOS) is increasingly recognised as a systemic illness extending beyond the scope of the reproductive disorder. Chronic low-grade inflammation is a key driver in the development and progression of cardiovascular disease (CVD) and inflammation has been reported in both PCOS and in those with excess abdominal adiposity. We assessed inflammation in PCOS phenotypes based on either excess abdominal adiposity or hyperandrogenism.

Methods: PCOS women were classified into four groups based on central adiposity (*healthy*/waist to height ratio (WHtR) 0.40-0.49 vs *high*/WHtR ≥0.6) and biochemical androgen status (*normal*/free androgen index (FAI) <5.0 vs *hyperandrogenism*/FAI>5.0. Groups were compared for cytokines (interleukins (IL-6, IL-1β, IL-8) and tumour necrosis factor α (TNFα)), BMI, HOMA-IR, blood pressure (BP), fibrosis-4-index (FIB-4), testosterone, DHEAS and FAI. Python (v3.14) was used for statistical analysis. $P < 0.05$ was considered statistically significant. Data is reported as median (IQR).

Results: The number of women in each sub-group were as follows: 15 with healthy WHtR, 23 with high WHtR, 32 with FAI ≤5.0 and 19 with FAI >5.0. Healthy and high WHtR groups had similar age, IL-1β, IL-8, TNFα, testosterone, DHEAS, FIB-4 and diastolic BP (DBP). High WHtR had higher % of non-White ethnicities 31 vs 8%, BMI 41.7(34.3-45.3) 23.6(21.7-24.5) kg/m^2 ($P < .0001$), IL-6 4.48(2.88-7.90) vs 1.61(1.21-1.98) ng/L (0.02), IL-6/TNFα 0.37(0.32-0.49) vs 0.16(0.113-0.20) (0.01), HOMA-IR 4.19(2.88-10.32) vs 1.16 (0.68-2.08) (0.02), FAI 5.25(2.08-6.50) vs 2.70 (2.20-3.40) (0.04) and systolic BP (SBP) 124(113-134) vs 108(116-118) mmHg (0.004). FAI ≤5.0 and >5.0 groups had similar age, % ethnicity, WHtR, cytokines, FIB-4, SBP and DBP. Those with FAI >5.0 had higher BMI 39.4(30.9-45.5) vs 27.9(23.7-34.9) kg/m^2 (0.02), testosterone 1.6(1.5-2.4) vs 1.3 (0.9-1.5) nmol/L (<0.0001), DHEAS 6.4(4.5-7.4) vs 2.3(1.9-3.3) umol/L (<0.0001) and HOMA-IR 3.15(2.56-5.04) vs 2.07(1.14-3.32) (0.04). There were no significant correlations between WHtR or FAI with any of the cytokines. However, numerous women exhibited circulating pro-inflammatory cytokines above the upper limits of normal, with elevated IL-6 in 64%, IL-8 and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

IL-1β in 48%, and TNFα in 28%. There was no difference in WHtR, FAI or IL-6 between White and non-White ethnicities.

Conclusions: In our cohort, excess abdominal adiposity was a stronger driver of IL-6, HOMA-IR and SBP with androgen excess driving primarily HOMA-IR. PCOS is associated with a heightened inflammatory burden, independent of BMI/androgen excess. These findings may suggest a role for active CVD risk stratification and prevention measures across all PCOS phenotypes.

Abstract citation ID: lvag096.487

P343 - ECE_2491 - The additive value of ovarian and adrenal hyperandrogenism in women with polycystic ovary syndrome and associations with age and weight. Insights from a large European cohort

Sarantis Livadas[1], Nicholas Angelopoulos[1], Dimitrios Papadimitriou[2], Jelica Bjekic Macut[3], Justyna Kuliczkowska-Płaksej[4], Ralitsa Robeva[5], Uglješa Barać[6], Rodis Paparodis[1], Tamara Baltić[3], Andromahi Vryonidou[7], Vaia Lambadiari[8], Andrzej Milewicz[4,9], George Mastorakos[10] and Djuro MacUt[6]
[1]Hellenic Endocrine Network, Athens, Greece; [2]Department of Pediatrics, Neonatal-Pediatric-Adolescent Endocrinology & Diabetes, Faculty of Medicine, University of Thessaly, Larisa, Greece; [3]Department of Endocrinology, KBC Bežanijska kosa, belgrade; [4]Department of Endocrinology, Diabetology and Isotope Therapy, University of Medicine, Wroclaw, Poland; [5]Ushate 'acad. IV. Penchev', Department of Endocrinology, Faculty of Medicine, Medical University, Sofia, Bulgaria; [6]Clinic for Endocrinology, Diabetes and Metabolic Diseases, belgrade; [7]Department of Endocrinology and Diabetes, Hellenic Red Cross Hospital, Athens, Greece; [8]2nd Propaedeutic Department of Internal Medicine, Research Unit and Diabetes Center, Attikon University Hospital, Athens, Greece; [9]School of Medicine, Wrocław, Poland; [10]Division of Endocrinology, Diabetes and Metabolism, Aretaieion University Hospital, Athens, Greece

Background: Hyperandrogenemia and insulin resistance (IR) are prevalent in PCOS. Since Androstenedione (A4) is produced by both ovaries and adrenals it is difficult to distinguish the source of hyparandrogenemia in these women. The ratio of testosterone to A4 ratio (T/A4) >1, is considered as a marker of ovarian contribution to androgen excess, whereas the ratio of Dehydroepiandrosterone sulfate (DHEAS) to A4 (DHEAS/A4) > 10 suggests a higher adrenal androgen production. Recent data suggest a potential favorable effect of T/A4 ratio in metabolism in lean women with PCOS.

Aim of the Study: To assess the association of ovarian (HO) and adrenal hyperandrogenemia (HA) with metabolic profile in PCOS.

Methods: Data from 2201 women with PCOS with a mean age of 25.0 years and BMI 24.7 kg/m^2 were analyzed. Participants were classified into HO and HA groups and findings were presented after adjustment for age and BMI.

Results: Women with T/A4 >1 displayed higher IR ($P = .004$), higher total glucose exposure during OGTT ($P = .034$) and impaired glucose tolerance (OR 5.51, $P = .018$). Furthermore, T/A4 was associated with elevated cholesterol ($P = .023$), LDL ($P < .001$), and lower HDL ($P = .002$). T/A4 > 1 was metabolically significant only in normal weight patients (HOMA-IR *P*: .012, HDL *P*:.034). Given the age-related decline in ovarian androgen levels, analyses were additionally stratified by age and it was disclosed a stronger impact of this ratio at younger ages for HOMA-IR with progressive attenuation (*P*:.029). Regarding HA, in the overall model adjusted for age and BMI, DHEAS/A4 >10 was not associated with HOMA-IR, whereas significant associations with lower total and LDL cholesterol were observed. However, these lipid associations were not consistent across BMI strata. Formal interaction analyses demonstrated that both age and adiposity significantly modified the metabolic expression of DHEAS/D4>10, since a significant age interaction was identified for HOMA-IR, while BMI-stratified analyses revealed lower HOMA-IR exclusively among women in the highest BMI tertile.

Conclusions: Collectively, these ratios resemble as functional indexes of androgen source, rather than absolute androgen burden. It seems that HA reflects heterogeneity in androgen source rather than a stable metabolically favorable phenotype. In contrast, HO is compatible with adverse metabolic profile especially in young lean women with PCOS, highlighting the ovary as the main regulator of dysmetabolism in this subset of women. Together, our findings argue against the use of T/A4 as a marker of favorable metabolic status in PCOS and instead support its role as an indicator of increased cardiometabolic risk.

Abstract citation ID: lvag096.488

P344 - ECE_3216 - Lipid accumulation product as a non–insulin-based marker of metabolic heterogeneity in polycystic ovary syndrome phenotypes

Lena Radic[1], Sanja Ognjanovic[1,2], Bojana Popovic[1,2], Dusan Ilic[1], Valentina Elezovic Kovacevic[1,2], Milica Opalic Palibrk[1], Katarina Krstic[1], Natalija Dragicevic[1], Bogdan Milenkovic[1], Uglješa Barać[1] and Djuro MacUt[1,2]
[1]Department for Endocrine Tumors and Hereditary Cancer Syndromes, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Belgrade, Serbia; [2]Faculty of Medicine University of Belgrade, Belgrade, Serbia

Introduction: Polycystic ovary syndrome (PCOS) is characterized by distinct metabolic heterogeneity, with insulin resistance representing a key pathophysiological feature. Given the limitations of insulin-based measures, non–insulin-based indices such as lipid accumulation product (LAP) have been proposed as simple and reliable marker of metabolic risk. However, data on the relationship between LAP, androgen-related parameters, and phenotypic metabolic heterogeneity in PCOS remain limited.

Subjects and Methods: This cross-sectional study included 200 women with PCOS, classified into phenotypes A–D according to the Rotterdam criteria (50 patients per group), and 50 healthy controls. Anthropometric, metabolic, and hormonal parameters were assessed. LAP was calculated using waist circumference and fasting triglyceride levels. Differences in LAP across study groups were analyzed using non-parametric methods, and associations between LAP and metabolic and hormonal parameters were evaluated using Spearman correlation analysis.

Results: The mean age of the study population was 26.2 ± 6.6 years, with no significant age differences between groups. Body mass index and waist circumference differed significantly across PCOS phenotypes and controls ($P < .001$). LAP values also differed significantly across study groups ($P < .001$), with higher values observed in hyperandrogenic PCOS phenotypes

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and lower values in phenotype D. In correlation analyses, LAP showed significant positive associations with body mass index ($r = 0.791$), waist circumference ($r = 0.885$), fasting insulin ($r = 0.369$), HOMA-IR ($r = 0.393$), triglycerides ($r = 0.760$), and free androgen index ($r = 0.411$), as well as significant negative associations with HDL-cholesterol ($r = -0.457$) and sex hormone–binding globulin ($r = -0.444$) (all $P < .001$). No significant correlation was observed between LAP and total testosterone. Similar patterns of association were confirmed when analyses were restricted to women with PCOS only.

Conclusions: LAP may represent a simple and clinically useful non–insulin-based marker for identifying metabolically unfavorable PCOS phenotypes, particularly those characterized by hyperandrogenism.

Abstract citation ID: lvag096.489

P345 - ECE_1583 - Impact of gender-affirming hormone treatment on body composition and muscle strength: 1-year follow-up data from a prospective study

Gesine Meyer[1], Anne-Sophie Fath[1], Kerstin Jacobs[1], Eva Herrmann[2] and Jörg Bojunga[1]
[1]*Endocrinology and Diabetes, Goethe University Frankfurt, University Hospital, Medical Clinic 1, Frankfurt, Germany;* [2]*Goethe University Frankfurt, Institute of Biostatistics and Mathematical Modelling, Frankfurt, Germany*

Objective: Several studies, predominantly using dual x-ray (DXA), showed rapid changes of body composition (BC) under virilising hormone treatment. However, the impact of muscle-building behaviour on these changes has not been considered so far.

Patients and Methods: Prospective measurement of BC using bioelectrical impedance analysis (BIA), hand-grip strenght and self-perception as well as workout habits using an established questionnaire (Drive for Muscularity Scale) in 42 transgender individuals ($n = 21$ transmen, $n = 21$ transwomen) before and 1 year after start of a gender-affirming hormone treatment (GAHT).

Results: During the first year pf GAHT body weight and BMI increased significantly in the entire cohort ($P = .015$, resp. $P = .024$). In transmen, BIA revealed a significant increase in lean body mass (+ 10.3%; $P < .001$) and a significant decrease in fat mass (−5.1%; $P = .02$). In transwomen lean body mass remain unchanged, while fat mass increased by 7.2%, though not significant. Hand-grip strength showed a significant increase in transmen (+8.8%; $P < .001$) and only a slight decrease in transwomen (−2.4%; n.s.). Muscularity-related cognition as well as behaviour did not change during the first year of GAHT. Differences of muscularity-related behaviour between transmen and transwomen were highly significant at both times of measurement ($P < .001$).

Conclusions: Our results of BIA are comparable to DXA measurements used in former studies, and demonstrate that virilising hormones lead to a significant increase of lean body mass and muscle strength in transmen even during the first year of treatment. According to former data, we could not see any significant changes in muscle mass or strength during the first year of a feminising hormone therapy. This is a remarkable finding, particularly considering the distinct lower degree of muscle-building behaviour in transwomen. A further measurement after five years of therapy will per performed to evaluate long-term effects.

Abstract citation ID: lvag096.490

P346 - ECE_3422 - Microglia rank signaling regulates GnRH neuronal function and the hypothalamic-pituitary-gonadal axis

Alejandro Collado Solé[1], Nozha Borjini[2,3,4], Jing Zhai[5,6], Francisco Ruiz-Pino[7,8], Gonzalo Soria-Alcaide[1], Cintia Folgueira[10], Celia García Vilela[11], Beatriz Romero-de la Rosa[7,8], Victor Lopez[1], Yassine Zouaghi[5,6], An Jacobs[12], Bella Mora-Romero[2,3,13], Alexandra Barranco[1], Guillermo Yoldi[14], Karine Rizzoti[15,16], Guadalupe Sabio[1,10], Gema Perez-Chacon[1], Patricia G. Santamaria[1], Jose Antonio Esteban[11], Nathalie Journiac[17,18], Vincent Prevot[17,18], Alberto Pascual[2,3], Manuel Tena-Sempere[7,8], Nelly Pitteloud[5,6] and Eva González Suárez[1,14]
[1]*Molecular Oncology, Spanish National Cancer Research Centre (CNIO), Madrid, Spain;* [2]*Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Spain, Seville, Spain;* [3]*Department of Medical Physiology and Biophysics, School of Medicine, University of Seville, Spain, Seville, Spain;* [4]*Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain;* [5]*Service of Endocrinology, Diabetology, and Metabolism, Lausanne University Hospital, Lausanne, Switzerland;* [6]*Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland;* [7]*Instituto Maimónides de Investigación Biomédica de Córdoba/Hospital Universitario Reina Sofia; Córdoba, Cordoba, Spain;* [8]*Department of Cell Biology, Physiology and Immunology, University of Córdoba, Cordoba, Spain;* [9]*CIBER Fisiopatología de la Obesidad y Nutrición, Instituto de Salud Carlos III, Córdoba, Spain;* [10]*Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain;* [11]*Department of Molecular Neuropathology, Centro de Biología Molecular Severo Ochoa (CSIC-UAM), Madrid, Spain;* [12]*Department of Medicine, Endocrinology, Diabetology, and Metabolism Unit, CHUV, Lausanne, Switzerland;* [13]*Departamento de Biología Celular, Facultad de Biología, Universidad de Sevilla, Seville, Spain;* [14]*Oncobell, Bellvitge Biomedical Research Institute, IDIBELL, Barcelona, Spain;* [15]*Laboratory of Stem Cell Biology and Developmental Genetics, The Francis Crick Institute, London, United Kingdom;* [16]*Centre for Endocrinology, William Harvey Research Institute, Faculty of Medicine and Dentistry, Queen Mary University of London,, London, United Kingdom;* [17]*Lille University, Inserm, CHU Lille, Lille Neuroscience and Cognition, UMR-S 1172, Labex DistAlz, Lille, France;* [18]*Laboratory of Development and Plasticity of the Neuroendocrine Brain, FHU 1000 Days for Health, EGID, Lille, France*

The hypothalamic-pituitary-gonadal axis (HPG) controls pubertal development, sexual maturation, and fertility. We hereby demonstrate a new role of hypothalamic microglia in controlling the HPG axis through Rank signaling, a pathway known for its role in bone and mammary gland biology. Whole-body and microglia Rank depletion leads to hypogonadotropic hypogonadism (HH) resulting from an alteration in gonadotropin-releasing hormone (GnRH) neuron function. In addition, we identify rare gene variants of *RANK* in patients with HH. Transcriptional profiling upon Rank loss reveals defective microglia activation and morphological alterations in the median

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

eminence, decreasing the contacts and engulfment of GnRH terminal projections and impairing GnRH neuronal responses to kisspeptin. Overall, our data uncover the role of microglia in regulating GnRH neuronal function through Rank signaling, with implications for reproductive maturation and fertility.

Abstract citation ID: lvag096.491

P347 - ECE_3228 - The use of pegvisomant to inhibit growth in a child with constitutional tall stature

Magdalena Stasiak, Renata Stawerska and Arkadiusz Zygmunt
Polish Mother's Memorial Hospital—Research Institute, Department of Endocrinology and Metabolic Diseases, Łódź, Poland

Constitutionally tall stature usually requires only the exclusion of gigantism, and no pharmacological treatment is necessary. However, when such height significantly exceeds the average height in a given population, it leads to peer rejection, a lack of self-acceptance, and, consequently, the development of depressive disorders.

Pegvisomant is a potent growth hormone (GH) receptor antagonist used in the treatment of acromegaly. This drug has not yet been reported to inhibit growth in children for indications other than pituitary gigantism.

We present the case of a 13-year-old boy whose height at the time of admission to our clinic was 195 cm and body weight 77 kg. His bone age was consistent with his chronological age. His predicted height based on his parents' height was 197.5 cm, and his final height, calculated using the Khamis-Roche formula, was 209.4 cm. Due to the growth prognosis, treatment with testosterone heptanoate was initiated at a dose of 200 mg every two weeks, and then—due to the lack of satisfactory efficacy—every 10 days. During treatment, bone age accelerated by 9 months, while height increased to 197 cm. The patient refused to continue treatment due to severe gynecomastia and height gain, as well as severe acne. At that moment, the calculated final height was 208 cm.

After obtaining approval from the bioethics committee, treatment with pegvisomant was initiated, using the standard dosage used in the treatment of acromegaly. An initial dose of 80 mg of pegvisomant was administered subcutaneously under medical supervision. Subsequently, the patient received 10 mg of the drug once daily. The boy self-administered the drug under his parents' supervision. During the 4-month treatment period significant growth retardation was observed (growth increased only by 1.4 cm) together with one-year bone age progression, although IGF-1 concentrations did not decrease below the reference range. As the initiation of the treatment took place exactly at the time of the beginning of the developmental growth spur, the initial IGF-1 concentration was 451.6 ng/mL (reference range 102-486) and it decreased to 230 ng/mL during treatment. The boy reported no side effects. No complications were observed during the 18-month follow-up. The final growth after growth completion is 199 cm, which is entirely acceptable for the patient.

Pegvisomant is an effective and safe treatment for patients with constitutionally very tall stature whose prognosed height significantly exceeds the height which can be psychologically accepted by a patient.

Abstract citation ID: lvag096.492

P349 - ECE_1673 - Multi-axis endocrine regulation of bone turnover in reproductive disorders

Jovanna Tsoutsouki[1,2], Edouard G Mills[1,2,3], Agathoklis Efthymiadis[1], Kanyada Koysombat[1], Megan Young[1], Sandhi Nyunt[1], Arthur Yeung[1], Aaran Patel[1], Maria Phylactou[1,2], Aureliane Pierret[1], Ali Abbara[1,2], Waljit Dhillo[1,2] and Alexander Comninos[1,2,3]
[1]*Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom;* [2]*Department of Endocrinology, Imperial College Healthcare NHS Trust, London, United Kingdom;* [3]*Endocrine Bone Unit, Imperial College Healthcare NHS Trust, London, United Kingdom*

Background: Bone health in reproductive disorders is traditionally attributed to oestrogen deficiency, neglecting that these conditions involve complex multi-axis endocrine perturbations. We hypothesised that bone turnover regulation reflects distinct endocrine signatures across reproductive states, challenging the purely oestrogen-centric paradigm.

Methods: We conducted a comparative cross-sectional study measuring fasting bone turnover markers (BTMs; P1NP, CTX) in hormonally-untreated women aged 20-36 years with distinct reproductive-endocrine phenotypes: healthy controls ($n = 26$), hypothalamic amenorrhoea (HA; $n = 29$), congenital hypogonadotrophic hypogonadism (CHH; $n = 9$), and polycystic ovary syndrome (PCOS; $n = 56$). Between-group differences were assessed using Kruskal-Wallis tests; within-group endocrine associations were evaluated using Spearman correlations.

Results: Bone turnover was markedly elevated in CHH (CTX 0.61 ng/mL; P1NP 86.7 ng/mL) compared with controls (CTX 0.38; P1NP 57.3), HA (CTX 0.39; P1NP 58.1), and PCOS (CTX 0.34; P1NP 53.1; all $P \leq .02$ compared to CHH). Interestingly, despite comparable oestradiol levels between CHH and HA, both resorption and formation markers were significantly higher in CHH, demonstrating that current sex-steroid exposure alone does not explain bone turnover patterns.

Androgens emerged as consistent positive correlates of bone turnover across all conditions. CTX correlated with androstenedione and dihydrotestosterone in controls ($r = 0.44$, $P = .04$) and HA ($r = 0.46$, $P = .03$), and with DHEAS in PCOS ($r = 0.29$, $P = .04$). P1NP correlated with dihydrotestosterone and androstenedione in controls ($r = 0.45–0.53$, $P < .03$) and HA ($r = 0.46–0.49$, $P < .03$), testosterone in PCOS ($r = 0.36$, $P = .01$), and strongly with DHEAS in CHH ($r = 0.82$, $P = .03$).

Condition-specific endocrine determinants were evident: in HA, P1NP correlated with markers of hypothalamic function (LH: $r = 0.51$, $P = .01$; oestradiol: $r = 0.53$, $P = .008$) and associated multi-axis disruption (IGF-1: $r = 0.44$, $P = .03$; fT3: $r = 0.49$, $P = .02$). In PCOS, CTX correlated inversely with BMI ($r = −0.31$, $P = .02$), suggesting adiposity-related suppression of bone resorption.

Conclusions: This comparative study reveals that bone turnover across reproductive-endocrine disorders reflects condition-specific endocrine regulation that extends beyond purely oestrogen exposure. Androgens demonstrate consistent anabolic associations, while HA and PCOS exhibit distinct multi-axis and metabolic modulation patterns. These findings challenge the traditional oestrogen-centric framework and support precision, phenotype-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

driven approaches to skeletal health assessment in reproductive endocrinology.

Abstract citation ID: lvag096.493

P350 - ECE_2546 - Steroid hormone levels across the menstrual cycle in women with PCOS: golden standard liquid-tandem mass spectrometry analysis

Meri-Maija Ollila[1], Sanni Parpala[1], Elisa Hurskainen[1], Marika Kangasniemi[1], Merja Häkkinen[2], Seppo Auriola[3], Matti Poutanen[4], Riikka Arffman[1] and Terhi Piltonen[5]
[1]*Department of Obstetrics and Gynaecology, Medical Research Center Oulu, Research Unit of Clinical Medicine, University of Oulu and Oulu University Hospital, Oulu, Finland;* [2]*Department of Public Health, Finnish Institute for Health and Welfare (THL), Kuopio, Finland;* [3]*Department of Health Sciences, School of Pharmacy, University of Eastern Finland, Kuopio, Finland;* [4]*Institute of Biomedicine, University of Turku, Research Centre for Integrative Physiology and Pharmacology, Turku, Finland;* [5]*Oulu, Finland*

Context: Women with PCOS are known to have alterations in the steroid hormone profile, yet there are no previous studies reporting different steroid hormone levels across menstrual cycle phases among the affected women analysed by liquid chromatography-tandem mass spectrometry (LC-MS).

Objective: To investigate the steroid hormone profile of women with PCOS according to menstrual cycle phases, with a special focus on ketosteroids.

Study Design: An age and BMI-matched case-control study including 89 women with PCOS and 80 control women, with multiple blood samples collected during different phases of the menstrual cycle.

Methods: Serum steroids were measured by LC-MS. Ovulation was detected by a urine test and confirmed by ultrasound. The baseline hormone levels were reported at the follicular phase. The changes in steroid hormone levels during the menstrual cycle between PCOS and control women were analysed using a generalized additive mixed model with five different time windows: cycle days [CD] CD 2-4, CD 6-8, and post ovulation luteinizing hormone level peak (LH)+2-3 days, LH+7-8 days, and LH +11-12 days.

Results: Serum testosterone ($P < .001$), free androgen index ($P < .001$), androstenedione ($P < .001$), progesterone ($P = .035$), 17α-hydroxyprogesterone ($P < .001$), 21-hydroxyprogesterone ($P = .035$) and estrone ($P < .001$) levels were significantly higher in women with PCOS compared to control women in the follicular phase of the menstrual cycle.

Serum levels of testosterone were 0.3 nmol/L higher (β = .33, 95% CI: 0.19-0.47, $P < .001$), androstenedione levels were 1.9 nmol/L higher (β = 1.86, 95% CI: 1.11-2.61, $P < .001$) and FAI was 0.8 higher (β = .82, 95% CI: 0.49-1.15, $P < .001$) throughout the menstrual cycle in women with PCOS compared to controls, and the levels changed non-linearly during menstrual cycle both in women with and without PCOS ($P < .001$ for all comparisons).

11-ketotestosterone (β = .06, 95% CI: −0.09-0.22, $P = .446$), 11-ketoandrostenedione β = .0003, 95% CI: −0.181-0.181, $P = .998$), and 11β-hydroxy-testosterone levels (β -.021, 95% CI: −0.092-0.051, $P = .569$) were comparable between PCOS and control women across the menstrual cycle.

Conclusions: Women with PCOS have significantly higher serum testosterone, androstenedione, and FAI levels than control women, regardless of menstrual cycle phase. In addition, in contrast to some previously published studies, levels of 11-oxygenated androgens measured were similar in women with and without PCOS with white European ethnicity, and the levels remained stable throughout the menstrual cycle.

Abstract citation ID: lvag096.494

P351 - ECE_2641 - Cortisol and stress levels in women with functional hypothalamic amenorrhoea (FHA) and polycystic ovary syndrome (PCOS)

Aureliane Pierret[1], Arthur Yeung[1], Kanyada Koysombat[1,2], Bijal Patel[1,2], Megan Young[1], Maria Phylactou[1,2], Jovanna Tsoutsouki[1], Sandhi Nyunt[1,2], Aaran Patel[1], Elisabeth Daniels[1], Ambreen Qayum[1,2], Pei Eng[1,2], Elizaveta Sheremetyeva[1,3], Edouard G Mills[1,2], Simon Hanassab[1,3], Channa Jayasena[1,2], Tricia Tan[1,2], Sophie Clarke[4], Alexander Comninos[1,2], Ali Abbara[1,2] and Waljit Dhillo[1,2]
[1]*Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom;* [2]*Department of Endocrinology, Imperial College Healthcare NHS Trust, London, United Kingdom;* [3]*Department of Computing, Imperial College London, London, United Kingdom;* [4]*University College Hospitals NHS Foundation Trust, London, United Kingdom*

Background: Menstrual disturbance affects one fifth of young women; the two commonest causes are functional hypothalamic amenorrhoea (FHA) and polycystic ovary syndrome (PCOS). Psychological stress is a key component of FHA, along with reduced energy availability and genetic susceptibility. FHA is associated with central hypercortisolism, with increased corticotrophin releasing hormone (CRH) believed to contribute to the reduction in GnRH neuronal activity. PCOS, which typically has increased GnRH neuronal activity, is also associated with psychological morbidity with increased rates of anxiety and depression. There are limited data directly comparing stress and cortisol in women with menstrual disturbance from different aetiologies.

Methods: We examined measures of stress and serum cortisol in women aged 18-35 years with FHA or PCOS, and healthy controls. Perceived stress was quantified using the validated perceived stress scale (PSS) and reported as mean (standard deviation). Group differences were calculated using one-way ANOVA with post-hoc Sidak's multiple comparisons test. 8am serm cortisol and ACTH concentrations were quantified using immunoassays and reported as median (IQR). Group differences were assessed using Krusak-Wallis with post-hoc Dunn's multiple comparisons test.

Results: We included 45 healthy controls, 37 women with FHA and 70 women with PCOS ($n = 46$ non-obese; $n = 24$ obese). PSS scores were similar between healthy women [13.08 (4.25)] and those with HA [16.62 (4.11), $P = .2048$], but significantly higher in PCOS [18.81 (6.642)] compared to healthy women ($P = .0005$). PSS scores did not differ with obesity in women with PCOS ($P = .8$). Serum cortisol (nmol/L) was significantly lower in PCOS [298.9 (237.1, 348.8)] than in FHA [374.1 (295.1, 435.4),

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

$P = .0099$], or healthy controls [389.5 (281.9, 470.2), $P = .0079$]. Cortisol trended lower in women with PCOS and obesity compared to those without, but did not reach statistical significance ($P = .13$). ACTH did not differ between the groups ($P > .8$).

Conclusions: In contrast to the expected association of FHA with stress, PSS scores and cortisol concentrations were not higher in FHA than in healthy women. Although women with PCOS had higher PSS scores, cortisol concentrations were lower than in healthy women or women with FHA. Cortisol concentrations are known to be reduced with obesity; however, we did not observe a significant reduction in cortisol concentrations with obesity in women with PCOS. Our data highlight the challenge in accurately distinguishing these two common causes of menstrual disturbance and that increased stress scores do not necessarily implicate FHA as the underlying aetiology.

Abstract citation ID: lvag096.495

P352 - ECE_2645 - Characterisation of pro-inflammatory cytokine profile across different BMI thresholds in women with Polycystic Ovary Syndrome

Martina Curcio[1,2], Fannie Lajeunesse-Trempe[3,4], Georgios K. Dimitriadis[1,5,6] and Royce Vincent[1,5]
[1]*King's College Hospital NHS Foundation Trust, London, United Kingdom;* [2]*Università Cattolica del Sacro Cuore, UCSC, Rome, Italy;* [3]*Quebec Heart and Lung Institute, Laval University, Quebec, Canada;* [4]*Nutrition Faculty, Laval University, Quebec, Canada;* [5]*Faculty of Life Sciences and Medicine, King's College, London, United Kingdom;* [6]*Eli Lilly and Company, Indianapolis, United States*

Background: Polycystic Ovarian Syndrome (PCOS) is an endocrine disorder affecting women of reproductive age, characterised by hyperandrogenism, menstrual irregularities, and the presence of polycystic ovaries. Pro-inflammatory cytokines, including interleukins (IL) and tumour necrosis factor (TNF), are elevated in both PCOS and in those with obesity, driving cardiovascular risk. Our aim was to characterise cytokine profiles across a wide range of body mass index (BMI) categories in women with and without PCOS.

Methods: Serum cytokine (IL-6, IL-1β, IL-8, TNF-α) levels from patients with and without PCOS presenting to a London teaching hospital were retrospectively analysed. Patients were classified into three groups, healthy-weight PCOS (BMI 18.5-24.9 kg/m^2; $n = 18$), PCOS with obesity (BMI ≥ 30 kg/m^2; $n = 29$), and with obesity but without PCOS ($n = 72$). Age was matched and BMI was adjusted to minimize confounding. Python (v3.14) was used for statistical analysis. Between-group comparisons were performed using one-way ANOVA, preceded by Levene's test for equality of variances. For localization of differences, Mann–Whitney U tests with Bonferroni correction were applied. Data are reported as median (IQR), and a $P < .05$ was considered statistically significant.

Results: Healthy-weight PCOS women exhibited higher TNF-α [14.6 (9.9-24.1) ng/L] than PCOS with obesity [9.7 (8.9-12.0) ng/L] and with obesity but without PCOS [11.9 (9.7-15.7) ng/L]. IL-1β showed a trend toward increased concentrations in healthy-weight PCOS women, compared with the other groups, but did not reach statistical significance. IL-6 and IL-8 were comparable between groups. No significant correlations were observed between cytokines and BMI in either the PCOS or non-PCOS groups. In PCOS women, TNF-α and IL-1β displayed a mild inverse trend with BMI ($r = -0.14$ and -0.09, respectively).

Conclusions: Healthy-weight PCOS women show a notable elevation of TNF-α, consistent with a BMI-independent inflammatory activation, possibly linked to intrinsic androgen or metabolic dysregulation. A limitation of these data is not assessing central adiposity or weight-to-height ratio. Larger studies are needed to better understand the higher inflammatory burden in women with PCOS and healthy weight.

Abstract citation ID: lvag096.496

P353 - ECE_3559 - Genetic variation in the gonadotropin signaling pathway and its role in PCOS pathogenesis

Giangela Stokes[1], Chloe Parker[1], Margrit Ubranek[1], Richard Legro[2] and Corrine Welt[3]
[1]*Northwestern University, Chicago, United States;* [2]*Penn State, Hershey, United States;* [3]*University of Utah, Salt Lake City, United States*

Background: Polycystic ovary syndrome (PCOS) is a common, complex endocrinopathy affecting 6-20% of reproductive age women. It is defined by elevated androgens, irregular or absent periods, and polycystic ovarian morphology. Physiological conditions contributing to PCOS pathogenesis include insulin resistance, and ovulatory and gonadotropin signaling dysfunction. Twin and family studies have shown PCOS to be highly heritable, and genome-wide association studies (GWAS) implicate several PCOS susceptibility loci near genes involved in gonadotropin and hypothalamic-pituitary secretion. The gonadotropin hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH), are neuroendocrine hormones that direct follicle development and overall ovarian health. Reproductive neuroendocrine dysfunction is a major pathophysiological component of PCOS. Women with PCOS have elevated LH levels contributing to hyperandrogenism and oligo/anovulation— two cardinal characteristics of PCOS.

Objective: Determine the impact of pathogenic variants in the gonadotropin signaling pathway on PCOS pathogenesis and elucidate the molecular mechanisms of impaired gonadotropin signaling.

Methods: To determine how disease-causing gonadotropin signaling variants contribute to PCOS pathogenesis, we sequenced the gonadotropin genes *FSHR, FSHB, LHCGR,* and *LHB* in two independent cohorts of women with PCOS. To elucidate the molecular mechanisms of gonadotropin signaling dysfunction, we used a cAMP assay to screen *FSHR* variants for impaired function.

Results: We found significant and reproducible evidence for association between variants in *FSHR* and *LHCGR* and PCOS ($P < 1e\text{-}15$) in two independent cohorts. We found that variation in *FSHB* is significantly associated with PCOS in our discovery cohort ($P < 1e\text{-}5$) and nominally associated in our replication cohort ($P = .02$). We identified 27 potentially pathogenic variants (PPVs) across the four gonadotropin genes in two independent cohorts.

Conclusions: *FSHR* variants have been identified in reproductive disorders such as hypogonadotropic hypogonadism (HH) or primary ovarian insufficiency (POI), but no pathogenic *FSHR*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

variants have identified in PCOS. We identified 26 PPVs in *FSHR* in two independent cohorts of women with PCOS. These studies demonstrate that rare variation in the gonadotropin signaling pathway is significantly enriched in PCOS, providing substantial evidence for their role in PCOS pathogenesis. Identifying and understanding genetic contributions to complex endocrinopathies like PCOS can increase our ability to find causal variants and improve treatment efficacy.

Abstract citation ID: lvag096.497

P354 - ECE_3594 - Triiodothyronine (T3) as a regulator of insulin receptor (INSR) expression in epithelial ovarian cancer

Aleksandra Sirek, Anna Ptak and Justyna Gogola-Mruk
Laboratory of Physiology and Toxicology of Reproduction, Jagiellonian University, Institute of Zoology and Biomedical Research, Kraków, Poland

Epidemiological and clinical data link thyroid dysfunction with ovarian cancer (OC) risk, progression, and prognosis, yet underlying molecular mechanisms remain unclear. Increasing evidence suggests that thyroid hormones, particularly triiodothyronine (T_3), may modulate processes in OC not only through classical genomic mechanisms mediated by nuclear thyroid hormone receptors (TRα, TRβ), whose expression has been demonstrated in ovarian tissue, but also indirectly by regulating the expression and secretion of other metabolic hormones. A key component of these pathways is the insulin receptor (INSR), which regulates cellular metabolism and proliferation.

The aim of this study was to assess the expression and prognostic significance of *INSR*, in OC and to investigate the dose-dependent effect of T_3 on INSR mRNA expression level in epithelial ovarian cancer (EOC).

SKOV-3 and COV318 cell lines, representing EOC, were cultured as 3D spheroids and treated with T_3 at concentrations reflecting physiological (1 nM), hypothyroid (0.1 nM), and hyperthyroid (10 nM) conditions. Basal expression of *TRα*, *TRβ*, and *INSR* as well, as changes in *INSR* expression following T_3 exposure in SKOV-3 and COV318 cells were quantified by RT-qPCR. Gene expression (mRNA level) in OC tissues was analyzed using GEPIA (http://gepia.cancer-pku.cn). Moreover, the association between INSR expression levels and the survival of OC patients was analyzed using the Kaplan–Meier plotter (https://kmplot.com/analysis).

Basal expression analysis revealed expression of *TRα* and *TRβ* and INSR in both analyzed EOC cell lines. Higher levels of *TRα* and *TRβ* in SKOV-3 compared to COV318 was observed. *INSR* expression level was similar in both EOC lines. Additionally, bioinformatic analysis confirmed that *INSR* mRNA expression was significantly downregulated in OC tissue ($n = 426$) compared to normal tissue ($n = 88$; $P < .05$). However, survival analysis showed that high *INSR* expression was not significantly associated with overall survival (OS) or progression-free survival (PFS), although a protective trend was observed (HR < 1). Interestingly, exposure to T_3 resulted in a reduction of INSR expression in both SKOV-3 and COV318 cell lines at concentrations of 1 nM and 10 nM, whereas at 0.1 nM only a non-significant downward trend was observed.

To sum up, thyroid hormone signaling, particularly via T_3, may influence on progression of EOC that express *TRα* and *TRβ* gene through modulation of *INSR* expression. T_3 mediated regulation of *INSR* suggests involvement of metabolic signaling pathways, with potential prognostic and therapeutic implications.

Abstract citation ID: lvag096.498

P355 - ECE_2205 - Menstrual disorders' risk factors in young women

Alla Shepelkevich, Eleonora Kislach and Diana Baalbaki
Endocrinology, Belarusian State Medical University, Minsk, Belarus

Background: Menstrual disorders are a spectrum of conditions that pose a prevalent challenge among young women. They can adversely impact the quality of life by significantly raising the risk of reproductive and long-term complications (metabolic and cardiovascular diseases), as well as an increased likelihood of premature mortality. Establishing diagnosis requires thorough medical investigation; for instance, secondary amenorrhea where evaluation of factors, like chronic stress, energy deficiency, excessive exercise, and sleep disturbances, is crucial for timely intervention.

Objectives: To assess menstrual disorders and secondary amenorrhea frequency in young women, and evaluate their behavioral and clinical risk factors.

Methods: A cross-sectional survey was conducted using questionnaires on general demographic and anthropometric data, menstrual cycle characteristics (regularity, menarche age, history of amenorrhea, chronic conditions and medication anamnesis), eating behavior (based on the Dutch Eating Behavior Questionnaire—DEBQ), stress level (Reeder Stress Inventory—RSI), physical activity (International Physical Activity Questionnaire—IPAQ), and assessment of sleep quality.

Results: Of the 940 participants (age 18-30), 750 (79.8%) had a regular menstrual cycle (21-35 days), while 190 (20.2%) had an irregular cycle; the latter's median age was 21 years with menarche age—13 years. Secondary amenorrhea was found in 48 participants (5.1%). Polycystic ovary syndrome was detected in 16.84% of participants with menstrual irregularities, hypothyroidism—4.74%, and hyperprolactinemia—3.16%. BMI was within the normal range in 67.9% of participants, whereas 17.9% were underweight and 14.2% were overweight or obese. Psychotropic (11.1%) medications were the most commonly reported. According to DEBQ, eating disorders were identified in 90.5% of women with irregular menstrual cycles: external type was observed in 83.1%, emotional—70.9%, and restrictive—57%. Using RSI, stress levels were high in 20.5%, moderate—57.9%, and low—21.6%. Based on IPAQ, our participants were mostly physically inactive—52.1%, insufficiently active—34.2%, and only 13.7% had optimal activity. Poor sleep quality was reported by 73.7% of participants with menstrual irregularities.

Conclusions: Menstrual disorders are observed in a significant number of young women—20.2% (secondary amenorrhea—5.1%). They were more likely to experience eating disorders, insufficient physical activity, high and moderate stress levels, and sleep problems. This highlights the importance of an in-depth assessment of behavioral and clinical factors of menstrual

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

health for early prevention of reproductive and metabolic complications.

Abstract citation ID: lvag096.499

P356 - ECE_2765 - Primary hypogonadism following open abdominal aortic aneurysm repair: an under-recognised complication?

Hafiz Awais Javed, Daisy Beard and Joohi Majeed
Endocrinology, Bury St Edmunds, West Suffolk Hospital, United Kingdom

Abdominal aortic aneurysm (AAA) is a major health concern with curative surgery requiring open or endovascular aortic repair (EVAR). Transient secondary (hypogonadotrophic) hypogonadism post-operatively is relatively common due to surgical stress or opioid analgesia. Primary (hypergonadotropic) hypogonadism is rare and usually permanent. Mechanisms include compromised gonadal blood supply through cross-clamping (open repair), inadvertent vessel ligation, thrombosis or microembolisation. We describe a case of de novo primary hypogonadism following open AAA repair.

A 67-year-old man underwent elective open repair of a 5.5 cm infrarenal AAA in December 2024. His peri-operative course was uncomplicated. He had no prior history of orchitis, testicular trauma, chemotherapy or radiotherapy. He had fathered two children and reported normal sexual function and secondary sexual characteristics prior to surgery. A few months post-operatively, he developed episodic sweating and hot flushes. His body hair, shaved pre-operatively, had failed to regrow over the axillae, torso, and pubic region and facial shaving was reduced to alternate days from daily. He had gained a stone in weight, attributed to smoking cessation pre-operatively. He also reported loss of spontaneous erections and reduced libido. There had not been any testicular pain.

On examination, he appeared hypogonadal, with loss of secondary sexual characteristics and small, soft, non-tender testes.

Testing in primary care in April 2025 had demonstrated undetectable 09:00 hrs testosterone (<0.09 nmol/L), mildly elevated prolactin (824 mIU/L), normal TSH (1.03 mIU/L) and low cortisol (115 nmol/L). Endocrine evaluation in May 2025 confirmed severe **primary hypogonadism** with low 09:00 hrs testosterone (1.82 nmol/L) and elevated gonadotropins (FSH 22.4 IU/L, LH 12 IU/L). Prolactin (290 mIU/L), thyroid function and cortisol (449 nmol/L) were normal. Testicular ultrasound doppler in December 2025 confirmed testicular atrophy, with bilateral small testes measuring 2.5 cm, showing uniform echotexture and preserved, albeit reduced, vascular flow.

Following testosterone replacement, his sweats settled, spontaneous erections returned and body hair regrowth resumed.

The temporal relationship of the presentation of primary hypogonadism to AAA repair strongly suggests a link and the ultrasound findings suggest it is permanent. This is theoretically more likely after open repair due to the increased and prolonged insult, including aortic cross-clamping. However, while there are reported cases of primary hypogonadism occuring after EVAR, we believe this is the first reported case occuring after open repair. Clinicians may need to consider androgen deficiency in men presenting with persistent non-specific symptoms post-AAA repair, including weight gain, loss of energy and libido.

Abstract citation ID: lvag096.500

P357 - ECE_2016 - Adiposity and male reproductive function in young men

Wiwat Rodprasert[1,2], Jorma Toppari[1,3,4], Heidi Elamo[1], Kreeta Viitala[1], Helena Ollila[5], Niels Erik Skakkebæk[6,7], Niels Joergensen[6,7], Katharina M. Main[7] and Helena Virtanen[1,4]
[1]*University of Turku, Research Centre for Integrative Physiology and Pharmacology, Institute of Biomedicine, Turku, Finland;* [2]*Division of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand;* [3]*Department of Pediatrics, Turku University Hospital, Turku, Finland;* [4]*Centre for Population Health Research, University of Turku and Turku University Hospital, Turku, Finland;* [5]*Department of Biostatistics, University of Turku and Turku University Hospital, Turku, Finland;* [6]*Department of Growth and Reproduction, Copenhagen University Hospital—Rigshospitalet, Copenhagen, Denmark;* [7]*Copenhagen University Hospital—Rigshospitalet and University of Copenhagen, International Centre for Research and Research Training in Endocrine Disruption of Male Reproduction and Child Health (EDMaRC), Copenhagen, Denmark*

Background: Adiposity has been associated with reduced total testosterone (TT) levels, while findings on free testosterone (FT) and semen quality are inconsistent. The roles of different fat regions in reproductive health remain unclear. This study investigated the relationship of adiposity with hypothalamic–pituitary–gonadal axis hormones and semen quality in Finnish men.

Methods: This cross-sectional study included men aged 18-23 years (mean 20.8, SD 0.98) from Turku, Finland. Participants completed questionnaires, underwent andrological examination and dual-energy X-ray absorptiometry (DXA), and provided blood and semen samples. DXA-derived fat mass index (FMI; fat mass [kg]/height^2 [m^2]) was categorized into quartiles. Serum hormone levels were measured at Rigshospitalet, Copenhagen, Denmark, and semen analysis followed the 5th WHO manual. FT level was calculated using Vermeulen's formula, and FT percentage was calculated as FT/TT × 100). Multivariable linear regression compared hormone and semen variables across FMI quartiles, adjusting for age, smoking, cryptorchidism, and andrological diseases. Separate regression analyses assessed associations between total, visceral, and leg fat mass and hormone levels.

Results: A total of 286 Finnish men provided semen samples and underwent DXA scanning; hormone levels were available in 179 men. Higher FMI quartiles were associated with lower adjusted TT and SHBG levels and higher FT percentage compared with lower quartiles (all $P < .001$). Inhibin B levels were lower in the highest versus the lowest FMI quartile ($P = .011$), and LH levels were lower in the highest versus the 3rd quartile ($P = .04$). However, calculated FT, FSH, estradiol levels, sperm concentration, total sperm count, total motility, and percentage of sperm with normal morphology did not differ across FMI quartiles. Adjusted semen volume was lower in the highest compared with the 3rd FMI quartile ($P < .001$). Standardized regression analyses demonstrated inverse associations between TT and total body fat ($\beta = -.376$; 95% CI [−2.705, −1.277]), visceral fat ($\beta = -.306$; 95% CI [−2.324, −0.876]), and leg fat ($\beta = -.319$; 95% CI [−2.439, −0.960]). Associations of total, visceral, and peripheral fat mass with all testosterone variables were similar.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: In young men, higher adiposity was associated with lower TT, mainly due to lower SHBG levels, whereas FT and semen quality were generally unaffected. Inhibin B levels were reduced only in men with the highest adiposity. Visceral and peripheral fat mass had a similar association with TT. These findings are in line with earlier BMI- and weight-based studies.

Abstract citation ID: lvag096.501

P358 - ECE_3215 - Diffusion-generated synthetic testicular ultrasound images for AI development in male infertility assessment

Daniele Renda Livraghi[1,2], Giorgia Spaggiari[1,2,3], Antonio Granata[1,3], Carlotta Pozza[4], Marta Tenuta[4], Andrea Isidori[4], Manuela Simoni[1,2], Nicola Morelli[5], Kevin Marchesini[5], Federico Bolelli[5], Costantino Grana[5] and Daniele Santi[1,2,3]

[1]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [2]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [3]Bentivoglio (Bologna), Italy; [4]Section of Medical Pathophysiology and Endocrinology, Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy; [5]Enzo Ferrari Department of Engineering, University of Modena and Reggio Emilia, Modena, Italy

Background: Testicular ultrasound is a cornerstone of male infertility assessment, particularly considering testicular volume and parenchymal inhomogeneity as key parameters associated with spermatogenic function. However, testicular parenchymal echogenicity assessment suffers from substantial operator dependency, limiting reproducibility and standardization. Artificial intelligence (AI) approaches offer transformative potential to convert subjective ultrasound features into objective, quantitative biomarkers. Nevertheless, the development of robust AI models is severely constrained by limited availability of large, shareable testicular ultrasound datasets due to privacy regulations and data scarcity. Denoising Diffusion Probabilistic Models (DDPMs) have demonstrated remarkable success in generating high-quality synthetic medical images across multiple modalities, yet their application to testicular ultrasound remains unexplored.

Aim of the Study: To investigate DDPMs to synthesize realistic B-mode testicular ultrasound images as privacy-preserving surrogates for AI model development and validation.

Methods: Synthetic image quality was rigorously evaluated through quantitative distribution-level metrics and a clinician-driven Visual Turing Test involving endocrinologists with varying expertise levels from two clinical centres (Modena and Rome). A two-stage filtering pipeline ensured feature-space consistency and anatomical plausibility. Images utility was assessed through two downstream tasks: (i) self-supervised pretraining for binary classification of testicular parenchymal homogeneity versus inhomogeneity and (ii) training of segmentation models for testicular region delineation, with synthetic data fully replacing real images during training.

Results: Twenty-two endocrinologists were involved and all of them, irrespective to their clinical expertise, evaluated 200 testicular images. All subjects were unable to reliably distinguish synthetic from real ultrasound images (accuracy:0.493 ± 0.092, sensitivity:0.473 ± 0.127, specificity:0.511 ± 0.154, d-prime -0.037), confirming visual realism. In downstream classification tasks, self-supervised pretraining on synthetic testicular images significantly improved performance compared to training from scratch and achieved results comparable to pretraining on real ultrasound data. Segmentation models trained exclusively on synthetic images achieved Dice similarity coefficients on real test images nearly equivalent to those obtained when training on real datasets, demonstrating effective substitutability. Application of the two-stage filtering pipeline further enhanced downstream task performance, validating the importance of quality control in synthetic data generation.

Conclusions: This study provides the first evidence that diffusion-generated synthetic testicular ultrasound images are visually realistic and useful for AI model development in male reproductive medicine. Our findings demonstrate that generative AI can provide privacy-preserving, scalable surrogate datasets that enable robust development of AI tools for objective assessment of testicular parenchymal characteristics. This approach has significant implications for advancing AI-assisted reproductive endocrinology while maintaining patient privacy and overcoming data scarcity limitations inherent to specialized medical imaging domains.

Abstract citation ID: lvag096.502

P360 - ECE_2498 - The impact of oral glucose tolerance test shape in the pathophysiology of women with polycystic ovary syndrome. Evidence from a large European cohort

Sarantis Livadas[1], Nicholas Angelopoulos[1], Dimitrios Papadimitriou[2], Jelica Bjekic Macut[3], Justyna Kuliczkowska-Płaksej[4], Ralitsa Robeva[5], Uglješa Barać, Tamara Baltić[3], Rodis Paparodis[1], Andrzej Milewicz[4,7], Andromahi Vryonidou[8], Vaia Lambadiari[9], George Mastorakos[10] and Djuro MacUt

[1]Hellenic Endocrine Network, Athens, Greece; [2]Department of Pediatrics, Neonatal-Pediatric-Adolescent Endocrinology & Diabetes, Faculty of Medicine, University of Thessaly, Larisa, Greece; [3]Department of Endocrinology, KBC Bežanijska kosa, belgrade; [4]Department of Endocrinology, Diabetology and Isotope Therapy, University of Medicine, Wroclaw, Poland; [5]Department of Endocrinology, Faculty of Medicine, Medical University, Ushate 'acad. IV. Penchev', Sofia, Bulgaria; [6]Clinic for Endocrinology, Diabetes and Metabolic Diseases, belgrade; [7]School of Medicine, Wrocław, Poland; [8]Department of Endocrinology and Diabetes, Hellenic Red Cross Hospital, Athens, Greece; [9]2nd Propaedeutic Department of Internal Medicine, Research Unit and Diabetes Center, Attikon University Hospital, Athens, Greece; [10]Division of Endocrinology, Diabetes and Metabolism, Aretaieion University Hospital, Athens, Greece

Background: Emerging data have shown that the shape of the glucose response curve during oral glucose tolerance test (OGTT) provides useful insights into insulin dynamics. A monophasic shape is defined as a simple increase to a peak with a subsequent decrease, whereas the biphasic shape was defined as a rise followed by a decrease and a subsequent increase ≥4.5 mg/

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

dL after the decline in glucose. However, the impact of these patterns, if any, on the pathophysiology of PCOS has not been fully elucidated yet.

Aim of the Study: To assess the association of OGTT shape with metabolic—hormonal profile in PCOS.

Methods: Data from 1328 women with PCOS with a mean age of 27.0 and BMI 26.7 kg/m^2 were analyzed and findings are presented before and after adjustment for age, BMI and area under the curve for glycemia (AUC).

Results: 461 subjects (34.7%) demonstrated a biphasic glucose response. The prevalence of impaired glucose tolerance (IGT) was higher in the biphasic group (20% vs 15%, *P*:.015), as well as testosterone levels (2.70 vs 2.58 mmol/L, *P*:.01) while HOMA-IR values, hormonal and lipid parameters were comparable among subgroups. Biphasic group was characterized by substantially lower glucose concentrations at 30-90′ and higher 120′ glucose levels, resulting in lower total glucose exposure (AUC_{0-120}) and markedly different late-phase slopes (ΔGLU60–90 and ΔGLU90–120), after adjustment for age and BMI. After adjustment for age and BMI the biphasic OGTT pattern remained strongly associated glucose values (30-90 min) and lower AUC_{0-120}, while exhibiting higher 120-minute glucose and it was also associated with higher odds of IGT. The favorable association of a biphasic response with lower glycemia was stronger at younger ages and progressively attenuated with increasing age (*P*: .0026). Also, an inverse relationship between AUC with increasing BMI was observed. Significant association between biphasic OGTT and testosterone (*P*:.002), FAI (*P*:.036) and DHEAS (*P*:.047) levels were disclosed after adjustment for age, BMI and AUC.

Conclusions: In our cohort those with biphasic OGTT exhibited lower early and mid-phase glucose values and lower total glucose exposure, and higher prevalence of IGT. However, younger age and normal weight are associated with less glycemic load. Furthermore, biphasic OGTT even after adjustment for age, BMI, and total glucose exposure was independently associated with higher androgen bioavailability. This finding suggests a potential link between OGTT glucose dynamics and steroidogenic regulation in PCOS.

Abstract citation ID: lvag096.503

P361 - ECE_3974 - Efficacy and safety of a therapeutic humanized FSH–blocking antibody in obesity and Alzheimer's disease models

Anusha Pallapati, Funda Korkmaz, Satish Rojekar, Steven Sims, Judit Gimenez-Roig, Anisa Gumerova, Uliana Cheliadinova, Anne McDonald, Vitaly Ryu, Ofer Moldavski, Tal Frolinger, Tony Yuen and Mone Zaidi
New York, United States

There is growing evidence for direct actions of follicle–stimulating hormone (FSH) on tissues other than the ovaries and testes. Blocking FSH action, either genetically or pharmacologically, protects against bone loss, fat gain, and memory loss in mice. We thus developed a humanized FSH–blocking antibody—MS-Hu6—as a lead therapeutic for three diseases of public health magnitude—osteoporosis, obesity and Alzheimer's disease (AD) that track together in post–menopausal women. Here, we report the crystal structure of MS-Hu6 and its interaction with FSH in atomistic detail. Using our Good Laboratory Practice (GLP) platform (21CFR58), we formulated MS-Hu6 and the murine equivalent Hf2 at an ultra–high concentration; both formulated antibodies displayed enhanced thermal and colloidal stability. A single injection of ^{89}Zr–labelled MS-Hu6 revealed a β–phase $t_{½}$ of 89 and 131 hours for female and male mice, respectively, with retention in regions of interest. Female mice injected subcutaneously with Hf2 displayed a dose–dependent reduction in body weight and body fat, in the face of reduced free (bioavailable) FSH and unperturbed estrogen levels. Hf2 also rescued recognition memory and spatial learning loss in a context– and time–dependent manner in AD–prone *3xTg* and *APP/PS1* mice. MS-Hu6 injected into African green monkeys (8 mg/kg) intravenously, and then subcutaneously at monthly intervals, was safe, and without effects on vitals, blood chemistries or blood counts. There was a notable ~4% weight loss in all four monkeys after the first injection, which continued in two of four monkeys. We thus provide IND–enabling data towards an upcoming first–in–human study.

Abstract citation ID: lvag096.504

P363 - ECE_1283 - The effect of submaximal doses of semaglutide with metformin on fertility outcomes in obese PCOS patients: a prospective observational study

Tomáš Bolek[1], Ivana Ságová[2], Matej Samoš[2], Peter Tudik[2] and Marian Mokan[3]
[1]*Jessenius faculty of medicine in Martin, Commenius University in Bratislava, Martin—Jahodníky;* [2]*Department of internal medicine 1st, Martin, Slovakia;* [3]*Department of internal medicine 1st, Martin—Jahodníky, Slovakia*

Background: Obesity-associated polycystic ovary syndrome (PCOS) is strongly linked to anovulation, subfertility, and adverse metabolic and pregnancy outcomes. While lifestyle modification and metformin alone often yield limited benefits, GLP-1 receptor agonists have shown promising metabolic and endocrine effects. Evidence on fertility outcomes using submaximal doses of semaglutide in combination with metformin remains scarce.

Aim: To assess menstrual and fertility outcomes following treatment with submaximal doses of semaglutide plus metformin in obese PCOS patients with secondary amenorrhea.

Methods: This prospective observational study included 20 obese PCOS patients (age 23-42; BMI 34.8 ± 4.3 kg/m^2) with amenorrhea. Patients were treated with metformin 1000 mg/day and semaglutide at submaximal doses (0.25-0.5-1.0 mg weekly), combined with standardized lifestyle counseling. Semaglutide was discontinued 30-60 days prior to planned conception. Follow-up lasted 6-8 months. Primary outcomes were menstrual normalization and pregnancy rate. Secondary outcomes included body composition changes and gestational outcomes.

Results: Normalization of menstrual cycles occurred in all participants within 3 months. Pregnancy was achieved in 12/20 patients (60%), all spontaneous. No gestational diabetes was observed on OGTT. Mean delivery occurred at 38 ± 2 weeks. Neonatal mean birthweight was 3400 ± 600 g (all eutrophic).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Significant improvements were observed in fat mass reduction and lean mass increase after 3 months of therapy.

Conclusions: Treatment with submaximal-dose semaglutide combined with low-dose metformin resulted in substantial menstrual recovery and a high rate of spontaneous conception in obese PCOS patients with prediabetes. Favorable pregnancy outcomes were observed despite discontinuation of therapy before conception. These findings highlight the potential of lower-dose GLP-1RA/metformin combination therapy as an effective preconception strategy in PCOS. Randomized controlled trials are needed to confirm these results.

Abstract citation ID: lvag096.505

P364 - ECE_3399 - Assessment of the performance of a routine progesterone assay using a novel high sensitivity LC-MS/MS method

Jonathan S Atkins and Brian Keevil
Department of Clinical Biochemistry, Manchester University NHS Foundation Trust, Manchester, United Kingdom

Introduction: Measurement of luteal phase serum progesterone is indicated to assess ovulatory function in female patients presenting with possible infertility. Progesterone concentrations peak 7 days following ovulation and can be measured to confirm occurrence of ovulation in patients with regular menstrual cycles. The predominant method of measuring progesterone in the UK is immunoassay. These are known to have variable performance when measuring steroid hormones due to non-specific binding of structurally similar steroids and issues liberating steroids from binding proteins for analysis to occur. Here, we aimed to develop an LC-MS/MS method to measure progesterone in serum and apply it to assess the performance of a routine immunoassay.

Methods: The method was developed on a Waters TQ-XS mass spectrometer. Calibrators and quality controls were gravimetrically prepared from separate stocks of certified reference material. The method utilised a 96-well plate format, with a progesterone-2,3,4-$^{13}C_3$ internal standard. Extraction was performed using supported liquid extraction with MTBE. Male samples ($n = 74$), were spiked with a methanolic progesterone standard to concentrations spanning the analytical range. These were analysed using the Roche Elecsys Progesterone III electrochemiluminescence immunoassay and results were compared to those produced using LC-MS/MS.

Results: Progesterone and its internal standard eluted with a symmetrical peak at 3.3 minutes. Concentrations ranging from 0.025 to 54 nmol/L could be quantitated, with concentrations up to 800 nmol/L reliably measured on dilution. The method demonstrated good recovery and minimal matrix effects. Spiked samples had concentrations ranging from 0.57 to 46.2 nmol/L. The Roche immunoassay compared well to LC-MS/MS with a slight positive bias. The Passing-Bablok fit was $y = 0.48 + 1.03x$ and Bland-Altman analysis showed a mean bias of 1 nmol/L (7.5%).

Conclusions: We present a robust and sensitive LC-MS/MS method to measure serum progesterone and its application to verify the performance of a routine progesterone immunoassay. These results suggest the Roche immunoassay performs sufficiently for assessment of ovulation in a routine setting. Our LC-MS/MS method may be applied for assessment of further routine immunoassay methods.

Abstract citation ID: lvag096.506

P365 - ECE_2464 - Pregnancy outcomes following assisted reproduction in 17-Hydroxylase/17,20-Lyase Deficiency: a micro-cohort study and pooled analysis

Haining Wang[1], Ye Liu[1], Aihua Liu[1], Rui Yang[2], Ying Wang[2] and Tianpei Hong[1]
[1]*Department of Endocrinology and Metabolism, Peking University Third Hospital, Beijing, China;* [2]*The Center for Reproductive Medicine, Peking University Third Hospital, Beijing, China*

Background: 17α-Hydroxylase deficiency (17OHD), a rare congenital adrenal hyperplasia (CAH) subtype caused by CYP17A1 pathogenic variants, impairs sex hormone and glucocorticoid synthesis in females, with concurrent mineralocorticoid excess, This leads to hypertension, hypokalemia, infertility, and other manifestations. While assisted reproductive technology (ART) enables live births in these patients, data on optimal pregnancy management, obstetric outcomes, and long-term reproductive health remain limited and fragmented.

Methods: This study combined retrospective micro-cohort analysis and systematic literature review. Eligible 17OHD patients (46,XX karyotype, confirmed diagnosis, fertility desire, clinical pregnancy, ≥1 year postpartum follow-up) received multidisciplinary treatment at our center from 2009 to 2025). A systematic literature search (updated to May 2025) identified previously reported 17OHD-associated pregnancies. Demographic, clinical, ART protocol, obstetric, neonatal, and long-term reproductive data were extracted and synthesized.

Results: Among 18 females with 17OHD followed at our center, 3 met the inclusion criteria and achieved singleton pregnancies via ART. Combined with 17 literature-retrieved cases, 20 females (median conception age: 29 years) and 23 live births were analyzed. Most (14/20) had spontaneous menarche (median age: 14 years). Key features included small uterine volume (6/11 evaluable), ovarian cysts (12/16 evaluable), and elevated follicular-phase progesterone. All pregnancies relied on IVF: 11 with long-acting GnRHa downregulation, 6 with PPOS protocol. All used frozen embryo transfer (FET), 90% (18/20) receiving pre-transfer glucocorticoids for progesterone suppression. Among 13 cases with complications, 46.2% (6/13) had gestational hypertension, diabetes, or preeclampsia. Only 25% (5/20) had term vaginal deliveries; others involved preterm birth or cesarean section. Four children with ≥1 year follow-up showed normal physical and neurodevelopment. Postpartum, menstrual irregularity and recurrent ovarian cysts persisted.

Conclusions: Females with 17OHD face notable reproductive challenges, with high obstetric complications and long-term morbidity. ART combining glucocorticoid-mediated progesterone suppression, ovarian downregulation, and FET effectively achieves live births. Meticulous multidisciplinary prenatal care is needed to reduce gestational hypertension, preeclampsia, and preterm birth risks. Long-term surveillance of menstrual and ovarian issues is crucial. Larger prospective studies are

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

required to refine guidelines and improve lifelong reproductive care.

Keywords 17-hydroxylase/17,20-lyase deficiency, congenital adrenal hyperplasia, assisted reproductive technology, frozen embryo transfer, pregnancy outcome, multidisciplinary management

Abstract citation ID: lvag096.507

P366 - ECE_3280 - Effect of genetic variability and plasma concentration of osteocalcin and its relationship with serum testosterone levels in men

Mariana António[1], Joana Ferreira[2,3], Mário Rui Mascarenhas[4], Manuel Bicho[2,3] and Ana Paula Barbosa[5]
[1]*Faculty of Medicine, Lisbon University, Lisbpn, Portugal;* [2]*Environmental Health Institute (ISAMB), Faculty of Medicine, University of Lisbon, Lisbon, Portugal;* [3]*Institute for Scientific Research Bento da Rocha Cabral, Lisbon, Portugal;* [4]*CEDML-Endocrinology Diabetes and Metabolism Clinic of Lisbon, Lisbon, Portugal;* [5]*Endocrinology University Clinic, Faculty of Medicine, Lisbon, Portugal*

Introduction: Bone is recognised as an endocrine organ, playing an active role in the regulation of energy metabolism and male reproductive function. Osteocalcin (OC), secreted by osteoblasts, stimulates testicular steroidogenesis through the bone–testis axis via the GPRC6A receptor in the Leydig cells. Despite evidence of this OC actions from animal models, human studies remain scarce. This study aimed to evaluate the association between serum testosterone (T) levels, metabolic and bone parameters, and the genetic variability of osteocalcin (*BGLAP*, rs1800247) and its receptor (*GPRC6A*, rs2274911) in men.

Materials and Methods: A retrospective cross-sectional study was conducted in adult men stratified into four groups according to total serum testosterone: ≤2.5; >2.5–≤3.2; >3.2–<4 and ≥4 ng/mL. Anthropometric, biochemical, hormonal and DXA bone mineral density data (QDR Discovery, Hologic) were collected. Genotyping of rs1800247 and rs2274911 was performed using endpoint genotyping. Statistical analysis included parametric and non-parametric tests, ANOVA, genetic association tests, and Pearson/Spearman correlations, with $P < .05$ considered significant.

Results: A group of 123 men, with a mean age of 57.2 years, a median weight ranging from 79.1 to 91.3 kg, and a mean height of 1.7, was studied. Statistically significant differences were observed between testosterone groups for several key parameters. The group with T ≥4 ng/mL presented higher levels of vitamin D ($P = .026$), bone alkaline phosphatase ($P = .027$), SHBG ($P = .001$), and estradiol ($P = .003$) compared to groups with lower testosterone concentrations. Conversely, groups with lower T levels showed an unfavourable metabolic profile, characterised by significantly higher total cholesterol ($P = .014$) and LDL-cholesterol ($P = .030$). Additionally, significant differences in bone densitometric parameters were observed between testosterone groups, with more favourable values in individuals with higher T concentrations ($P < .05$). Regarding genetics, no statistically significant differences were found in the distribution of rs1800247 and rs2274911 genotypes among the four testosterone groups ($P > .05$). However, relevant metabolic trends were identified: carriers of the CC genotype (rs1800247) presented lower osteocalcin levels and higher HOMA-IR values, while the GG genotype (rs2274911) was associated with higher LH and estradiol levels, suggesting compensatory mechanisms within the gonadal axis.

Conclusion: This study suggests that higher testosterone levels are associated with more favourable bone and metabolic profiles. Although osteocalcin and GPRC6A polymorphisms do not directly determine serum testosterone concentrations, the observed trends, particularly the relationship between osteocalcin and insulin resistance, reinforce the relevance of the interaction between bone metabolism, energy homeostasis, and male reproductive function.

Abstract citation ID: lvag096.508

P367 - ECE_3602 - Impact of insulin delivery modality on gonadal axis hormonal profiles in men with type 1 diabetes mellitus

Paola Girardi[1], Edoardo Vergani[1], Alessandro Oliva[1], Linda Tartaglione[1], Alessandro Rizzi[2], Dario Pitocco[1], Domenico Milardi[1], Antonio Mancini[1] and Alfredo Pontecorvi[1]
[1]*UOC Medicina Interna, Endocrinologia e Diabetologia, Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy;* [2]*Rome, Italy*

Background: In men with type 1 diabetes mellitus (T1DM), multiple daily insulin injections (MDI) generally ensure satisfactory glycaemic control; however, continuous subcutaneous insulin infusion (CSII) is required in selected patients to achieve optimal metabolic stability. Although insulin plays a key role in hepatic sex hormone-binding globulin (SHBG) regulation and androgen bioavailability, evidence regarding gonadal axis alterations in men with T1DM under different insulin delivery modalities remains scarce and inconclusive.

Objective: To assess the impact of different insulin administration strategies on the gonadal axis in male patients with T1DM.

Methods: Between 2023 and 2025, 108 male subjects aged 18-69 years were enrolled and allocated into three groups:

- patients with T1DM treated with CSII (Group A, $n = 36$);
- patients with T1DM treated with MDI (Group B, $n = 36$);
- age-matched healthy controls (Group C, $n = 36$).

Serum concentrations of SHBG, total testosterone (TT), calculated free testosterone (cFT), estradiol, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) were measured.

An age-stratified analysis was performed to evaluate hormonal variations across age groups.

Results: Mean SHBG concentrations were significantly higher in the CSII group compared with both the MDI group (57.22 ± 3.16 vs 46.69 ± 2.69 nmol/L) and healthy controls (57.22 ± 3.16 vs 38.78 ± 1.98 nmol/L), although values remained within the reference range. cFT levels were comparable among the three groups, while TT and LH exhibited a non-significant trend toward higher levels in CSII-treated patients. Estradiol concentrations were significantly lower in healthy controls compared with both T1DM groups. Age-stratified analysis demonstrated a more pronounced decline in cFT among patients with T1DM, regardless of insulin delivery modality, compared with controls.

Conclusions: In men with T1DM, insulin delivery strategy is associated with distinct differences in gonadal hormonal profiles,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

particularly SHBG concentrations. Moreover, T1DM appears to be associated with an accentuated age-related decline in free testosterone, independent of insulin administration modality. These findings suggest a complex interplay between insulin therapy, hepatic SHBG regulation, and androgen availability in T1DM.

Abstract citation ID: lvag096.509

P369 - ECE_1256 - "Risk factors for endocrine complications in sickle cell disease: a 25-year review of the impact of age, iron burden, puberty, genetics, and nutrition"

Ashraf Soliman[1], Shayma Ahmed[1], Nada Alaaraj[1], Mohamed Yassin[2], Noor Hamed[1], Fawziya Alyafei[1] and Noora Alhemaidi[1]
[1]*Hamad Medical Center, Pediatric Endocrinology, DOHA, Qatar;* [2]*Hamad Medical Center, Hematology Oncology, DOHA, Qatar*

Background: Sickle cell disease (SCD) is a chronic hemoglobinopathy with increasing survival into adulthood, revealing a substantial burden of endocrine complications. These include growth failure, delayed puberty, hypogonadism, thyroid and adrenal dysfunction, glucose abnormalities, and poor bone health. The underlying mechanisms are multifactorial and reflect the combined effects of chronic hemolysis, recurrent vaso-occlusion, inflammation, iron overload, undernutrition, and genetic heterogeneity.

Objective: To review the prevalence, patterns, and determinants of endocrine complications in SCD and assess the contribution of major risk factors including age, genotype, pubertal development, iron overload, chelation adherence, sickling frequency, and nutritional status.

Methods: A structured review of studies published between 1999 and 2024 was undertaken using PubMed and major hematology–endocrinology sources. Included studies examined endocrine outcomes in pediatric and adult SCD populations. Data on anthropometry, endocrine profiles, iron parameters, and associated risk factors were synthesized into comparative impact estimates.

Results: Endocrine complications were highly prevalent and displayed clear risk factor dependency. **Age** was a major determinant: older adolescents and adults demonstrated higher frequencies of hypogonadism, osteopenia/osteoporosis, and disordered glucose metabolism (≈40% impact). **Genotype** contributed substantially, with HbSS patients experiencing more severe and frequent endocrine abnormalities than HbSC (≈25% impact). **Pubertal delay** affected up to 45% of adolescents, with associated short stature and reduced IGF-1 levels.

Iron overload emerged as the strongest modifiable risk factor (≈50% impact). Elevated ferritin or hepatic iron concentration correlated with hypogonadism, impaired glucose tolerance, hypothyroidism, and reduced IGF-1, while **regular chelation therapy** was associated with lower rates of endocrinopathy (≈30% protective effect). **Sickling frequency**—reflected in pain crises and hospitalization rate—was linked to growth failure, adrenal insufficiency, and elevated cortisol turnover (≈35% impact).

Nutritional deficiencies, particularly vitamin D deficiency (70-85% prevalence), contributed to low bone mineral density, poor linear growth, and increased fracture risk (≈40% impact). Across studies, children with SCD consistently exhibited lower BMI, reduced lean mass, and compromised GH–IGF-1 axis activity, reflecting chronic undernutrition and systemic disease stress.

Conclusions: Endocrine complications in SCD are common, multifactorial, and strongly influenced by iron burden, pubertal status, genotype, disease severity, and nutrition. Early endocrine monitoring—especially of growth, puberty, bone health, adrenal function, and glucose metabolism—combined with optimized chelation and nutritional therapy is essential to improve long-term outcomes and quality of life.

Abstract citation ID: lvag096.510

P371 - ECE_1289 - Intergenerational effects of maternal testosterone levels and polycystic ovary syndrome on sleep duration and timing in seven-year-old children. Odense child cohort

Anne Kjær[1], Dorte Glintborg[1], Camilla Viola Palm[2], Henrik Christesen[3], Hajir Al-Jorani[1], Anders Grøntved[4] and Marianne Andersen[1]
[1]*Department of Endocrinology and Metabolism, Odense University Hospital, Odense, Denmark;* [2]*Department of Gynecology and Obstetrics, Odense University Hospital, Odense, Denmark;* [3]*Odense University Hospital, Hans Christian Andersen Children's Hospital, Odense C, Denmark;* [4]*University of Southern Denmark, Department of Sports Science and Clinical Biomechanics, Research Unit for Exercise Epidemiology, Odense, Denmark*

Background: Sleep is essential for child health and development. Prenatal testosterone exposure decreased sleep in female rodents, but not in males, suggesting sex-specific developmental sensitivity. Human studies on whether prenatal maternal testosterone or PCOS diagnosis influence sleep in offspring are lacking.

Aim: To examine whether maternal third-trimester testosterone or PCOS diagnosis, were associated with sleep outcomes in 7-year-old children.

Materials and Methods: We included 737 mother-child dyads (363 girls and 374 boys) from the Odense Child Cohort. Exposures were maternal third trimester total testosterone (TT) and free testosterone (FT), and PCOS diagnosis ($n = 81$). Sleep was assessed by 24h/7days accelerometry. Outcomes included bedtime, chronotype (midsleep time on free days), sleep period time (SPT), total sleep time (TST), and waketime. Linear regression models were adjusted for maternal age, parity, and educational level.

Results: In all children, 1 nmol/L increase in maternal TT was associated with earlier weekend bedtime, $\beta = -.06$ h, (95%CI: −0.12; −0.02), $P = .01$. In girls, 1 nmol/L increase in maternal TT was associated with earlier weekend bedtime, $\beta = -.11$ h, (95% CI: −0.19; −0.04), $P = .01$ and 0.1 nmol/L increase in FT may be associated with earlier weekend bedtime, $\beta = -3.7$ h (95% CI: −6.78; 0.69), $P = .02$. In girls, 1 nmol/L increase in TT was associated with earlier chronotype, $\beta = -.10$ h (95% CI: −0.18; −0.01), $P = .02$. In boys, no significant associations were seen. In all children, maternal PCOS was associated with earlier weekday bedtime, $\beta = -.19$ h (95% CI: −0.36; −0.02), $P = .03$ and longer SPT and TST, $\beta = .19$ h (95% CI: 0.03; 0.36), $P = .02$ and $\beta = .18$ h (95% CI: 0.03; 0.34), $P = .02$, respectively.

Conclusions: In all children, maternal TT and PCOS showed subtle associations with sleep at 7 years of age. Associations with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

maternal testosterone exposure were more evident in girls than in boys. Future follow-up in the Odense Child Cohort may help clarify whether these early differences in sleep duration and timing persist later in childhood.

Abstract citation ID: lvag096.511

P372 - ECE_1802 - Characterization of a dihydrotestosterone-induced mouse model of polycystic ovary syndrome (PCOS) using whole-ovary 3D imaging and metabolic profiling

Line Zachariassen, Annika Runegaard Thomsen, Malene Lundgaard Riis, Susanne Pors, Marie Biviano Rosenkilde, David Ari Ostenfeldt, Jacob Lercke Skytte and Allison Butt
Gubra A/S, Hørsholm, Denmark

Background and Aim: Polycystic ovary syndrome (PCOS) affects approximately 10-15% of women of reproductive age and is a leading cause of anovulation and infertility. PCOS is frequently accompanied by hyperandrogenism, insulin resistance, and altered body composition. Androgen-induced mouse models reproduce key reproductive and metabolic features of PCOS and are widely used in translational research. However, conventional ovarian histology relies on sectional sampling and semi-quantitative estimates of follicle number and size, limiting accurate assessment of especially antral follicular dynamics. This study aimed to characterize a dihydrotestosterone (DHT)-induced mouse model of PCOS using reproductive and metabolic endpoints, using whole-ovary 3D imaging as a fully quantitative method to assess ovarian morphology.

Methods: Female C57BL/6JRj mice were implanted subcutaneously at four weeks of age with slow-releasing DHT pellets (40 µg/day) or empty implants and maintained on a Western diet. After eight weeks of androgen exposure, mice received vehicle daily injections for four weeks prior to termination to mimic pharmacotherapy. Endpoints included body weight, body composition, anogenital distance, estrous cycle monitoring, and metabolic and endocrine plasma biomarkers. At termination, ovaries were imaged ex vivo using whole-ovary 3D light sheet fluorescence microscopy (LSFM) imaging, enabling complete volumetric reconstruction. From the volumes, follicle populations were detected and quantified using deep learning-based image analysis.

Results: DHT-treated mice exhibited a rapid and sustained increase in body weight, fat and lean tissue mass and anogenital distance, confirming androgenization. Estrous cyclicity was completely disrupted, with no animals entering estrus during the monitoring period. DHT-treated mice showed impaired glycemic control with elevated fasting glucose and insulin levels. Whole-ovary 3D imaging confirmed anovulation by the absence of corpora lutea and enabled unbiased quantification of follicular populations. DHT-PCOS mice displayed a marked increase in the number of large antral follicles and thinning of the granulosa cell layer compared with controls which confirm PCOS-like ovarian morphology.

Conclusions: The DHT-induced PCOS mouse model recapitulates key reproductive, metabolic, and androgenic features of PCOS. Whole-ovary 3D LSFM imaging provides a robust, fully quantitative assessment of ovarian morphology and represents a powerful translational tool for evaluating therapeutic interventions targeting PCOS.

Abstract citation ID: lvag096.512

P373 - ECE_2421 - Lobectomy versus total thyroidectomy in intermediate-risk papillary thyroid carcinoma: rethinking surgical extent

Jungah Lim[1], Min Joo Kim[2], Seung Eun Yoo[2], Jae Hoon Moon[2], Woo-Jin Jeong[2], Wonjae Cha[2], Jeong-Yeon Ji[2], Hunjong Lim[2], Sang Il Choi[2], Hee Young Na[2], So Yeon Park[2], Ja Kyung Lee[2], Hyeong Won Yu[2], June Young Choi[2] and Ka Hee Yi[3]
[1]Department of Internal Medicine, National Medical Center, Seoul, South Korea; [2]Seoul National University Bundang Hospital, Seongnam, South Korea; [3]Seoul, South Korea

Background: Thyroid lobectomy is increasingly being performed on patients with low-risk papillary thyroid carcinoma (PTC) following the expanded guideline recommendations. However, the oncological safety of lobectomy for patients with intermediate-risk PTC remains uncertain. The present study aimed to compare recurrence-free survival (RFS) between lobectomy and total thyroidectomy in a large cohort of patients with intermediate-risk PTC.

Materials and Methods: We retrospectively reviewed patients with intermediate-risk PTC who underwent surgery at a tertiary referral center between 2016 and 2020. Propensity score matching (PSM) was performed in a 1:1 ratio based on age, sex, preoperative lymph node status, and tumor size. RFS was compared using Kaplan–Meier curves and Cox proportional hazards regression.

Results: A total of 848 matched patients were analyzed, with 424 in each group. During a mean follow-up period of 63.5 months, recurrence occurred in 2.1% of the lobectomy group and 3.8% of the total thyroidectomy group ($P = .223$). Cox proportional hazards regression analysis showed that surgical extent was not significantly associated with RFS (HR 0.75, 95% CI 0.26-2.16, $P = .594$).

Conclusions: In this large cohort study of patients with intermediate-risk PTC, lobectomy showed no significant difference in recurrence rates compared to total thyroidectomy. These results suggest that for appropriately selected intermediate-risk PTC patients, lobectomy is a safe and feasible surgical option, offering reduced surgical morbidity and preserved thyroid function without compromising oncologic outcomes.

Abstract citation ID: lvag096.513

P375 - ECE_3484 - Clinicopathological and molecular features of papillary thyroid microcarcinoma

Marie Rodová[1], Vlasta Kuklikova[1], Barbora Bulanova[1], Olivia Cillikova[1], Katerina Vyhnalova[1], Karolina Dobiasovska[1], Eliska Vaclavikova[1], Jitka Carkova[1], Petr Lastuvka[2], Rami Katra[3], Petr Vlcek[4], Daniela Kodetova[5], Petr Bavor[6], Martin Chovanec[7], Jana Drozenova[8], Jaromir Astl[9], Jiří Soukup[10], Josef Vcelak[1] and Bela Bendlova[1]
[1]Department of Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic; [2]Department of Otorhinolaryngology and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Head and Neck Surgery, 1st Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [3]Department of Ear, Nose, and Throat, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [4]Department of Nuclear Medicine and Endocrinology, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [5]Department of Pathology and Molecular Medicine, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [6]Department of Surgery, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [7]Department of Otorhinolaryngology, 3rd Faculty of Medicine, Charles University in Prague and University Hospital Kralovske Vinohrady, Prague, Czech Republic; [8]Department of Pathology, 3rd Faculty of Medicine, Charles University in Prague and University Hospital Kralovske Vinohrady, Prague, Czech Republic; [9]Department of Otorhinolaryngology and Maxillofacial Surgery, 3rd Faculty of Medicine and Military University Hospital, Prague, Czech Republic; [10]Department of Pathology, 3rd Faculty of Medicine and Military University Hospital, Prague, Czech Republic

Objective: Papillary thyroid carcinoma (PTC) is the most common subtype of thyroid cancer, with a substantial proportion being microcarcinomas (uPTCs). Currently, there is no clear strategy for their treatment. This study focused on the most frequent pathogenic variant, V600E, of the *BRAF* gene. The aim was to correlate tumor size with clinicopathological characteristics and subsequent response to treatment.

Methods: A total of 969 fresh-frozen tissue samples from primary PTC tumors were analyzed for the presence of the most prevalent genetic alterations in PTC, including *BRAF, TERT, RAS*, and 23 fusion genes (*ALK, BRAF, GLIS3, NTRK1, NTRK3, PPARG*, and *RET*). Of the total PTC cohort, 253 (26.1%) cases were uPTCs. For the correlation between tumor size and aggressiveness, only PTCs harboring the *BRAF* V600E mutation were included. Multifocal PTCs were classified as carcinomas or microcarcinomas based on the largest lesion and included in the statistical analysis accordingly. If a clinicopathological feature was present in only one lesion, it was considered valid. Samples were excluded if a genetic alteration other than *BRAF* V600E was detected even in another lesion.

Results: In uPTCs, the risks of lymph node or distant metastasis, angioinvasion, invasiveness, and extrathyroidal extension were 19.8%, 6.3%, 23.3%, and 13.4%, respectively. In PTCs larger than 10 mm (*PTCs) and uPTCs, respectively, *BRAF* mutations were detected in 439 and 148 patients, *RAS* mutations in 61 and 18 patients, *TERT* mutations in 58 and 6 patients, and fusion genes in 156 and 43 patients. Of the 515 PTCs harboring only the *BRAF* V600E mutation, 138 (26.8%) were uPTCs. The only statistically significant differences ($P \leq .05$) between *PTCs and uPTCs were angioinvasion and tumor invasiveness with higher incidence in *PTCs. No statistically significant differences were observed in tumor metastasis or extrathyroidal extension. A 24-month follow-up was available for 196 (52.0%) *PTC patients and 64 (46.4%) uPTC patients. An excellent, indeterminate, structural incomplete, and biochemical incomplete response to treatment was observed in 62.8%, 23.0%, 8.2%, and 6.1% of *PTC patients and in 71.9%, 25.0%, 1.6%, and 1.6% of uPTC patients, respectively.

Conclusions: The risk of aggressive behavior in uPTCs harboring the *BRAF* V600E mutation is not negligible. Therefore, uPTCs should be managed cautiously, and molecular testing should be incorporated into their diagnostic and therapeutic evaluation.

Funding: Supported by AZV NU21-01-00448 and MH CZ RVO 00023761.

Abstract citation ID: lvag096.514

P376 - ECE_1960 - Enhanced formation of neutrophil extracellular traps in patients with hyperthyroidism but not in those with hypothyroidism: effects of thyroid hormone normalization

Kamila Undas[1], Joanna Natorska[2,3], Alicja Hubalewska-Dydejczyk[4] and Anetta Undas[2,3]
[1]Jagiellonian University Medical College, Kraków, Poland; [2]Department of Thromboembolic Disorders, Jagiellonian University Medical College, Institute of Cardiology, Kraków, Poland; [3]St. John Paul II Hospital, Krakow Centre for Medical Research and Technologies, Kraków, Poland; [4]Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland

Formation of neutrophil extracellular traps (NETs; so-called NETosis), released by activated neutrophils and containing DNA, histones and antimicrobial proteins, has been shown in multiple infectious, inflammatory, and prothrombic diseases. Associations of increased NETs with arterial and venous thromboembolism have been reported mainly in cardiovascular and autoimmune disorders. A well-established marker of severity of NETosis is the circulating citrullinated histone 3 (citH3). To our knowledge, formation of NETs has not been explored in thyroid disorders yet.

The aim of this study was to investigate plasma citH3 in hyper- and hypothyroid individuals before and after therapy leading to euthyroidism. Moreover, we evaluated associations of citH3 with several prothrombotic markers including plasma fibrin clot parameters.

We enrolled 31 patients with hyperthyroidism and 29 with hypothyroidism at similar age (44.80 ± 16.19 years) along with 29 sex- and age-matched controls. Apart from citH3, we evaluated thyroid-stimulating hormone (TSH), free thyroxine (FT4) and triiodothyronine (FT3) concentrations as well as fibrin clot parameters (including clot lysis time), fibrinolysis proteins, thrombin generation, and platelet activation markers, all before and after 3-month therapy leading to thyroid hormone normalization. The study protocol was approved by the Jagiellonian University Ethical Committee. Informed written consent was acquired from study participants.

Pre-treatment citH3 concentrations were higher among hyperthyroid individuals by 88% and 106% in comparison to the hypothyroid group and controls, respectively (both $P < .001$) without any difference between the latter groups. Pre-treatment citH3 concentrations were positively correlated with FT4 and FT3 ($R = 0.870$, $P < .001$ and $R = 0.709$, $P < .001$, respectively) only in the hyperthyroid group. Plasminogen activator inhibitor-1 (PAI-1) antigen was also strongly positively correlated with citH3 in the hyperthyroid group ($R = 0.538$, $P = .002$), without any associations of any prothrombotic markers, including lysis time. There were no associations of pre-treatment citH3 with any demographic, clinical, and routine laboratory investigations including inflammatory markers. A decrease in citH3 concentrations of 43% was observed following treatment among hyperthyroid patients but not in hypothyroid

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

ones ($P < .001$). No associations of citH3 with on-treatment thyroid hormones or any prothrombotic markers were found.

This study is the first to show enhanced NETs formation in hyperthyroid patients, but not hypothyroid individuals, as reflected by increased citH3 concentrations, with a significant reduction after hormone normalization. Our report suggests that NETs-related prothrombotic mechanisms could be involved in thrombotic manifestations in hyperthyroid patients. These findings increase our knowledge on the impact of hyperthyroidism on blood coagulation, in particular on PAI-1-related fibrinolysis in relation to NETosis.

Abstract citation ID: lvag096.515

P377 - ECE_2478 - Thyroid antibody testing in practice: an audit on TPO measurement requests in a tertiary hospital

Kevin Veerasamy, Laura Ryan, Erum Rasheed and Anne Marie Hannon
University Hospital Limerick, Limerick, Ireland

Thyroid peroxidase (TPO) antibodies are commonly present in individuals with Hashimoto's thyroiditis and, less frequently, in those with Graves' disease. The National Institute for Health and Care Excellence (NICE) recommends measuring TPO antibodies once in adults with elevated thyroid-stimulating hormone (TSH) levels and advises against repeat testing due to their limited diagnostic value. This audit was undertaken to evaluate TPO antibody testing practices in the Midwest region and assess compliance with established guidelines.

A retrospective review was conducted of all TPO antibody tests performed in 2023 and 2024, including corresponding thyroid function tests. Individuals under 18 years were excluded. Laboratory-specific reference ranges were used to define normal TSH and TPO values. A total of 9960 TPO antibody tests were performed on 7425 individuals with 1279 (17.2%) having repeat TPO testing. On average, TPO testing was repeated 2.6 times, with the frequency of duplicates ranging between 2 to 11 times. The majority (77%) were female, with a median age of 47 years. Most requests originated from primary care (76.3%), followed by obstetrics and gynaecology (13.8%) and secondary care (3.1%). Only 10% ($n = 1032$) of tests were associated with a TSH above 4.2 mU/L, the threshold that justifies testing. Among these, 866 had subclinical hypothyroidism and 166 had overt hypothyroidism. While appropriate TPO testing can support the diagnosis of autoimmune thyroid disease, this audit highlights a high volume of potentially unnecessary testing. These findings support the need for improved adherence to clinical guidelines to ensure appropriate and cost-effective use of thyroid antibody testing.

Abstract citation ID: lvag096.516

P378 - ECE_2680 - Association of TSH and FT4 levels with incident dementia: a population-based cohort study

Gloria Hoi-Yee Li[1], Jiawen Lu[1], Elaine Yun-Ning Cheung[2], Kathryn Choon-Beng Tan[3], Wai-Chi Chan[4] and Ching-Lung Cheung[5]
[1]*Department of Health Technology and Informatics, The Hong Kong Polytechnic University, Hung Hom, Hong Kong;* [2]*Department of Medicine and Therapeutics, The Chinese University of Hong Kong, CUHK Medical Centre, Sha Tin, Hong Kong;* [3]*Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Pok Fu Lam, Hong Kong;* [4]*Department of Psychiatry, The University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong;* [5]*Department of Pharmacology and Pharmacy, The University of Hong Kong, Pokfulam, Hong Kong*

Introduction: Contradictory findings were reported on the relationship of thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels with risk of dementia in cross-sectional studies, or prospective studies of limited sample size or short follow-up. In this study, we aimed to evaluate the association of TSH and FT4 levels, both across the full and normal reference ranges, with risk of dementia.

Methods: We used a population-based electronic health record database from Hong Kong to identify individuals aged ≥55 with valid TSH and/or FT4 measurements between 2006 and 2009. They were followed from the date of TSH/FT4 measurement (index date) until the first diagnosis of dementia, first prescription of anti-dementia medication, death, or study end on 31 December 2019, whichever earlier. Individuals who received any thyroid-related treatment after the index date were censored. The Fine-Gray competing risk model, with death as a competing event, was used to estimate the subdistribution hazard ratio (SHR) of incident dementia per unit increase in TSH/FT4, both in full and normal reference ranges.

Results: A total of 366 300 individuals had valid TSH records (median follow-up: 7.22 years) and 135 906 had valid FT4 (median follow-up: 3.53 years) records from 2006 to 2009. TSH, as a continuous trait, was inversely associated with incident dementia in both the full (SHR = 0.946; 95% confidence interval [CI]: 0.937-0.954; $P < .001$) and normal reference ranges (SHR = 0.937; 95% CI: 0.925-0.95; $P < .001$). Compared to the 3rd quintile, individuals in the 4th and 5th quintiles of TSH had a reduced risk of dementia in both the full (4th quintile: SHR = 0.965; 95% CI: 0.933-0.998; $P = .036$; 5th quintile: 0.838; 95% CI: 0.808-0.869; $P < .001$) and normal reference range (4th quintile: SHR = 0.963; 95% CI: 0.929-0.998; $P = .036$; 5th quintile: SHR = 0.884; 95% CI: 0.852-0.917; $P < .001$). As a continuous trait, FT4 in full range was positively associated with risk of dementia (SHR = 1.007; 95% CI: 1.001-1.014; $P = .031$), but such association was not observed for FT4 within normal range. Individuals in the 1st quintile of FT4 had a lower risk of incident dementia when compared to the 3rd quintile (Full range: SHR = 0.845; 95% CI: 0.79-0.905; $P < .001$; Normal range: SHR = 0.926; 95% CI: 0.866-0.991; $P = .027$). Sensitivity analysis excluding individuals with prior thyroid-related treatment (TSH cohort: $n = 339\,916$; FT4 cohort: $n = 112\,127$) yielded similar results.

Conclusions: TSH level, even within normal reference range, was inversely associated with risk of dementia. These findings support the need to define optimal thyroid function ranges based on risk of adverse health outcomes.

Abstract citation ID: lvag096.517

P379 - ECE_2673 - Genotype–phenotype correlation of biallelic DUOX2 mutations in transient and permanent congenital hypothyroidism

Dau-Ming Niu[1,2], Yung-Hsiu Lu[1], Sheng-Bin Liang[1], Chih-Ya Cheng[1], Yun-Ru Chen[1], Yann-Jang Chen[1,2] and Chia-Feng Yang[1,2]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Department of Pediatrics, Taipei Veterans General Hospital, Taipei Veterans General Hospital, Taipei, Taiwan; [2]National Yang Ming Chiao Tung University Yangming Campus, Beitou District, Taiwan

Background: Congenital hypothyroidism (CH) due to biallelic DUOX2 mutations shows marked clinical heterogeneity. While some patients recover thyroid function during early childhood, others require long-term levothyroxine (LT4) therapy. Predictors of thyroid function recovery remain uncertain.

Aim: To investigate whether baseline biochemical severity, thyroid morphology, bone maturation, and biallelic DUOX2 variant severity are associated with thyroid function recovery in DUOX2-related CH.

Methods: We retrospectively analyzed 71 patients with CH carrying biallelic pathogenic DUOX2 variants. Patients were categorized into three outcome groups: LT4 discontinued by age 4 years ($n = 19$), LT4 discontinued after age 4 years ($n = 25$), and continued LT4 with biochemical worsening requiring dose escalation ($n = 27$). Baseline thyroid function tests (TSH, T3, T4, free T4, thyroglobulin), thyroid volume, and bone maturation were compared across groups. Bone maturation was assessed by distal femoral epiphyseal area (DFEA) and classified as normal (DFEA ≥ 0.22 cm^2) or delayed. Genotype–phenotype relationships were examined, including clinical variability among patients with identical biallelic genotypes. Putative severe alleles were evaluated to assess variant severity.

Results: Baseline thyroid function tests did not differ significantly among outcome groups (TSH $P = .222$; T3 $P = .314$; T4 $P = .422$; free T4 $P = .505$; thyroglobulin $P = .363$). Thyroid volume ($P = .246$) and bone maturation status ($P = .238$) were also not significantly different. The distribution of putative severe DUOX2 alleles was comparable across groups ($P = .862$). Patients with identical biallelic DUOX2 genotypes were observed in different outcome categories, demonstrating divergent clinical courses including both thyroid function recovery and persistent hypothyroidism requiring ongoing LT4 therapy.

Conclusions: Baseline biochemical severity, thyroid volume, bone maturation, and inferred DUOX2 variant severity do not reliably predict thyroid function recovery in DUOX2-related CH. Substantial within-genotype heterogeneity suggests the influence of compensatory H_2O_2-generating pathways and/or additional modifying genetic or environmental factors. Further studies are needed to identify biomarkers that can guide individualized long-term management.

Abstract citation ID: lvag096.518

P381 - ECE_3918 - Clinical utility of whole-exome sequencing in the etiological diagnosis of congenital hypothyroidism and thyroid axis disorders

Josef Vcelak and Karolina Hrckulakova
Department of Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic

Background: Neonatal screening for congenital hypothyroidism (CH) is well established across Europe and enables early initiation of treatment. However, determination of the underlying etiology remains challenging in a substantial proportion of patients. Genetic testing is crucial for precise etiological classification, differentiation between transient and permanent CH, and optimization of long-term management. Whole exome sequencing (WES) allows comprehensive analysis of coding regions of the genome and enables simultaneous detection of causative variants and additional genetic comorbidities.

Methods: WES was performed in 40 pediatric probands diagnosed with congenital hypothyroidism and associated abnormalities of the thyroid axis. Genomic DNA was extracted from peripheral blood leukocytes. In cases suggestive of autosomal recessive inheritance with potential compound heterozygosity, parental testing was conducted using trio-based analysis. All families received genetic counseling, including the option of targeted testing of siblings and first-degree relatives.

Results: A definitive or likely genetic cause of disease was identified in 16 of 40 probands, yielding a diagnostic rate of 40%. Pathogenic and likely pathogenic variants were most frequently detected in genes associated with thyroid dysgenesis (*TSHR, PAX8, NKX2-1*), thyroid dyshormonogenesis (*SLC5A5, TG, TPO, DUOX2, DUOXA2*), and thyroid hormone resistance (*THRB, THRA*). Variants in genes linked to broader endocrine or syndromic disorders were also identified (*KDM6A, POU1F1, ALB*). Genetic findings led to refinement of diagnosis, improved prognostic stratification, and informed long-term clinical management in a substantial proportion of patients.

Conclusions: Whole exome sequencing represents a highly effective diagnostic tool for elucidating the genetic basis of congenital hypothyroidism and related thyroid axis disorders. Genetic diagnosis directly informs clinical decision-making, supports individualized thyroid hormone replacement strategies, and facilitates distinction between transient and permanent forms of disease. Our data challenge the outdated perception of genetic testing as inaccessible or impractical and support its integration into routine diagnostic algorithms. Incorporation of WES into clinical guidelines for congenital hypothyroidism and other hereditary endocrinopathies has the potential to significantly improve patient care and long-term outcomes.

Funding: Supported by Ministry of Health, Czech Republic—conceptual development of research organization (Institute of Endocrinology—EÚ, 00023761)

Abstract citation ID: lvag096.519

P382 - ECE_3010 - Total thyroidectomy in Graves' orbitopathy: impact on TRAB levels and clinical activity score—a paired cohort analysis

Gratiela Bratu[1,2], Vlad Radulescu[1,2], Medeea Moraru[1], Daniela Alexandrescu[3], Romeo Smarandache[1], Cristina Stancu[1,4], Monica Livia Gheorghiu[1,2] and Corin Badiu[1,2]
[1]National Institute of Endocrinology CI Parhon, Bucharest, Romania; [2]University of Medicine and Pharmacy Carol Davila, Bucharest, Romania; [3]Bucharest, Romania; [4]Endocrinology, National Institute of Endocrinology "C.I. Parhon", Bucharest, Romania

Introduction: Graves' ophthalmopathy (GO), a sight-threatening extrathyroidal manifestation of Graves' disease (GD), poses significant challenges in management. Apart antithyroid drugs, thyroidectomy and radioiodine represent radical treatment methods for GD. While GO is clearly worsened after radioiodine,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

its progression following total thyroidectomy (TT) is still debated.

Patients and Methods: Review of the patient's records from a tertiary endocrine center admitted between 2015-2025 with GD, aged 18-80 years at diagnosis, who underwent TT. Inclusion criteria encompassed euthyroid status preoperatively, thyroid-stimulating hormone receptor autoantibodies (TRAb) positivity (>1.75 IU/L), and minimum 12-month follow-up. Patients with GO and steroid pulse therapy were included. This retrospective cohort study evaluates the evolution of GO post-TT in 54 GD patients, incorporating TRAb levels and standardized GO classification before and after surgery, using the European Group on Graves' Ophthalmopathy (EUGOGO) severity criteria (mild, moderate-to-severe, sight-threatening) and Clinical Activity Score (CAS). Patients with GD without GO, submitted to TT were in control group ($n = 14$).

Results: Preoperatively, 31.5%(17/54) of patients presented with mild GO (EUGOGO), 57.4% (31/54) moderate-to-severe, and 11.1% (6/54) sight-threatening, alongside elevated median TRAb levels (19.27 IU/L, range 1.0-47). CAS scores averaged 3.33 ± 1.26 (preoperative). No significant TRAB-CAS correlation existed at baseline (Spearman $r = -0.044$, $P = .751$), although some studies linked TSH receptor antibodies to orbital fibroblast activation and glycosaminoglycan synthesis. TT aimed to ablate thyroid antigen source, potentially mitigating cross-reaction autoimmunity.

Post-TT outcomes revealed GO improvement: mild 55.6% (30/54); moderate-to-severe 35.2%(19/54) and severe 9.3%(5/54). TRAB decreased at median of 5.85 IU/L ($P = .004$, 95%CI 1.93-9.77) and CAS improved 0.44 points ($P < .001$, 95%CI 0.22-0.67). Persistent TRAB predicted residual activity (TRAB_POST-CAS_POST $r = 0.369$, $P = .006$). Thyroidectomy achieves significant autoimmune and inflammatory reduction but requires TRAB-guided monitoring for progressive orbital fibrosis.

In controls ($n = 14$), TRAB levels decreased significantly from mean 17.17 ± 13.66 IU/L preoperatively to 4.51 ± 4.75 IU/L postoperatively, demonstrating a role of TT in autoimmune resolution process in GD.

Conclusions: According to our study, we demonstrated statistically significant reductions in TRAb levels and CAS scores between baseline and follow-up assessments. Limitations include retrospective design and lack of randomization. These findings indicate a meaningful improvement in disease activity and orbital inflammatory status, supporting the therapeutic efficacy of the intervention. Further studies with controlled designs and longer follow-up periods are warranted to confirm these results and assess long-term clinical outcomes.

Abstract citation ID: lvag096.520

P383 - ECE_3656 - Slightly elevated calcitonin values in unselected thyroid nodules can be safely managed over time

Giulia Lisi[1], Carla Gambale[1], Alessio Faranda[1], Alessandro Prete[1], Elisa Minaldi[1], Eleonora Molinaro[1], Gabriele Materazzi[2], Liborio Torregrossa[3], Rossella Elisei[1] and Antonio Matrone[1]

[1]*Unit of Endocrinology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy;* [2]*Endocrine Surgery Unit, Department of Surgical, Medical and Molecular Pathology and Critical Area, University of Pisa, Pisa, Italy;* [3]*Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Pisa, Italy*

Background: Calcitonin (CTN) is the most sensitive biomarker for pre-operative diagnosis of medullary thyroid cancer (MTC). However, one of the most criticisms in routinely using this marker is the interpretation of CTN values slightly above the upper limit of the normal ranges not necessarily diagnostic of MTC. We aimed to evaluate the prevalence and the clinical meaning of cases with these CTN values.

Methods: We evaluated 13 315 consecutive patients (2017-2024) who underwent their first clinical evaluation, neck US, and CTN measurement at the Unit of Endocrinology of the University of Pisa for thyroid nodule(s). CTN was measured with CLIA assay (normal range <11.5 and 18.2 ng/L in females and males, respectively)

Results: CTN values slightly above the normal range (median 20.8 ng/L—IQR 14.7-25.5) was found in 116/13 315 (0.87%) patients. Because the CTN values would have been the only reason for surgery, we decided to monitor the trend of CTN values and keep these patients under surveillance.

In 24/116(20.7%) patients (median CTN 21.1ng/L–IQR 14.43-23.6), we did not have follow-up data and were excluded from this analysis. In the remaining 92(79.3%) patients, the median CTN value at the first evaluation was 20.8ng/L (IQR 14.7-25.5) with a median follow-up time of 15.9 months (IQR 4.7-38.8). In 48 of these 92 (52.2%) patients (group1), whose CTN median values at first examination was 17.8 ng/L (IQR 13.3-22), CTN values returned to normal values in a median follow-up of 13.6 months (IQR 2.8-28.2). Ten of these 48 (20.83%) patients showed a new slightly increase of CTN during follow-up with CTN values no different from those of the first examination.

In 44/92(47.8%) patients (group2), whose CTN median values at first examination was 23.7 ng/L (IQR 19.8-32.5), CTN persisted slightly elevated during a median follow-up of 19.4 months (IQR 6.5-7.1) Median CTN values significantly decreased during follow-up (from 23.7 to 20.25ng/L; $P = .007$), and patients were kept under surveillance. A statistically significant difference was found between patients of group1 and group2 regarding the CTN values at first examination ($P < .0001$).

Conclusions: In our series of consecutive patients with thyroid nodules, the prevalence of slightly elevated CTN was very low (0.87%) and most of these patients are still under surveillance after about two years from initial observation. Indeed, in many cases CTN spontaneously normalized or showed stable values. These findings support a relaxed approach, reserving surgery for patients with significantly higher or progressively increasing CTN levels.

Abstract citation ID: lvag096.521

P384 - ECE_1658 - Genetic correlations across 22 autoimmune diseases: a sibling study of 6 million individuals

Daniel Eriksson[1], Ralf Kuja-Halkola[2], Olle Kämpe[2,3], Sophie Bensing[2,3] and Jakob Skov[2,4]

[1]*Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden;* [2]*Department of Medicine, Karolinska*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Institutet, Solna, Stockholm, Sweden; [3]Department of Endocrinology, Metabolism and Diabetes, Karolinska University Hospital, Stockholm, Sweden; [4]Region Värmland, Center for Clinical Research, Karlstad, Sweden

Background: Autoimmune diseases (ADs) often co-occur within individuals and families, suggesting shared genetic risk factors. However, the extent to which genetic contributions overlap across the autoimmune spectrum remains unclear.

Methods: This register-based nationwide sibling study included all Swedish individuals born between 1932 and 1983. Participants were identified through the Swedish Total Population Register, with the Multi-Generation Register used to identify full sibling pairs. The occurrence of 22 ADs was determined using diagnostic records in the National Patient Register and prescription data in the Prescribed Drug Register from 1969 to 2013. Pairwise genetic correlations of ADs were estimated based on sibling recurrence patterns. Network analysis and principal component analysis were used to explore the genetic interconnections of ADs.

Results: A total of 3 839 400 full-sibling pairs were identified in a cohort of 6 336 615 individuals, of whom 706 107 (11.1%) had at least one AD. In all, 802 335 AD-cases were recorded. The studied ADs formed a network of significant genetic correlations (mean $r_g = 0.23$) with clusters of more closely related ADs ($r_g \geq 0.3$). We found no evidence of a universal factor predisposing to autoimmunity.

Conclusions: This study demonstrates that ADs share substantial cluster-specific genetic overlap that largely aligns with affected tissue types, leading to distinct groupings of connective tissue diseases, gastrointestinal disorders, and endocrinopathies. This suggests that shared biological mechanisms may drive coaggregation within disease groups. Clinically, these insights highlight the importance of monitoring patients and their relatives for related autoimmune disorders.

Abstract citation ID: lvag096.522

P385 - ECE_2762 - Evaluation of the management of incidentally detected thyroid nodules prior to solid organ transplantation

Deniz Türküm Atikcan, Ekin Reyhan, Nihan Bakirtas, Uygar Ozkan, Hazım Cankaya, Parham Piltan, Shaheer Maaz, Ozlem Turhan Iyidir and Neslihan Başçıl Tütüncü
Istanbul, Türkiye

Introduction: The increasing use of cross-sectional imaging has led to more frequent incidental detection of thyroid nodules, particularly among solid organ transplant candidates undergoing extensive pre-transplant evaluation. In this population, the presence of a thyroid nodule may raise concerns regarding malignancy and potentially influence transplant eligibility or timing. However, current thyroid nodule management guidelines are based on the general population and do not offer transplant-specific recommendations. As a result, transplant candidates may be subjected to lower biopsy thresholds and more aggressive diagnostic approaches, increasing the risk of unnecessary procedures and delays in transplantation. Determining whether incidentally detected thyroid nodules in transplant candidates differ in ultrasonographic features, cytological findings, or malignancy risk compared with non-transplant patients is therefore essential to support appropriate and evidence-based clinical management.

Materials and Methods: This retrospective cohort study included 116 adult solid organ transplant candidates with incidentally detected thyroid nodules identified during routine pre-transplant imaging between January 2020 and December 2024. A control group of 135 age- and sex-matched patients with incidentally detected thyroid nodules unrelated to transplantation was also analyzed. Thyroid ultrasound examinations were reviewed for nodule size, echogenicity, margins, calcifications, vascularity patterns, and TI-RADS categories. FNAB indications followed standard ultrasonographic and clinical criteria. Cytological results were classified according to the Bethesda system, and histopathological findings were recorded for patients who underwent thyroid surgery.

Results: A total of 350 thyroid nodules were evaluated, including 172 nodules in transplant candidates and 178 nodules in the control group. Median nodule size was significantly smaller in transplant candidates compared with controls (10 mm vs 15 mm, $P < .001$). Vascularity patterns differed significantly between groups ($P = .003$), whereas echogenicity, margins, calcifications, and TI-RADS categories were similar. FNAB cytology distributions did not differ significantly between groups. Malignant or suspicious cytology was observed in 4.7% of nodules in transplant candidates and 7.3% in controls (Table 1). Rates of thyroidectomy and final histopathological malignancy were comparable.

Conclusions: Incidentally detected thyroid nodules in solid organ transplant candidates demonstrate ultrasonographic, cytological, and histopathological characteristics similar to those observed in non-transplant patients. These findings support the use of standard FNAB criteria for risk stratification in transplant candidates and highlight the need to avoid unnecessary invasive procedures that may delay transplantation.

Abstract citation ID: lvag096.523

P388 - ECE_3395 - The cytology of focal thyoid lesion classified as atypia of undetermined significance in fine-needle aspiration biopsy

Magdalena Turowska[1,2], Maria Szmigielska[1,2], Bernadetta Kałuża[1,2], Małgorzata Kołos[3] and Edward Franek[1,2,4]
[1]Warsaw, Poland; [2]Department of Internal Medicine, Endocrinology and Diabetology, National Medical Institute of the Ministry of the Interior and Administration in Warsaw, Warsaw, Poland; [3]Pathomorphology Centre, National Medical Institute of the Ministry of the Interior and Administration in Warsaw, Warsaw, Poland; [4]Department of Human Epigenetics, National Medical Institute of the Ministry of the Interior and Administration in Warsaw, Warsaw, Poland

Background: The Bethesda system is used to categorize fine-needle aspiration biopsy (FNAB) results of focal thyroid lesions. Bethesda category III comprises a heterogeneous group of lesions, including such subcategories as atypia of undetermined significance (AUS), follicular lesion of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

undetermined significance (FLUS), cellular and architectural atypia (AUS/FLUS), Hurthle cell atypia (AUS and/or FLUS), and indeterminate atypia. The aim of this study was to characterize the focal lesions of the thyroid sampled via ultrasound-guided FNAB and classified as AUS.

Materials and Methods: For the purpose of this study, we reviewed the hospital database from the years 2023-2025 and, out of all ultrasound-guided FNAB, selected Bethesda category III samples ($n = 107$), and divided them into two groups: FLUS ($n = 65$) and AUS ($n = 42$).

Results: The compared groups differed in terms of the following parameters: groups of normal thyrocytes (78.46 vs 50.00%, $P = .002$), sheets of normal-type thyrocytes (50.77 vs 30.95%, $P = .04$), scattered thyrocytes (55.38 vs 30.95%, $P = .01$), small follicular structures (56.92 vs 2.38%, $P = .001$), microfollicular structures (30.77 vs 4.76%, $P = .001$), colloid (84.62 vs 47.62%, $P = .001$), oxyphilic metaplasia (27.69 vs 57.14%, $P = .002$), nuclear grooves (1.5 vs 11.9%, $P = .02$), anisocytosis (15.38 vs 50.0%, $P = .0001$), anisonucleosis (10.77 vs 40.48%, $P = .001$); however, they did not differ in terms of such parameters as macrofollicular structures (4.62 vs 0%, $P = .16$), nuclear enlargement (12.31 vs 4.76%, $P = .19$), hyperplasia (32.31 vs 23.81%, $P = .34$), nucleolar prominence (9.23 vs 11.9%, $P = .66$). Univariate logistic regression analysis indicated that the factors increasing the risk of AUS development include oxyphilic metaplasia (OR 3.481 [1.537-7.887], $P = .003$), anisocytosis (OR 5.5 [2.224-13.602], $P = .001$), and anisonucleosis (OR 5.634 [2.078-15.275], $P = .001$), whereas the factors increasing the risk of FLUS were normal-thyrocyte groups (OR 3.643 [1.563-8.488], $P = .003$) or sheets (OR 2.3 [1.018-5.198], $P = .045$), normal-type thyrocytes, and scattered normal thyrocytes (OR 2.769 [1.224-6.267], $P = .015$), small-follicular (OR 54.179 [7.019-418.171], $P = .0001$) and microfollicular structures (OR 8.889 [1.954-40.427], $P = .005$), and colloid (OR 6.05 [2.445-14.969], $P = .0001$).

Conclusions: Bethesda category III in ultrasound-guided FNAB of the thyroid is heterogenous, with numerous features, among which oxyphilic metaplasia, anisocytosis, and anisonucleosis best characterize the AUS subtype.

Abstract citation ID: lvag096.524

P389 - ECE_3639 - Associations between kallistatin and lipid parameters in Hashimoto's thyroiditis

Sára Bak-Csiha[1,2,3], István Molnár[2,3], Hajnalka Lőrincz[4], Anna Somogyi[2,3], Mónika Katkó[1], Mariann Harangi[3,4], Gyorgy Paragh[4], Endre Nagy[1], Miklos Bodor[1,2] and Eszter Berta[2,4]

[1]Division of Endocrinology, Department of Medicine, Faculty of Medicine, University of Debrecen, Debrecen, Hungary; [2]Department of Clinical Basics, Faculty of Pharmacy, University of Debrecen, Debrecen, Hungary; [3]University of Debrecen, Doctoral School of Health Sciences, Debrecen, Hungary; [4]Faculty of Medicine, Division of Metabolism, Department of Medicine, University of Debrecen, Debrecen, Hungary

Chronic lymphocytic thyroiditis, also called Hashimoto's thyroiditis, is a form of autoimmune thyroid disease with hypothyroidism. Hypothyroidism is known to induce atherogenic alterations in lipid metabolism; however, the effects of autoimmune inflammatory processes on atherosclerosis are not fully understood.

Kallistatin belongs to the superfamily of endogenous serine protease inhibitors and has multiple biological functions, including antioxidant, anti-inflammatory, and anti-atherosclerotic effects. Although disturbances in thyroid function are known to increase cardiovascular risk, the potential role of kallistatin in this process, has not yet been investigated.

We examined the associations between serum kallistatin levels, thyroid function, and lipid parameters in HT patients [$n = 88$; 82 women and 6 men; age: 45 ± 14 years; BMI: 25.4 (23.6-31.6)] recruited from the Endocrinology Outpatient Clinic of the Internal Medicine Clinic, University of Debrecen, and in healthy controls [$n = 86$; 80 women and 6 men; age: 46 ± 14 years; BMI: 26.3 (22.3-30)].

Kallistatin levels were significantly higher in the patient group compared to controls (7495 vs 6140 ng/mL; $P < .0001$). Furthermore, patients exhibited higher median TSH and fT4 levels (2.81 vs 1.82 mU/L;$P < .005$ and 17.6 vs 15.4 pmol/L;$P < .0001$), while their fT3 levels were lower (4.6 vs 5.0 pmol/L;$P < .0001$) compared with controls.

In the patient cohort, disease duration also showed a significant negative correlation with kallistatin levels ($r = -0.2908$; $P = .0255$). Additionally, positive correlations were detected between kallistatin and non-HDL-C ($r = 0.2724$; $P = .0107$), ApoB ($r = 0.3209$; $P = .0027$), log PAI-1 ($r = 0.2606$; $P = .0142$), and the FGF21/adiponectin ratio ($r = 0.2302$; $P = .0310$).

Our findings suggest that kallistatin is closely associated with lipid metabolism and levels of atherogenic lipids. Based on these results, kallistatin may play a role in modulating the lipid profile, and its levels could potentially serve as a biomarker for evaluating cardiometabolic risk in patients with Hashimoto's thyroiditis.

Funding: SUPPORTED BY THE EKÖP-25-3-II-DE-218 University Research Scholarship Program Of The Ministry For Culture And Innovation from the source of the National Research, Development And Innovation Fund.

Abstract citation ID: lvag096.525

P390 - ECE_1526 - Predictors of malignancy and false-negative risk in large (≥3 cm) thyroid nodules: insights from a single-center cohort

Ömer Komaç, Elif Bilgili, Merve Yetişken, Deniz Çetin, Nesibe Kahraman Çetin, Ogün Aydoğan, Göksel Tuzcu, İmran Kurt Ömürlü, Mustafa Unubol, Mustafa Gökhan Ünsal and Engin Güney

Kocaeli, Türkiye

Background: In everyday clinical practice—particularly along non-tertiary referral pathways—large thyroid nodules are frequently perceived as inherently "high risk," often prompting early surgical referral before structured ultrasound-based risk assessment or fine-needle aspiration biopsy (FNAB). This size-driven perception persists despite guideline recommendations and may lead to avoidable surgery. We aimed to clarify how often malignancy is actually present in nodules ≥3 cm, which features meaningfully stratify risk beyond size, when benign cytology is sufficiently reassuring, and whether tumour behaviour changes as nodules enlarge.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Methods: We retrospectively analyzed 285 consecutive thyroidectomy patients (2018-2024) with a dominant thyroid nodule ≥3 cm (one patient = one analytic unit). EU-TIRADS category and suspicious cervical lymphadenopathy (LAP) were recorded from preoperative ultrasound when available ($n = 261$). FNAB was recoded by Bethesda. Primary outcomes were dominant-nodule malignancy and false-negative (FN) benign cytology (malignancy on final histology despite Bethesda II in the sampled dominant nodule; incidental microcarcinomas in non-dominant foci were excluded). Multivariable logistic regression identified independent predictors.

Results: Dominant-nodule malignancy was 13.3% (38/285), predominantly papillary thyroid carcinoma, indicating that large size alone does not confer a high cancer probability. Malignancy demonstrated a marked ultrasound risk gradient (EU-TIRADS TR3 3.6%, TR4 25.3%, TR5 64.3%). Independent predictors were TR4–5 (OR 7.59) and suspicious LAP (OR 5.97), with additional effects of solid composition (OR 3.34) and size ≥4 cm (OR 2.62). Thus, size contributed to risk only in conjunction with adverse imaging features.

Among 111 Bethesda II nodules, the overall FN rate was 4.5% (5/111); importantly, all FN events occurred in nodules ≥4 cm (7.5% vs 0% in 3-4 cm; $P = .023$). FN cases frequently showed cystic or infiltrative patterns, consistent with sampling limitations in heterogeneous large nodules. With increasing nodule size, we also observed a broader malignant histologic spectrum, including a notable proportion of aggressive thyroid cancers (~21% of malignancies; lymphomas excluded), suggesting that tumour behaviour—not only prevalence—may shift as nodules enlarge.

Conclusions: Large size alone should not mandate surgery. In nodules ≥3 cm, malignancy risk is best defined by EU-TIRADS category, nodal status, and internal composition rather than diameter in isolation. A benign FNAB is generally reassuring in 3-4 cm nodules, whereas ≥4 cm nodules—particularly those with TR4–5 patterns, solid structure, or suspicious LAP—require careful risk stratification, repeat or targeted FNAB, core biopsy, and avoidance of purely size-driven surgical decisions.

Abstract citation ID: lvag096.526

P391 - ECE_1887 - LH and hCG induce opposite signals via TSH receptor

Carmela Perri[1,2], Giada Mercanile[1], Clara Lazzaretti[1], Samantha Sperduti[1,3], Manuela Simoni[1,3,4], Giulia Brigante[1,4] and Livio Casarini[1,3]

[1]*Unit of Endocrinology, University of Modena and Reggio Emilia, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia. Baggiovara Hospital, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy;* [2]*Department of Biomedical, Metabolic and Neural Sciences, International Ph.D. School in Clinical and Experimental Medicine (CEM), University of Modena and Reggio Emilia, Modena, Italy;* [3]*Department of Biomedical, Metabolic and Neural Sciences, Center for Genomic Research, University of Modena and Reggio Emilia, Modena, Italy;* [4]*Department of Medical Specialties, Azienda Ospedaliero-Universitaria di Modena. Baggiovara Hospital, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy*

Human chorionic gonadotropin (hCG) has high structural identity with thyrotropin (TSH), and may cross-activate TSH receptor (TSHR), sustaining thyroid hormone production during pregnancy. hCG shares the same receptor (LHCGR) of the luteinizing hormone (LH), which mediates gametogenesis although it is unclear if it may bind TSHR as well. Therefore, we compared the effects of hCG and LH on TSHR-mediated pathways.

Transfected COS7 cells overexpressing human TSHR were exposed to increasing (nM-μM range) LH and hCG concentrations *in vitro*, before to explore the activation of Gs and Gq protein-related pathways. Intracellular cyclic adenosine monophosphate (cAMP) and inositol monophosphate (IP1) levels were measured by homogeneous time-resolved fluorescence (HTRF). cAMP response element (*CRE*)-dependent transcriptional activity was assessed using a luciferase reporter assay. Cells treated with 300 nM TSH served as a positive control, while human thyroid organoids were used to confirm the effects of hCG on native tissues. All experiments were run in quadruplicate ($n = 4$) and statistical analyses were performed by Kruskal-Wallis test and Dunn's post hoc comparisons ($P < .05$).

1 μM hCG induced significant increase of intracellular cAMP levels, confirmed by the activation of *CRE*-dependent activity. These data are consistent with hCG-dependent activation of the TSHR/Gs pathway. Surprisingly, sub-μM LH doses did not induce cAMP accumulation and *CRE* activation, which were even inhibited by 1 μM LH. Neither hCG nor LH increased intracellular IP1 levels, although 1 μM LH (but not hCG) resulted in the reduction of TSH-induced IP1 accumulation when the two hormones were co-administered to cells. These results indicated LH-dependent inhibitory activity of TSHR-mediated Gq pathway. hCG-specific effects were confirmed in thyroid organoids, where the hCG supported sample viability and preserved its cAMP responsiveness to TSH. These findings demonstrate that hCG selectively cross-activates TSHR-dependent cAMP/*CRE* signals and thyroid tissue responsiveness, consistent with its role in gestation. LH behaves as a TSHR antagonist, negatively modulating both Gs and Gq pathways.

Previous studies demonstrated that LH and hCG elicit different LHCGR-mediated signaling pathways. Therefore, this study strengthens the concept of different LH vs hCG signaling and proposes TSHR as a new partner receptor for gonadotropins, opening to new mechanisms regulating thyroid pathophysiology.

Abstract citation ID: lvag096.527

P394 - ECE_3872 - The role of the calcium stimulation test in the early detection of medullary thyroid carcinoma

Selin Celik[1], Aykut Celik[2], Tugba Matlim Ozel[2], Zeynep Elüstü Belten[1], Ozge Sahin Kimyon[1], Utku Erdem Soyaltin[3], Sema Ciftci[1] and Hamide Piskinpasa[1]

[1]*Department of Endocrinology and Metabolism, University Of Health Sciences, Bakirkoy Dr. Sadi Konuk Research and Training Hospital, İstanbul, Türkiye;* [2]*Department of General Surgery, Division of Endocrine Surgery, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, İstanbul, Türkiye;* [3]*Department of Endocrinology and Metabolism, Ege University Faculty of Medicine, İzmir, Türkiye*

Background: Medullary thyroid carcinoma (MTC) is a malignancy originating from parafollicular-C cells and characterized by

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

calcitonin (CT) secretion. Although basal calcitonin(bCT) levels have high sensitivity, mildly elevated CT levels may lead to diagnostic uncertainty. Since CT secreted by C cells is expected to rise in response to calcium stimulation, we aimed to assess the diagnostic value of the calcium stimulation test in patients with mildly CT levels who underwent surgery.

Methods: Forty-two patients with nodular thyroid disease and mildly elevated serum CT levels who underwent thyroidectomy were included in this study. None of the patients had any chronic disease known to cause elevated calcitonin. bCT and calcium-stimulated CT(casCT) levels were measured preoperative in all patients. CT reference values were considered positive at >6.4pg/mL for women and >9.5pg/mL for men. Given the known sex-releated differences in CT reference values, bCT and casCT levels were normalized by calculating the fold increase compared to the upper limit of normal(ULN). bCT and casCT levels were evaluated in relation to postoperative pathology for assessing diagnostic value.

Results: Among the 42 patients (19F/23M) with a mean age of 48 ± 12 years included in the study, MTC was diagnosed in 23.8% (6F/4M), while 76.2% (13F/19M) had non-MTC pathology. There were no significant differences between the groups in terms of age, sex, autoimmune thyroid disease, smoking or ppı use($P > .05$). Median bCT levels were significantly higher in the MTC group (20pg/mL;range 11-98) than non-MTC group (13pg/mL; range 9-57)($P = .048$). Similarly, the fold increase in bCT relative to the reference value was significantly higher in patients with MTC(2.75-fold;range 1.19-15.31) compared with the non-MTC group (1.57-fold;range 1.05-8.91)($P = .045$). Median casCT levels were significantly higher in the MTC group (631.5pg/mL;range 164-1820) than non-MTC group(213pg/mL;range 31-855)($P = .020$). The fold increase in casCT relative to the reference value was also significantly higher in patients with MTC (66.33-fold;range 25.63-284.38)compared with the non-MTC group(29.24-fold;range 4.84-97.66)($P = .017$). ROC analysis showed that casCT cut-off of 37.4×ULN provided 70% sensitivity and 66% specificity for MTC diagnosis (AUC = 0.748, 95% Cl:0.582-0.915;$P = .019$).

Conclusions: Both bCT and casCT levels, as well as their fold increases relative to reference values, are significantly higher in patients with MTC. CasCT, particularly when expressed as multiples of the ULN, provides additional diagnostic value in patients with mildly elevated CT levels. A casCT cutoff of 37.4×ULN offers an acceptable balance between sensitivity and specificity for identifying MTC, although validation in larger prospective studies is warranted.

Abstract citation ID: lvag096.528

P395 - ECE_1206 - Impact of subclinical hypothyroidism on renal outcomes: a systematic review and meta-analysis

Paolo Augusto Romero Merino[1], Carlos Valladares[2], Stefanni Vivanco[3], Jenny Zablah[4], Brigida Tueros[5], Rommel Portilla[6], Sebastian Vega[7] and Jia Chia[8]

[1]*Hospital Clinico Universitario of Valladolid, Valladolid, Spain;* [2]*University of Miami Miller School of Medicine, Miami, United States;* [3]*Universidad de San Martin de Porres, Lima, Peru;* [4]*Universidad Tecnológica Centroamericana, Tegucigalpa, Honduras;* [5]*Universidad Nacional Federico Villareal, Lima, Peru;* [6]*Universidad de las Américas, Quito, Ecuador;* [7]*Universidad Peruana Cayetano Heredia, Lima, Peru;* [8]*Texas Tech University Health Science Center, El paso, Texas, United States*

Background: Subclinical hypothyroidism (SCH), characterized by elevated serum TSH with preserved free thyroxine levels, is frequently identified in adult populations and has been suggested as a potential contributor to impaired renal function. Nevertheless, the strength and consistency of the association between SCH and the development of chronic kidney disease (CKD) remain unclear.

Methods: We carried out a systematic review and meta-analysis following PRISMA 2020 recommendations. A comprehensive search of major electronic databases identified observational studies that reported incident CKD among individuals with SCH. Five studies fulfilled the inclusion criteria, collectively encompassing more than 4 million participants. Random-effects models were used to estimate pooled risk ratios (RR). The quality and risk of bias of the included studies were assessed using the ROBINS-I tool.

Results: Across the pooled analysis, SCH was associated with a higher likelihood of developing CKD (RR 1.19; 95% CI 1.10-1.29). Heterogeneity across studies was moderate ($I^2 = 48.9\%$). Multiple sensitivity analyses, including exclusion of high-risk studies and alternative SCH definitions, showed consistent results, reinforcing the stability of the observed association. Evaluation of funnel plot symmetry did not reveal meaningful publication bias.

Conclusions: Individuals with SCH exhibit a modest but significant increase in the risk of incident CKD. These findings support the relevance of thyroid function abnormalities in renal risk profiling and raise the possibility that earlier recognition or intervention in SCH could influence long-term kidney outcomes. Future prospective studies and interventional trials are needed to clarify whether managing SCH may prevent or delay CKD progression.

Keywords subclinical hypothyroidism, chronic kidney disease, renal impairment, thyroid function, meta-analysis

Abstract citation ID: lvag096.529

P396 - ECE_1610 - Batoclimab induces very rapid and sustained post-treatment euthyroidism in Graves' disease

George Kahaly[1], Jan Wolf[1], Anna-Lena Ganz[1], Maximilian Luffy[1], Katherine Albert[2], Farah Ali[2], E Lin[2] and William Maclas[2]

[1]*Department of Medicine I, Johannes Gutenberg University Medical Center, Mainz, Germany;* [2]*Immunovant, Inc., New York, NY, United States*

Objective: To report post-treatment outcomes among hyperthyroid patients with Graves' disease (GD) who received batoclimab, a neonatal fragment crystallizable receptor blocker, in a phase 2a, proof-of-concept open-label study.

Methods: Overtly hyperthyroid GD participants with elevated thyrotropin receptor autoantibodies (TRAb) despite ≥12 weeks on moderate-to-high dose antithyroid drugs (ATD) received weekly subcutaneous injections of batoclimab for 24 weeks (Weeks 0-11,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

680 mg; Weeks 12-23, 340 mg). At Week 24, participants with FT3/FT4 at or below the upper limit of normal (ULN) entered a 24-week treatment-free follow-up period (Weeks 24-48).

Results: By Week 2, 15/25 (60%) patients achieved FT3/FT4 levels at or below ULN without increasing their ATD dose; this increased to 20/25 (80%) patients at Week 12 or end of high-dose treatment, including 15 (60%) who were off ATD. At Week 24 or end of treatment (EOT), 18 (72%) patients had FT3/FT4 ≤ULN without increasing their ATD dose, including 10 (40%) who were off ATD. Six months following EOT, 17/25 (68%) patients had FT3/FT4 ≤ULN; of these, 8 were off ATD and 5 were on ≤2.5 mg ATD/day only. Mean (SD) TSH increased from 0.01 (0.01) mIU/L at baseline to 0.32 (0.61) mIU/L and 0.77 (0.85) mIU/L at Weeks 24 and 48, respectively. Patients who were off ATD 24 weeks after EOT had a mean (SD) TSH of 0.55 (0.47) mIU/L and low TRAb (<2xULN) at EOT/Week 24. Mean (SD) TRAb levels rapidly decreased from 17.96 (12.12) IU/L at baseline to 8.13 (8.82) IU/L, 6.16 (8.85) IU/L, and 9.94 (12.03) IU/L at Weeks 2, 24, and 48, respectively ($P < .0001$ vs baseline for all). Total IgG rebounded after treatment stopped, with a mean (SD) level of 11.72 (2.64) g/L at baseline compared with 4.10 (1.76) g/L at Week 24 ($P < .001$) and 11.14 (2.78) g/L at Week 48 ($P = .42$). In patients with eye signs/symptoms at baseline (20/25), EOT improvements in proptosis and Clinical Activity Score were sustained at Week 48. Batoclimab was well tolerated with no new safety signals observed.

Conclusions: Batoclimab resulted in very rapid and sustained normalization of FT3/FT4. Six months after stopping treatment, 52% of patients remained euthyroid either off ATD or on ≤2.5 mg ATD/day.

Abstract citation ID: lvag096.530

P397 - ECE_2810 - The impact of severe overt primary hypothyroidism on outcomes of hospitalized patients with bacteremia

Dor Eldar[1], Naftali Gross[2], Meir Frankel[1], Eli Ben-Chetrit[3], Noa Sylvetsky[1], Gavriel Lichewitz[3], Michal Manovich[1] and Gabriel Munter[1]

[1]*Shaare Zedek Medical Center, Hebrew University School of Medicine, Endocrinology, Diabetes & Metabolism Unit, Jerusalem, Israel;* [2]*Jerusalem, Israel;* [3]*Shaare Zedek Medical Center, Hebrew University School of Medicine, Endocrinology, Diabetes & Metabolism Unit, Jerusalem, Israel*

Background: Thyroid dysfunction is common among hospitalized patients and may adversely influence clinical outcomes during acute illness. This study evaluated whether severe overt primary hypothyroidism at admission is associated with worse outcomes among inpatients with blood culture proven bacteremia.

Methods: A retrospective cohort study was conducted at Shaare Zedek Medical Center (Jerusalem, Israel) between the years 2000 and 2024. Adult inpatients (≥18 years) with a history of hypothyroidism or levothyroxine use, and available thyroid function tests (TFTs) at admission were included. At our center, TSH is routinely measured for all hospitalized patients on admission. Hypothyroidism was defined by documented diagnosis, chronic levothyroxine use, or TSH > 20 mU/L. Uncontrolled hypothyroidism was defined as TSH > 10 mU/L. Primary outcomes included, among others, in-hospital mortality, and length of stay (LOS)

Results: Among 1756 patients (mean age 82.4 ± 11.8 years; 72.4% female), in-hospital mortality increased progressively with higher TSH levels: 14% for TSH 0.35-5 mU/L, 19.3% for TSH 5-10 mU/L, 22.9% for TSH 10-20 mU/L, and 32.7% for TSH > 20 mU/L. Adjusted Cox regression demonstrated that TSH > 20 mU/L was independently associated with mortality (HR 1.89, 95% CI 1.28-2.79, $P = .001$). A continuous TSH model confirmed an incremental risk (HR 1.02 per 1 mU/L TSH increase, $P < .001$). Additional independent correlates of mortality included older age (HR 1.05, $P < .001$), female sex (HR 1.35, $P = .037$), and vasopressor use (HR 1.77, $P < .001$), whereas higher albumin levels were significantly protective (HR 0.54, $P < .001$). Median LOS also increased with higher TSH: 8.0 days (IQR 5.0-16.0) for TSH 0.35-5 mU/L, 8.5 days (IQR 6.0-17.0) for TSH 5-10 mU/L, 11.0 days (IQR 6.0-26.0) for TSH 10-20 mU/L, and 13.0 days (IQR 7.0-21.25) for TSH > 20 mU/L.

Conclusions: Uncontrolled hypothyroidism, particularly TSH > 20 mU/L, is an independent predictor of higher in-hospital mortality and is associated with prolonged hospitalization among patients with bacteremia. These findings suggest that thyroid status serves as a significant prognostic marker in this high-risk population and warrant further prospective studies to evaluate targeted management strategies.

Abstract citation ID: lvag096.531

P400 - ECE_3966 - Treatment with intramuscular levothyroxine in refractory hypothyroidism: a case report

Ana Luísa Barbosa, Mafalda Canudas Costa, Marta Borges Canha, Sandra Belo and Joana Queirós

Department of Endocrinology, Diabetes and Metabolism, São João Local Health Unit, Porto, Portugal

Background: Oral levothyroxine is the standard treatment for hypothyroidism, with most patients achieving stable hormone levels. When standard therapy is ineffective and doses exceeding 1.9 μg/kg/day are required, the differential diagnosis includes levothyroxine malabsorption and pseudomalabsorption (nonadherence to therapy), and alternative approaches, including injectable levothyroxine, can be considered.

Case Report: We present a 66-year-old woman with a history of hypothyroidism following total thyroidectomy eleven years earlier for a follicular neoplasm, on oral levothyroxine therapy. Due to persistent hypothyroidism despite escalating doses of oral levothyroxine (up to 2.6μg/kg/day), she was referred to the Endocrinology clinic. Laboratory evaluation did not reveal signs of malabsorption, with normal haemoglobin, albumin, ferritin, vitamin B12 and folic acid, negative antibodies for celiac disease and autoimmune gastritis and a negative urea breath test for Helicobacter pylori infection. Due to suspected nonadherence, she was treated with oral levothyroxine twice weekly under supervision at her local health centre, with the dose escalated up to 4000μg/week. Nevertheless, hypothyroidism persisted with worsening biochemical parameters (thyroid-stimulating hormone [TSH] >100 [0.35-4.94] μUI/mL, low free thyroxine [FT4] 0.42 [0.70-1.48] ng/dL) and clinical manifestations including fatigue, brain fog, hair loss and peripheral and periorbital edema. She was admitted to the Endocrinology ward and treated with intravenous levothyroxine (100-150μg/day) for fourteen days,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

resulting in normalization of thyroid function. Subsequently, a levothyroxine absorption test performed after an overnight fast, with supervised intake of 1600μg of levothyroxine, showed peak elevation of FT4 two hours after ingestion (from 1.01 ng/dL to 1.72ng/dL, representing an increase of more than 0.4ng/dL), with a concomitant decrease in TSH (from 7.13μUI/mL to 3.07μUI/mL), thereby ruling out levothyroxine malabsorption. The patient was discharged on 1800μg of oral levothyroxine twice weekly under supervision at her local health centre. Laboratory evaluation performed four months later showed TSH 53μUI/mL and FT4 0.64ng/dL. Treatment with weekly intramuscular levothyroxine (800μg), administered at her local health centre, was initiated, resulting in normalization of thyroid function after one month (TSH 2.99μUI/mL, FT4 1.36ng/dL).

Discussion: This case illustrates the challenges in managing refractory hypothyroidism and demonstrates that intramuscular levothyroxine can be an effective alternative in such situations. It highlights the importance of an individualized approach, considering all therapeutic options to achieve adequate thyroid hormone control and prevent progression to severe disease.

Abstract citation ID: lvag096.532

P401 - ECE_1443 - Refining ACR TI-RADS risk stratification with strain elastography: reducing unnecessary fine-needle aspirations in thyroid nodules

Nicholas Angelopoulos[1], Dimitrios Goulis[1], Ioannis Chrisogonidis[1], Ioannis Iakovou[1] and Fraklin Tessler[2]
[1]*Aristotle University of Thessaloniki, AHEPA Hospital, Nuclear Medicine, Thessaloniki, Greece;* [2]*Department of Radiology, University of Alabama at Birmingham, Birmingham, United States*

Background: The American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) relies exclusively on grayscale ultrasonography (US) for malignancy risk stratification, without incorporating clinical variables or adjunctive imaging modalities. Despite its effectiveness, a substantial number of benign thyroid nodules still undergo unnecessary fine-needle aspiration (FNA), particularly in low- and intermediate-risk categories.

Objective: To evaluate whether the integration of strain elastography, color Doppler ultrasonography (CDUS), and selected clinical parameters improves malignancy risk stratification and optimizes FNA utilization beyond current ACR TI-RADS recommendations.

Methods: In this prospective study, 556 adults with thyroid nodules ≥10 mm who met ACR TI-RADS criteria for FNA were enrolled between May 2023 and April 2025. All nodules underwent standardized B-mode US, CDUS, and strain elastography. A semi-quantitative elastography ratio (ER) was calculated as the ratio of nodule stiffness to the adjacent sternocleidomastoid muscle. Cytological results were classified using the Bethesda System, with histopathology serving as the reference standard when surgery was performed. Receiver operating characteristic (ROC) analyses were conducted to determine optimal ER thresholds overall and within each ACR TI-RADS category.

Results: Among the 556 nodules evaluated, 55 papillary thyroid carcinomas were identified. Overall, elastography demonstrated good diagnostic performance for malignancy prediction (AUC 0.886). When analyzed by ACR TI-RADS category, ER showed excellent discriminatory ability in TI-RADS 3 nodules (AUC 0.994), with an optimal threshold of ER >1.60 achieving 100% sensitivity and 99.4% specificity. Category-specific ER thresholds (>1.60 for TI-RADS 3, >0.44 for TI-RADS 4, and >0.54 for TI-RADS 5) allowed a reduction in FNAs from 501 to 260 (48%) without missing any malignant cases. Elastography provided the greatest additive value in low-risk nodules, where unnecessary biopsies are most frequent.

Conclusions: The integration of strain elastography into the ACR TI-RADS framework substantially improves risk stratification and safely reduces unnecessary FNAs, particularly in low- and intermediate-risk thyroid nodules. These findings support the incorporation of elastography-derived thresholds into future revisions of thyroid nodule risk stratification systems.

Abstract citation ID: lvag096.533

P402 - ECE_1170 - Development of a practical risk score for malignancy prediction in Bethesda III thyroid nodules: integrating clinical, ultrasonographic, and cytological predictors in a multicenter study

Manuel Carpio Salmerón[1], Georgios Kyriakos[1], Antonio Rios Vergara[1], Mariano Tébar Caballero[2], Irene Martin Perez[1], Paula Villalba Armario[1], Clara Marín Sospedra[1], Ana Casas Miras[3], Alfonso Agüera Sánchez[4], Ana Balibrea Ruiz[5] and Luis Marin Martinez[1]
[1]*General University Hospital Santa Lucía, Endocrinology and Nutrition, Cartagena (Murcia), Spain;* [2]*Reina Sofía University General Hospital, Internal Medicine, Murcia, Spain;* [3]*General University Hospital Santa Lucía, Pathological Anatomy, Cartagena (Murcia), Spain;* [4]*Reina Sofía University General Hospital, Pathological Anatomy, Murcia, Spain;* [5]*General University Hospital Santa Lucía, Family and Community Medicine, Cartagena (Murcia), Spain*

Introduction and Objectives: Bethesda III (atypia of undetermined significance) remains a major management challenge, and there is a need for simple malignancy risk-stratification tools to guide decision-making. This study aimed to identify clinical, ultrasonographic and cytological predictors of malignancy in Bethesda III thyroid nodules and to develop an easy-to-use score to estimate individual malignancy risk in histologically confirmed cases.

Methods: We conducted an observational, retrospective, multicentre study (2019-2024) including patients with a Bethesda III cytological diagnosis who subsequently underwent thyroid surgery. Clinical, ultrasonographic and cytological features of benign and malignant nodules were systematically compared. Univariate and multivariate logistic regression analyses were used to identify independent predictors of malignancy. Based on the final beta-coefficients, we constructed a 0-12 point risk score and defined three risk categories with suggested management strategies.

Results: Eighty-five Bethesda III nodules were analysed; 65 (76.5%) were benign and 20 (23.5%) malignant. Independent predictors of malignancy were: high-risk ACR-TIRADS category 4-5 (OR 6.15; 95% CI 1.17-32.37; $P = .032$), lymphocytic thyroiditis (OR 3.81; 95% CI 1.06-13.73; $P = .041$) and nuclear atypia (OR 5.23; 95% CI

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

1.53-17.90; $P = .008$). A cut-off of ≥8 points maximised Youden's index (0.54), with 75% sensitivity, 79% specificity, PPV 54% and NPV 91%.

Three risk strata were defined:- SCORE ≥8 (high/very high risk): recommendation for surgery.

- SCORE 5-7 (intermediate risk): consider repeat FNA and/or molecular testing.

- SCORE ≤4 (low risk): ultrasound follow-up.

Malignancy rates increased across categories, from low in the SCORE ≤4 group to approximately one in two nodules in the SCORE ≥8 group.

The model's discriminative capacity was high, with an area under the curve (AUC) of 0.83, indicating very good performance in differentiating benign from malignant nodules in the Bethesda III category. Limitations include retrospective design and modest sample; prospective validation planned.

Conclusions: In Bethesda III thyroid nodules, malignancy was independently associated with high-risk ACR-TIRADS categories, lymphocytic thyroiditis and nuclear atypia. The proposed 0-12 point score provides practical and individualised malignancy risk stratification and may help optimise the indication for surgery, repeat FNA or molecular testing in this uncertain diagnostic category.

Abstract citation ID: lvag096.534

P403 - ECE_1776 - Identification of a senescent-like cell population with a low differentiation state in BRAFV600E-mutated follicular cell-derived thyroid carcinoma

Alexandra Monnot[1,2], Myriam Decaussin-Petrucci[2,3], Marie Chanal[2], Flore Deroux[2], Gabriela Makunyte[2], Francoise Borson-Chazot[1], Lifante Jean-Christophe[4], David Bernard[2], Lasolle Hélène[1,2] and Philippe Bertolino[2]

[1]Endocrinology Department, Hospices Civils de Lyon, Hôpital Louis-Pradel, Bron, France; [2]Inserm U1052, CNRS UMR5286, Cancer Research Center of Lyon, Lyon 1 University, Lyon, France; [3]Hospices Civils de Lyon, Groupement Hospitalier Sud, Pathology Department, Pierre Bénite, France; [4]Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, Endocrine Surgery Department, Pierre Bénite, France

Introduction: The role of senescence in follicular cell-derived thyroid carcinoma (FCDTC) has been confirmed *in vitro* and *in vivo*. While senescence markers, including SA-β-gal activity, p16, and p21 expression, vary across tumor contexts and thyroid cancer progression, the role of thyroid senescent tumor cells and their secretome has been confirmed at the invasive front where these cells contribute to collective migration and invasion. Here we explore the spatial heterogeneity and relationship between senescent markers and tumor differentiation to refine the characterization of senescent cells in BRAFV600E FCDTC.

Methods: Published single-cell transcriptomic datasets and Xenium spatial sequencing data from BRAFV600E FCDTC were analyzed. Thyroid Differentiation Score (TDS) and senescence signatures (Fridman_up, SenMayo) were assessed in clustered and spatially sequenced tumors. Differential gene expression analyses were conducted to identify novel markers of senescent tumor cells. Immunohistological validations were performed on differentiated and high-grade FCDTC to further assess senescence markers (SA-β-gal, p16, and p21) and validate a candidate marker (LAMC2, a known senescence-associated candidate gene).

Results: Single-cell transcriptomic analysis of 109956 cells integrated from 18 samples identified a FCDTC cell population with a lower Thyroid Differentiation Score that was enriched for *CDKN2A* expression and senescence signatures. Histological stainings demonstrated a tumor-specific, yet spatially heterogeneous expression of P16 in tumor tissues compared to normal thyroid controls, while expression of P21 was more homogeneous between tumor and control tissues. Spatial transcriptomic analysis of 2 BRAFV600E-FCDTC (DTC and HGFCDTC) identified two tumor cell clusters with distinct TDS profiles. Senescence markers were enriched in TDS-Low cells, which were frequently observed at the invasive front and displayed a mutually exclusive spatial distribution compared to TDS-High clustered cells. Thyroglobulin (TG) immunohistochemistry confirmed the exclusive spatial distribution between P16 and TG-expressing cells. Differential gene expression identified 74 candidate marker genes in TDS-Low senescent tumor cells. Histological expression and spatial distribution of LAMC2, an identified candidate marker, was confirmed in TDS-low tumor regions.

Conclusions: Integrated analysis of single-cell, spatial transcriptomic and histological staining supports that senescence markers are enriched in a tumor cell population that is located at the invasive front of BRAFV600E FCDTC. Our results further support that these cells exhibit a reduced expression of thyroid differentiation markers. The identification of a gene signature associated with these TDS-Low senescent cells refines the biological characterization of intratumoral FCDTC heterogeneity. It further provides a foundation for exploring the prognostic value of TDS-Low senescent cells and their potential therapeutic interest in thyroid cancer.

Abstract citation ID: lvag096.535

P405 - ECE_3240 - Risk of Parkinson's disease in long-term survivors of thyroid cancer: a nationwide population-based cohort study

Se Hee Park, Min Heui Yu, Jung Ho Kim and Namki Hong

Seoul, South Korea

Background: As the survival of patients with thyroid cancer (TC) increases, understanding long-term treatment-related complications has become essential. While thyroid hormone levels are known to influence neurodegenerative processes, the association between postoperative levothyroxine therapy and the risk of Parkinson's disease (PD) remains unclear. This study aimed to investigate the risk of PD in patients who underwent thyroidectomy for TC using a large-scale nationwide database.

Methods: We conducted a retrospective cohort study using data from the Korean National Health Insurance Service (2004-2019). A total of 269 963 patients aged 40 years or older who underwent thyroidectomy for TC were matched 1:1 by age and sex with controls without a history of cancer or PD. The primary outcome was the risk of developing PD, estimated using multivariable Cox proportional hazards models adjusted for age, sex, income level, and Charlson Comorbidity Index. Sub-analyses further evaluated the impact of thyroidectomy extent, radioactive iodine (RAI) therapy, and levothyroxine dose categories on PD risk.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: During the follow-up period, PD incidence rates were 8.86 vs 8.36 per 10 000 person-years in the TC and control groups, respectively. The overall risk of PD in TC patients was not significantly higher after adjusting for multiple comorbidities (adjusted hazard ratio (aHR) 1.02, 95% confidence interval (CI) 0.95-1.08, $P = .611$). However, a significant dose-response relationship was observed regarding the average postoperative levothyroxine dose. Compared to the control group, patients receiving high-doses of levothyroxine exhibited a significantly increased risk of PD: aHR 1.15 (95% CI, 1.01-1.31; $P = .041$) for 125-149 μg/day and aHR 2.28 (95% CI, 2.04-2.56; $P < .0001$) for ≥150 μg/day. In the subgroup analysis of levothyroxine ≥150 μg/day group, the risk was significantly more pronounced in females (aHR 1.62; 95% CI, 1.27-2.06) than in males (aHR 1.05; 95% CI, 0.72-1.55; P-interaction = .033). PD incidence did not differ significantly based on the extent of surgery or the use of RAI therapy.

Conclusions: While the overall risk of PD in thyroid cancer survivors is comparable to that of the general population, high-dose levothyroxine therapy is associated with a markedly increased risk of PD, especially at doses ≥150 μg/day. These findings suggest that the intensity of long-term TSH suppression therapy should be carefully balanced against potential neurodegenerative risks.

Abstract citation ID: lvag096.536

P406 - ECE_1051 - Thyroid hormone resistance or TSH-secreting pituitary adenoma: a diagnostic dilemna

Kevin Kwek[1] and Aaron Ng[2]
[1]Endocrinology, Khoo Teck Puat Hospital, Singapore; [2]Tan Tock Seng Hospital, Singapore

While interpretation of thyroid testing is generally straightforward, hyperthyroxinemia with inappropriately raised TSH presents a diagnostic challenge for Endocrinologists. Careful clinical, biochemical, radiological and genetic investigation are required to clinch an accurate diagnosis.

A 54-year-old gentleman with notable history of hypertension and pre-diabetes diagnosed 5 years prior was evaluated at our clinic for a screening thyroid function test (Roche Cobas E801 assay) showing free thyroxine (fT4) of 34.2 pmol/L (RR 12-22) and of TSH 1.74 mIU/L (RR 0.27-4.2). Of note, a previous thyroid function test at our institution 4 years prior showed a similarly elevated fT4 of 32.3 pmol/L with TSH of 1.84 mIU/L.

On clinical evaluation, he volunteered history of intermittent palpitations and tremors since childhood. Resting tachycardia (HR 110-120bpm) was observed. Thyroid eye disease, pretibial myxedema or palpable goitre were not observed. He had no family history of hyperthyroidism, pituitary tumour or other endocrinopathies. He was not consuming any potential interfering drugs or biotin-containing supplements.

Table 1 Repeat biochemistry

Test	Result	Reference Range
fT4 (Roche Cobas)	34.8 pmol/L	12-22
TSH (Roche Cobas)	1.75 mIU/L	0.27-4.2
Free triiodothyronine (Roche cobas)	7.8 pmol/L	3.1-6.8
fT4 (Abbott Alinity)	24 pmol/L	9-19.1
TSH (Abbott Alinity)	1.35 mIU/L	0.35-4.94
Total thyroxine (Abbott Alinity)	207 nmol/L	63-151

Concordant results (Table 1) obtained with the Abbott Alinity assay suggest against assay interference. Testing for thyrotropin receptor and anti-thyroid peroxidase antibodies was negative. Thus, we performed further evaluation to distinguish between TSH-producing pituitary adenoma (TSHoma) and resistance to thyroid hormone (RTH).

Table 2 Further testing

Test	Result	Reference Range
Alpha-subunit	0.1ng/ml	<0.5
TSH	1.57 mIU/L	0.27-4.2
Ferritin	136ng/ml	30-400
Sex hormone binding globulin (SHBG)	47 nmol/L	17-78

The normal alpha-subunit:TSH molar ratio (0.63) and normal tissue markers of thyroid hormone action suggest RTH over TSHoma. A TRH stimulation test demonstrated brisk response of TSH (1.75 mIU/L > 13.3 mIU/L (30min) > 7.84 mIU/L (60mins)) consistent with RTH. T3 suppression testing was contraindicated due to resting tachycardia. Thus, we performed genetic screening (Blueprint genetics thyroid hormone resistance panel), which unexepectedly did not detect any known disease-causing variants.

We performed pituitary magnetic resonance imaging to re-evaluate the diagnosis, which revealed 3x2x3mm pituitary tumour. As this may represent an incidental non-functioning microadenoma or a TSHoma, octreotide suppression testing was offered. At present, he is responding well to symptomatic therapy with beta blockade.

This diagnostic dilemma demonstrates the limitations of existing diagnostic algorithms in differentiating TSHoma and RTH. We await further advances, especially in genetic testing, which may shed further light on this case.

Abstract citation ID: lvag096.537

P407 - ECE_1277 - Preclinical evaluation of calcitriol in Graves' disease under varying vitamin D status

Daham Kim, Yaru Bao, So Jeong Lee, Se Hee Park and Eun Jig Lee
Yonsei University College of Medicine, Seoul, South Korea

Graves' disease (GD) is an autoimmune thyroid disorder driven by immune dysregulation. Vitamin D has immunomodulatory effects, but its activation is tightly controlled by rate-limiting hydroxylation steps. While supplementation offers limited benefit

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

in vitamin D-replete individuals, the active form of vitamin D (calcitriol) bypasses these steps and may provide stronger immune regulation. This study evaluated the effects of calcitriol in a preclinical GD model under vitamin D-sufficient and vitamin D-deficient conditions.

Rosa26_hTSHRa (Balb/c) mice were maintained on either a standard diet or a vitamin D-deficient diet initiated four weeks before the experimental schedule. Within each dietary condition, mice were assigned to three groups: Control, GD, and GD+calcitriol. The GD and GD+calcitriol groups received 250 U of TAT-Cre by intramuscular injection into one thigh at 8 weeks of age, followed by an injection into the contralateral thigh three weeks later. The GD+calcitriol group was treated with calcitriol (5 μg/kg, subcutaneously, three times weekly) beginning at week 7. Serum T4 and TSHR antibody levels were measured at weeks 6 and 13 using ELISA.

At week 6, both dietary conditions showed a significant elevation of TSHR antibodies in the GD and GD+calcitriol groups compared with the control group, with similar titers between the two groups. This increase was numerically greater in the vitamin D-deficient diet experiment. Serum T4 levels also began to rise, and in the standard diet experiment, a significant difference from the control group appeared earlier.

At week 13, although the difference between the GD and GD +calcitriol groups did not reach statistical significance, the vitamin D-deficient diet experiment demonstrated a greater reduction in TSHR antibodies in the GD+calcitriol group compared with the GD group. In the standard diet experiment, T4 levels tended to be higher in the GD group but no significant differences were observed between groups; however, the GD+calcitriol group showed a significant decrease in T4 levels relative to its week-6 level. In the vitamin D-deficient diet experiment, the GD group exhibited a significant increase in T4 compared with the control group, whereas the GD+calcitriol group maintained T4 levels comparable to those of the control group.

These findings suggest that calcitriol exerts a protective effect against GD-associated thyroid dysfunction, particularly under vitamin D-deficient conditions, by attenuating T4 elevation and promoting a reduction in TSHR antibody levels. Calcitriol may therefore serve as a potential adjunctive therapeutic strategy for GD, especially in individuals with inadequate vitamin D status.

Abstract citation ID: lvag096.538

P409 - ECE_2414 - Association of hashimoto thyroiditis with tumor characteristics and recurrence in papillary thyroid carcinoma

Solji An, Joonseon Park, Kwangsoon Kim and Ja Seong Bae
Seoul, South Korea

Background: The relationship between Hashimoto thyroiditis (HT) and papillary thyroid carcinoma (PTC) remains controversial. This study aimed to evaluate the clinicopathologic characteristics and prognostic impact of coexisting HT in patients with PTC.

Methods: A total of 6581 patients who underwent surgery for PTC were retrospectively analyzed. Patients were classified into control ($n = 5396$) and HT ($n = 1185$) groups based on histopathologic diagnosis. Clinicopathologic features, molecular profiles, surgical extent, and recurrence-free survival (RFS) were compared. Multivariate logistic regression analysis was performed to identify factors associated with coexisting HT. RFS was analyzed using the Kaplan–Meier method.

Results: Patients with HT were more likely to be female and younger (both $P < .001$). Total thyroidectomy and central lymph node dissection were more frequently performed in the HT group ($P = .005$ and $P = .003$, respectively). HT was associated with higher rates of multifocality ($P < .001$) but showed no significant differences in tumor size, vascular invasion, lymphatic invasion, extrathyroidal extension, or lateral lymph node metastasis. The HT group demonstrated a lower prevalence of BRAF mutation (72.2% vs 84.7%, $P < .001$), while TERT mutation rates were comparable. Preoperative TSH, thyroglobulin, and anti-thyroglobulin antibody levels were significantly higher in patients with HT (all $P < .001$). On multivariate analysis, female sex, younger age, multifocal disease, absence of extrathyroidal extension, absence of BRAF mutation, and higher preoperative anti-thyroglobulin antibody levels were independently associated with coexisting HT. During follow-up, recurrence rates did not differ significantly between groups (3.2% vs 3.4%, $P = .726$), and Kaplan–Meier analysis showed no significant difference in RFS ($P = .73$).

Conclusions: Coexisting Hashimoto thyroiditis in PTC is associated with distinct clinicopathologic and molecular characteristics, including female predominance, multifocality, and lower BRAF mutation rates. However, HT does not appear to influence recurrence-free survival. These findings suggest that while HT affects tumor presentation, it has limited prognostic impact on long-term outcomes in PTC.

Abstract citation ID: lvag096.539

P410 - ECE_2915 - Surgical extent, tumor size, and calcitonin levels in medullary thyroid carcinoma: impact on oncologic outcomes in a retrospective cohort study

Ekin Yiğit Köroğlu[1], Berna Evranos Ogmen[2], Muzaffer Serdar Deniz[1], Barış Saylam[3], Hilal Ahsen[4], Cevdet Aydin[2], Oya Topaloglu[2], Reyhan Ersoy[2] and Bekir Cakir[2]
[1]Endocrinology and Metabolism Diseases, Ankara Bilkent City Hospital, Ankara, Türkiye; [2]Endocrinology and Metabolism Diseases, Ankara Yıldırım Beyazıt University, Ankara, Türkiye; [3]Breast and Endocrine Surgery, General Surgery, Ankara Bilkent City Hospital, Ankara, Türkiye; [4]Medical Pathology, Ankara Bilkent City Hospital, Ankara, Türkiye

Background: Medullary thyroid carcinoma (MTC) treatment guidelines recommend surgical extent based primarily on calcitonin levels, yet the oncologic impact of deviating from these protocols remains incompletely characterized. This study evaluates whether individualized treatment approaches based on comprehensive tumor characterization compromise disease outcomes compared to guideline-adherent management, and examines the relative importance of tumor size, calcitonin levels, and surgical extent in predicting persistent disease.

Methods: This retrospective cohort study included 91 patients with histologically confirmed MTC followed at a tertiary center from January 2019 to March 2025. Surgical procedures were

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

compared against ATA-2015, ESMO-2019, and NCCN-2025 guideline recommendations and classified as concordant, less extensive, or more extensive. Primary outcomes included persistent disease (biochemical or structural incomplete response ≥6 months), reoperation rates, and postoperative complications. Associations between preoperative calcitonin levels and lymph node (LN) metastasis patterns were analyzed. Multivariable logistic regression identified independent predictors of persistent disease.

Results: Surgical procedures deviated from guidelines in 32.3% (ATA), 70.8% (ESMO), and 40.0% (NCCN) of cases. Deviation from guideline-recommended extent did not significantly impact persistent disease rates, reoperation requirements, or complication rates. Overall, 23.1% of patients had persistent disease at final follow-up. On multivariable analysis, independent predictors of persistent disease were higher preoperative calcitonin levels (OR 1.02 per 100 pg/mL increase, 95% CI 1.00-1.04, $P = .042$) and presence of LN metastasis (OR 4.52, 95% CI 1.01-20.24, $P = .049$), but not surgical extent classification. Primary tumor size correlated with metastatic involvement across all cervical compartments, while preoperative calcitonin levels predicted only ipsilateral lateral LN metastasis. A calcitonin threshold of 189.5 pg/mL predicted ipsilateral lateral metastasis with 92.3% sensitivity and 61.8% specificity.

Conclusions: Individualized surgical approaches based on comprehensive preoperative assessment do not compromise oncologic outcomes when compared to guideline-adherent protocols. Disease persistence is determined by tumor biology rather than adherence to standardized surgical algorithms. Integration of tumor size with calcitonin measurements may improve risk stratification and enable treatment personalization while maintaining disease control.

Abstract citation ID: lvag096.540

P411 - ECE_3079 - Diagnostic Value of Contrast-Enhanced Ultrasound in the Multimodal Assessment of Bethesda III and IV Thyroid Nodules

Agnieszka Żyłka[1], Katarzyna Dobruch-Sobczak[2], Jacek Gałczyński[1], Piotr Góralski[1], Elwira Bakuła-Zalewska[3] and Marek Dedecjus[1]

[1]Department of Endocrine Oncology and Nuclear Medicine, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [2]Radiology Department II, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [3]Department of Pathology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background: Indeterminate thyroid nodules classified as Bethesda category III and IV remain a major diagnostic challenge and frequently result in potentially unnecessary surgery. Conventional B-mode ultrasound provides limited diagnostic accuracy in this subgroup. Contrast-enhanced ultrasound (CEUS) has been proposed as an adjunct imaging modality, but its role in risk stratification remains unclear.

Methods: This single-centre imaging study included 63 patients (51 women, 12 men) with Bethesda III ($n = 19$) or IV ($n = 44$) thyroid nodules scheduled for surgery. All nodules underwent standardized B-mode ultrasound evaluation, including EU-TIRADS and strain elastography (Asteria score), followed by CEUS prior to surgery. CEUS assessment included enhancement intensity, homogeneity, wash-out pattern, and enhancement type after intravenous administration of 1.5 mL of contrast agent and was independently evaluated by two observers blinded to final histopathological diagnosis. Histopathology served as the reference standard. Diagnostic performance was assessed using ROC analysis with AUC calculation. Associations with malignancy were explored using univariate and confirmatory multivariate logistic regression.

Results: Malignancy was confirmed in 39.7% of nodules ($n = 25$), with papillary thyroid carcinoma (PTC) as the predominant histological subtype ($n = 11$, 40%). In the benign group, follicular adenoma was the dominant pathology ($n = 22$, 57.9%). Age, sex, and nodule size did not differ between malignant and benign nodules. In univariate analysis, several B-mode ultrasound features were significantly associated with malignancy, including hypoechogenicity (OR 8.57, $P = .048$), Asteria score 4 (OR 7.66, $P = .018$), and non-smooth margins (OR 3.26, $P = .029$), all demonstrating modest diagnostic performance (AUC range 0.612-0.643). Selected combinations of B-mode and CEUS features showed stronger associations with malignancy in univariate analysis, particularly non-smooth margins combined with hypoenhancement (OR 14.39, 95% CI 2.32-279.84; $P = .016$), as well as combinations of non-smooth margins with heterogeneous enhancement or fast wash-out, and hypoechogenicity combined with heterogeneous enhancement (OR range 2.92-3.71; all $P < .05$). Among these, the combination of non-smooth margins and CEUS hypoenhancement demonstrated the most robust diagnostic profile, with very high specificity (97%) and remained independently associated with malignancy in multivariate analysis (OR 10.46, 95% CI 1.53-210.66; $P = .040$).

Conclusions: In Bethesda III and IV thyroid nodules, conventional B-mode ultrasound remains fundamental for malignancy risk assessment, while contrast-enhanced ultrasound may provide incremental value when interpreted alongside standard ultrasound features. A multimodal ultrasound approach may improve diagnostic confidence and support clinical decision-making, although further validation in larger patient cohorts is required.

Abstract citation ID: lvag096.541

P412 - ECE_2422 - Serum selenium positively correlates with 25-hydroxyvitamin D in patients with Graves' disease

Cheng-Yu Tsai and Chia-Hung Lin

New Taipei City, Taiwan

Introduction: Serum selenium (Se) and 25-hydroxyvitamin D (25(OH)D) concentrations have been reported to differ between patients with and without Graves' disease (GD), yet the relationship between these two parameters remains unclear. Furthermore, whether GD status influences this relationship is also unknown. Thus, we aimed to investigate the association between serum Se and 25(OH)D and determine whether GD status modifies this relationship.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Methods: We analyzed data from a prospective cohort in a selenium-sufficient population at National Taiwan University Hospital. Participants with and without GD were enrolled, excluding those taking Se supplements. The association between serum Se and 25(OH)D was evaluated using Pearson's correlation and linear regression analyses stratified by GD status.

Results: A total of 116 subjects were enrolled, comprising 59 subjects with GD and 57 subjects without GD (non-GD). Serum Se levels were significantly higher in GD patients compared to non-GD controls (128.58 vs 119.32 μg/L, $P = .024$), while there was a trend toward lower 25(OH)D levels in GD patients (21.44 vs 24.05 ng/mL, $P = .071$). Serum Se levels were positively correlated with 25(OH)D (Pearson's correlation coefficient $r = 0.186$, $P = .045$). Correlation analysis stratified by GD status revealed a significant correlation between Se and 25(OH)D only in the GD group ($r = 0.287$, $P = .028$) but not in the non-GD group ($r = 0.153$, $P = .255$). Linear regression demonstrated a significant overall association between Se and 25(OH)D ($\beta = .299$, $P = .028$). Upon GD status stratification, a significant positive association was observed only in the GD group ($\beta = 0.568$, $P = .012$), whereas no such relationship was found in the non-GD group ($\beta = .135$, $P = .349$). After adjusting for age and fasting plasma glucose, the association between 25(OH)D and serum Se in the GD group still showed a trend toward statistical significance ($\beta = .376$, $P = .088$). In contrast, the association between serum Se and 25(OH)D remained non-significant in the non-GD group.

Conclusions: To our knowledge, this study is the first to investigate whether GD status modifies the association between serum Se and 25(OH)D levels in Taiwan, a selenium-sufficient country. We identified a distinct positive correlation between serum Se and 25(OH)D levels in subjects with GD, which was absent in subjects without GD. These findings imply a potential disease-specific link between selenium and vitamin D that warrants further investigation in larger cohorts and interventional studies.

Abstract citation ID: lvag096.542

P414 - ECE_3563 - Destructive thyroiditis due to metastatic thyroid infiltration in a patient with adenocarcinoma of unknown primary origin

Mafalda Canudas Costa[1], Juliana Gonçalves[1], Ana Rita Leite[1], Ines Pereira[1], Ana Luísa Barbosa[1], Ana Varela[1], João Neves[1], Luís Guimarães[2] and Joana Queirós[1]

[1]Department of Endocrinology, Diabetes and Metabolism, São João Local Health Unit, Porto, Portugal, Oporto, Portugal; [2]Department of Radiology, São João Local Health Unit, Porto, Portugal, Oporto, Portugal

Background: Metastases to the thyroid gland from nonthyroid neoplasms are uncommon and most patients remain euthyroid. Destructive thyroiditis in this context is an uncommon cause of thyrotoxicosis. Recognition of this entity is essential, as management differs from primary hyperthyroidism.

Case Presentation: We describe a 70-year-old male with stage IV tubular adenocarcinoma of unknown primary origin with loss of SMARCA4 expression, admitted for recurrent episodes of presyncope. He had a previous medical history of non-toxic multinodular goiter. He initially presented to the emergency department with palpitations and was found to have clinical thyrotoxicosis (TSH < 0.001 (0.35-4.94)μUI/mL, free T4 1.90 (0.70-1.48)ng/dL). He was discharged with methimazole and propranolol. He was subsequently admitted due to recurrent presyncope, at which point endocrinology consultation was requested for persistent thyrotoxicosis. In the weeks preceding admission, he reported palpitations, nocturnal sweating and mild heat intolerance.

Thyroid hormone levels transiently worsened during hospitalization, with peak free T3 10.26 (1.71-3.71)pg/mL and free T4 3.33ng/dL. During the endocrine evaluation, TSH-receptor antibodies and anti-thyroid antibodies were negative. A cervical CT performed two months prior to the onset of thyrotoxicosis, showed a thyroid gland of normal size and morphology, without structural abnormalities apart from a suspicious left level IV cervical lymphadenopathy. He repeated cervical CT which demonstrated near complete replacement of the thyroid gland by neoplastic tissue. Thyroid ultrasound with Doppler, revealed a diffusely enlarged, heterogeneous, pseudonodular gland with marked hypovascularity, along with bilateral laterocervical adenopathies. These findings, supported the diagnosis of destructive thyroiditis secondary to neoplastic infiltration.

Systemic corticosteroid therapy, previously initiated during hospitalization by the oncology team, was maintained, and antithyroid therapy was discontinued. Pre-existing beta-blocker therapy with bisoprolol was optimized. Thyroid hormone levels progressively declined, with concomitant clinical improvement. After 4 days, free T4 had decreased to 2.27ng/dL and free T3 to 3.83pg/mL. At outpatient follow-up seven days later, further biochemical improvement was documented (free T4 1.69ng/dL, free T3 3.18pg/mL), allowing gradual tapering of corticosteroids. Three weeks later, thyroid function continued to improve (TSH 0.01μUI/mL, free T4 1.34ng/dL).

Conclusions: This case illustrates a rare cause of thyrotoxicoses due to destructive thyroiditis in the context of rapid and extensive neoplastic thyroid infiltration. Awareness of this entity is crucial in patients with disseminated malignancy to avoid unnecessary antithyroid therapy and to ensure appropriate multidisciplinary management.

Abstract citation ID: lvag096.543

P415 - ECE_3878 - Resistance to thyroid hormone due to a novel THRB variant and coexisting pituitary lesion: A case report

Georgios Kostopoulos[1], Evangelia Makri[1], Athina Ververi[2], Sokratis Katafigiotis[2], Thomais Stavridoi[3] and Foteini Adamidou[1]

[1]Endocrinology, Hippokration General Hospital, Thessaloniki, Greece; [2]Department of Genetics for Rare Diseases, Papageorgiou General Hospital, Thessaloniki, Greece; [3]Private Practice, Castoria, Greece

Background: Elevated free thyroid hormone levels with non-suppressed thyrotropin (TSH) represent a diagnostic challenge and require differentiation between resistance to thyroid hormone (RTH), TSH-secreting pituitary adenoma (TSHoma), and familial dysalbuminemic hyperthyroxinemia (FDH). Most cases of resistance to thyroid hormone beta (RTH) are caused by

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

heterozygous mutations in the thyroid hormone receptor beta gene (*THRB*) and follow an autosomal dominant inheritance pattern. The reported coexistence of RTHβ with pituitary incidentalomas further complicates the diagnostic approach.

Case Presentation: A 69-year-old male with a history of type 2 diabetes mellitus, chronic hepatitis B and solitary kidney was referred for persistently elevated free T4 and free T3, with high normal TSH levels on repeated routine testing. Clinically, the patient was asymptomatic, apart from sinus bradycardia. Mild cognitive impairment was noted. Thyroid antibodies were negative, sex hormone binding globulin was normal, and thyroid ultrasound revealed a multinodular goiter. Notably, the patient's mother had undergone total thyroidectomy for a benign multinodular goiter and required addition of T3 supplementation to thyroxine replacement to normalize her persistently elevated TSH. Extensive laboratory evaluation excluded assay interference and anterior pituitary dysfunction. Pituitary MRI revealed a 5x7 mm pituitary lesion. Dynamic endocrine testing, including TRH stimulation and T3 suppression test, favored the diagnosis of RTH over TSHoma.

Based on the biochemical profile and family history, the patient underwent Whole Exome Sequencing, which identified a novel heterozygous missense variant in the THRB gene, c.1054G>C (p.Ala352Pro). According to ACMG criteria, this variant was initially classified as a variant of uncertain significance (VUS). Subsequent familial testing demonstrated the presence of the same variant in the patient's mother. Segregation of the variant within the family supported its pathogenicity and was consistent with a diagnosis of resistance to thyroid hormone beta (RTHβ).

Conclusions: The differential diagnosis of apparently inappropriate TSH secretion as in RTH, calls for integrated clinical evaluation and family history, dynamic hormonal testing, thyroid and pituitary imaging and genetic testing to avoid unnecessary therapeutic interventions.

Abstract citation ID: lvag096.544

P416 - ECE_2108 - Perchlorate and thiocyanate environmental contaminants in mother-baby cohort in N.I

Doua S Ahmed[1], Paul McMullan[1], Jayne V Woodside[2], Elizabeth N. Pearce[3] and Karen Mullan[1]

[1]Regional Centre for Endocrinology and Diabetes, Belfast Health and Social Care Trust, Belfast, United Kingdom; [2]Centre for Public Health, Queen's University Belfast, Belfast, United Kingdom; [3]Boston University Chobanian & Avedisian School of Medicine, Boston, United States

Sufficient iodine supply is essential for thyroid hormone synthesis, which is crucial for foetal neurodevelopment. Perchlorate (ClO_4^-) and thiocyanate (SCN^-) are environmental pollutants that inhibit iodine uptake into thyroid cells. Contamination has been found in water, milk, and some food supplies and originates from products such as cigarettes, nitrogen fertilisers, and rocket fuel. These pollutants may potentially compound iodine deficiency and partly explain the significant rise in congenital hypothyroidism described in Northern Ireland (N.I), Ireland, and other Western countries over the last 40 years.

A prospective cohort of 241 mothers in N.I provided urine samples for storage during each trimester of pregnancy and postpartum, with a subset of 80 providing an offspring sample (6-24 weeks).

Mothers were iodine deficient throughout pregnancy and postpartum, while babies were iodine replete, as previously reported. Maternal median urinary iodine concentrations (mUIC) across the three trimesters and postpartum were 73 mcg/L, 94 mcg/L, 117 mcg/L, and 90 mcg/L, respectively. Infant mUIC was 40 µg/L. Perchlorate and thiocyanate were highly prevalent in maternal urine samples, detected in 95% and 100%, respectively, indicating ubiquitous exposure. Maternal median perchlorate levels across the three trimesters and postpartum were 3.6, 4.1, 3.3, and 3.8 mcg/L, respectively, and 1.9 mcg/L in offspring (detected in 65% of infants). Maternal median thiocyanate levels were 353, 709, 572, and 751 mcg/L, respectively, and 136 mcg/L in offspring (detected in 100% of infants). Smoking was associated with a four-fold increase in maternal thiocyanate levels in the second trimester compared with non-smokers (2970 vs 657 µg/L, $P < .001$). Formula feeding was associated with higher perchlorate levels in infants. Median urinary perchlorate concentrations were 0.9 mcg/L in breastfed infants and 1.8 mcg/L in formula-fed infants ($P = .011$). There was no significant ClO_4^- or SCN^- contamination detected in contemporaneous water samples from across the island of Ireland (median <0.05 and <0.5 µg/L, respectively). Only 2/29 locations had measurable, but low, levels.

To our knowledge, this is the first European cohort shown to have evidence of thyroid hormone synthesis blocker contamination in infants. Results are similar to a mother-infant cohort in Boston, USA. However, in the Boston cohort, mothers were iodine replete, which may provide some protection not afforded to Ireland and UK, which have no iodine fortification programmes. These findings highlight the need for public health strategies to optimise iodine nutrition in Northern Ireland and raise concerns regarding concurrent exposure to environmental thyroid disruptors.

Abstract citation ID: lvag096.545

P417 - ECE_1959 - Thyroid hormone receptor β1 as a key regulator of hepatic gene expression and bile secretion

Liudmyla Kaminska[1,2] and John Blacked[1]

[1]NIHR Liverpool Clinical Research Facility, Liverpool, United Kingdom; [2]University of Liverpool, Biosciences, Liverpool, United Kingdom

Background: The ATP-binding cassette transporter ABCB4 (MDR3) is essential for the excretion of phosphatidylcholine (PC) into bile, a critical process for maintaining hepatobiliary lipid homeostasis. Impaired ABCB4 expression or function leads to cholestatic liver disease and bile duct injury. Thyroid hormones are key regulators of hepatic lipid metabolism; however, the role of thyroid hormone receptor β1 (THRβ1), the predominant hepatic isoform, in modulating ABCB4 expression remains unclear.

Methods: Human hepatocyte models were treated with triiodothyronine (T3) to assess dose- and time-dependent effects on ABCB4 transcription. THRβ1-selective agonists, including GC-1 and KB-141, were used to evaluate isoform-specific regulation.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

In vivo studies in mice examined the impact of THRβ1 activation on hepatic ABCB4 expression and biliary PC secretion. Conserved THR response elements upstream of the ABCB4 gene were identified using genomic analyses.

Results: T3 stimulation induced robust, dose- and time-dependent upregulation of ABCB4 mRNA in human hepatocytes. THRβ1-selective agonists elicited greater transcriptional activation than native T3, confirming isoform-specific regulation. In mice, KB-141 treatment increased hepatic ABCB4 expression and significantly enhanced biliary PC secretion. Conserved THR response elements located ~6 kb upstream of the ABCB4 locus were identified in both human and murine genomes, providing direct mechanistic evidence for THRβ1-mediated transcriptional control.

Conclusions: THRβ1 functions as a novel transcriptional activator of ABCB4, promoting increased canalicular transporter levels and facilitating phosphatidylcholine secretion into bile. These findings establish a direct link between thyroid hormone signaling and hepatobiliary lipid metabolism, highlighting THRβ1 as a key modulator of bile duct homeostasis. Furthermore, selective THRβ1 agonists may represent a promising therapeutic strategy for enhancing ABCB4-mediated biliary lipid excretion and improving liver function in cholestatic disorders.

Abstract citation ID: lvag096.546

P419 - ECE_3387 - miRNA expression profiles of CCDC6/RET- and ETV6/NTRK3-fusion positive papillary thyroid carcinoma

Katerina Vyhnalova[1], Karolina Dobiasovska[2], Vlasta Kuklikova[1], Barbora Bulanova[1], Olivia Cillikova[1], Marie Rodová[1], Eliska Vaclavikova[1], Jitka Carkova[1], Rami Katra[3], Petr Vlček[4], Daniela Kodetova[5], Martin Chovanec[6], Jana Drozenova[7], Radoslav Matej[7], Jaromir Astl[8], Jiri Hlozek[9], Jiří Soukup[9], Josef Vcelak[1] and Bela Bendlova[10]

[1]Institute of Endocrinology, Department of Molecular Endocrinology, Prague, Czech Republic; [2]Prague, Czech Republic; [3]Department of Ear, Nose, and Throat, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [4]Department of Nuclear Medicine and Endocrinology, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [5]Department of Pathology and Molecular Medicine, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [6]Department of Otorhinolaryngology, 3rd Faculty of Medicine, Charles University in Prague and University Hospital Kralovske Vinohrady, Prague, Czech Republic; [7]Department of Pathology, 3rd Faculty of Medicine, Charles University in Prague and University Hospital Kralovske Vinohrady, Prague, Czech Republic; [8]3rd Faculty of Medicine and Military University Hospital, Praha, Czech Republic; [9]3rd Faculty of Medicine and Military University Hospital, Prague, Czech Republic; [10]Institute of Endocrinology, Prague, Czech Republic

Objective: *CCDC6/RET* (also known as *RET/PTC1*) and *ETV6/NTRK3* gene fusions represent recurrent oncogenic drivers in papillary thyroid carcinoma (PTC), particularly in radiation-associated and pediatric cases, but are also detected in adult sporadic tumors. Although these fusions are generally associated with favorable outcomes, increasing evidence suggests substantial heterogeneity in clinical behavior, ranging from indolent tumors to aggressive disease with locoregional invasion or distant metastases. MicroRNAs (miRNAs) are key post-transcriptional regulators involved in thyroid tumorigenesis and may contribute to differences in tumor aggressiveness. The aim of this study was to characterize miRNA expression profiles associated with aggressive versus indolent clinical behavior in *CCDC6/RET*- and *ETV6/NTRK3*-positive PTC.

Methods: A total of 60 PTC samples were analyzed, including 30 tumors harboring the *CCDC6/RET* fusion and 30 tumors positive for the *ETV6/NTRK3* fusion. *CCDC6/RET*-positive PTCs comprised 15 indolent and 15 aggressive tumors, while the *ETV6/NTRK3*-positive cohort included 16 indolent and 14 aggressive PTCs. Tumors were classified as aggressive based on advanced local disease, lymph node involvement, angioinvasion, or presence of distant metastases, whereas indolent tumors were defined as T1–T2, N0, M0 with excellent response to therapy. Total RNA was isolated from fresh-frozen thyroid tissues, and miRNA libraries for next-generation sequencing were prepared using the QIAseq miRNA Library Kit (Qiagen). Differential miRNA expression analysis was performed using the miRge3.0 pipeline and the DESeq2 package in R, with comparisons focused on aggressive versus indolent tumors within each fusion-positive group.

Results: In *CCDC6/RET*-positive PTCs, aggressive tumors showed significantly altered expression of 12 miRNAs compared with indolent tumors, including 10 upregulated and two downregulated miRNAs. The most statistically significant upregulated miRNAs were hsa-miR-224-5p, hsa-miR-193a-5p, and hsa-miR-12136, while hsa-miR-3065-3p and hsa-miR-3065-5p were the most significantly downregulated. In *ETV6/NTRK3*-positive PTCs, aggressive tumors exhibited upregulation of 6 miRNAs compared with indolent tumors, with no miRNAs showing significant downregulation. The most significantly upregulated miRNAs included hsa-miR-1248, hsa-miR-27a-5p, and hsa-miR-323a-3p.

Conclusions: Our results demonstrate distinct miRNA expression patterns associated with aggressive clinical behavior in *CCDC6/RET*- and *ETV6/NTRK3*-positive PTC. These findings suggest that miRNA profiling may contribute to improved risk stratification and help identify fusion-positive PTC patients with a higher likelihood of aggressive disease, potentially supporting more personalized clinical management.

Funding: Supported by the Ministry of Health of the Czech Republic in cooperation with the Czech Health Research Council under project NU21-01-00448 and MH CZ RVO 00023761.

Abstract citation ID: lvag096.547

P422 - ECE_1738 - Endocrine immune-related adverse events and survival in cancer immunotherapy: a bias-corrected meta-analysis

Lavanya Mangla

Maulana Azad Medical College, Delhi, India

Background: Endocrine immune-related adverse events (e-irAEs) are common during immune checkpoint inhibitor (ICI) therapy and have been associated with improved survival in observational studies. However, most prior analyses are vulnerable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

to immortal time bias—whereby patients must survive long enough to develop endocrine toxicity, artificially inflating survival estimates—limiting causal interpretation from an endocrine standpoint. Clarifying whether endocrine toxicity reflects true immune activation or methodological artefact is clinically relevant for endocrinologists managing these patients, particularly with respect to surveillance intensity and prognostic counselling.

Methods: We conducted a systematic review and meta-analysis following PRISMA guidelines, identifying studies published between 2019 and 2025 that evaluated survival outcomes in patients developing endocrine irAEs during ICI therapy. Primary analyses were restricted to studies employing landmark-adjusted or time-dependent Cox models, excluding naïve time-to-event analyses. Overall survival (OS) was analysed using a random-effects Bayesian framework. Meta-regression explored differences by endocrine organ, cancer type, and ICI regimen. Trial Sequential Analysis (TSA) assessed evidence sufficiency, and sensitivity analyses evaluated robustness.

Results: Four studies employing bias-corrected methods were included. Development of endocrine irAEs was associated with improved OS (posterior hazard ratio [HR] 0.68, 95% credible interval [CrI] 0.49-0.93; $I^2 = 2\%$), indicating a high posterior probability of survival benefit. Thyroid irAEs showed a trend toward improved survival (posterior HR 0.67, 95% CrI 0.41-1.11, crossing unity), reflecting substantial uncertainty, while pituitary and adrenal toxicities showed insufficient evidence to determine an association**.** Despite the small number of studies, TSA demonstrated that the cumulative Z-curve crossed the monitoring boundary in favour of benefit after the second study, indicating a low probability that the overall association is due to chance. Sensitivity analyses confirmed robustness of the primary finding.

Conclusions: After correction for immortal time bias, endocrine immune-related adverse events are associated with improved overall survival during cancer immunotherapy. These findings support endocrine toxicity as a prognostic correlate of systemic immune activation, rather than definitive evidence of a clinically actionable biomarker. Whether endocrine irAEs can be used for risk stratification or treatment decision-making—for example, in selecting patients for treatment intensification or de-escalation—requires prospective endocrine-focused validation.

Abstract citation ID: lvag096.548

P423 - ECE_1702 - Management of refractory thyrotoxicosis to facilitate salvage multivisceral transplantation in a critically ill patient

Sarishka Singh, Zin Tun, Saira Yousaf, Shafiq Yusuff and Hassan Ibrahim
Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

Introduction: Distinguishing between severe non thyroidal illness and primary hyperthyroidism in the intensive care unit is challenging. In the context of salvage multivisceral transplantation (MVT) achieving biochemical stability is vital for perioperative safety. We describe a case of severe thyrotoxicosis refractory to high dose therapy necessitating complex perioperative planning and multidisciplinary collaboration.

Case Presentation: A 38 year old female was transferred from Ireland for MVT assessment following mesenteric ischaemia and septic shock. History included portal vein thrombosis, ascites, and spontaneous bacterial peritonitis. Her course required intensive care, haemofiltration, and surgeries resulting in short bowel syndrome.

Thyroid function progressed through three distinct stages. Local reference ranges were TSH (0.35-5.50 mU/L), Free T3 (3.50-6.5 pmol/L), and Free T4 (11.5-22.7 pmol/L). Initial tests on admission (TSH 0.59 mU/L, FT3 2.4 pmol/L, FT4 8.5 pmol/L) suggested non-thyroidal illness. Four months later, she demonstrated T3 thyrotoxicosis (TSH <0.03 mU/L, FT3 7.3 pmol/L, FT4 19.7 pmol/L), progressing by nine months to overt thyrotoxicosis (TSH <0.03 mU/L, FT4 12.9 pmol/L, FT3 53.6 pmol/L) associated with tachycardia and high stoma output.

Work up excluded assay interference and heparin effect. TSI and TPO antibodies were negative. Thyroid ultrasound showed benign nodules (<1cm, BTA U2) without increased vascularity. Thyroid uptake was markedly reduced at 0.2%, consistent with thyroiditis. While multiple contrast exposures contributed, the deterioration in thyroid function observed four months after the last exposure might suggest a cumulative staggering effect rather than a purely contrast-driven aetiology.

To facilitate MVT, carbimazole was titrated to 60 mg daily but the response was refractory possibly due to malabsorption from short bowel syndrome. A contingency plan involved iopanoic acid to inhibit 5′-deiodinase and reduce peripheral conversion of T4 to T3.

Pre-operatively, her tests demonstrated TSH <0.03 mU/L; FT3 9.4 pmol/L; FT4 33.3 pmol/L. Following MVT, thyroid function corrected rapidly. Five days post-surgery, FT3 was 2.8 pmol/L and FT4 12.5 pmol/L. Improvement could possibly be related to iodine washout during intraoperative and early post-operative haemofiltration and resolution of illness. Subsequent autoantibody screens remained negative, suggesting transient thyroiditis evolving into non-thyroidal illness.

Conclusions: This case illustrates the complexities of managing thyrotoxicosis in surgical intensive care. It highlights the impact of gastrointestinal failure on oral medication efficacy and the utility of alternative strategies for perioperative stabilisation. Furthermore, it demonstrates that clinical features suggesting hyperthyroidism may ultimately represent non-thyroidal illness or transient thyroiditis.

Abstract citation ID: lvag096.549

P424 - ECE_1949 - Cytokine signatures predicting thyroid toxicity during immune checkpoint therapy

Ketevan Lomidze[1], Nino Kikodze[2] and Marine Gordeladze[3]
[1]*Tbilisi State Medical University, Tbilisi, Georgia;* [2]*Immunology, Tbilisi State Medical University, Tbilisi, Georgia;* [3]*Endocrinology, Tbilisi State Medical University, Tbilisi, Georgia*

Background: Hypothyroidism is one of the most common endocrine immune-related adverse events associated with immune checkpoint inhibitor (ICI) therapy. Current guideline-recommended monitoring strategies rely on uniform biochemical surveillance and do not incorporate individual immunological risk profiles. Identification of clinically applicable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

biomarkers may enable more precise prediction and management of ICI-associated thyroid dysfunction.

Methods: We conducted a prospective observational study including 35 patients with advanced solid tumours treated with PD-1 or combined PD-1/CTLA-4 inhibitors. Serum levels of interleukin-6 (IL-6), interleukin-10 (IL-10), and interferon-gamma (IFN-γ) were measured at baseline and during early treatment. Cytokine concentrations were compared between patients who developed hypothyroidism and those who remained euthyroid using non-parametric testing. Predictive performance was evaluated using receiver operating characteristic (ROC) analysis, with optimal thresholds determined by Youden's index.

Results: Patients who developed hypothyroidism exhibited significantly lower circulating levels of IL-10 and IL-6 compared with disease-free individuals ($P < .01$), whereas IFN-γ showed no statistically significant difference. ROC analysis demonstrated strong predictive performance for IL-10 (AUC 0.93) and IL-6 (AUC 0.82), while IFN-γ showed moderate discriminative ability (AUC 0.72). Power analysis confirmed adequate statistical power for IL-10 and IL-6. Substantial overlap in IFN-γ levels limited its utility as a standalone systemic biomarker.

Conclusions: Reduced IL-10 and IL-6 levels define a cytokine profile associated with increased susceptibility to ICI-induced hypothyroidism. Cytokine-based biomarkers represent a feasible and biologically grounded approach to precision clinical medicine, enabling biomarker-driven risk stratification and individualized monitoring strategies for immune-related endocrine toxicity.

Abstract citation ID: lvag096.550

P425 - ECE_3457 - The epidemiology of focal thyroid lesions classified as category iv lesions in fine-needle aspiration biopsy

Maria Szmigielska[1,2], Magdalena Turowska[1,2], Bernadetta Kałuża[1,2], Małgorzata Kołos[3] and Edward Franek[1,2,4]

[1]*Department of Internal Medicine, Endocrinology and Diabetology, National Medical Institute of the Ministry of the Interior and Administration in Warsaw, Warsaw, Poland;* [2]*Warsaw, Poland;* [3]*Pathomorphology Centre, National Medical Institute of the Ministry of the Interior and Administration in Warsaw, Warsaw, Poland;* [4]*Department of Human Epigenetics, Mossakowski Medical Research Centre Polish Academy of Sciences, Warsaw, Poland*

Background: Bethesda system category IV determined via fine-needle aspiration biopsy (FNAB) of the thyroid is consistent with suspected follicular neoplasm; with the postoperative pathology report possibly indicating follicular adenoma, a highly cellular hyperplastic nodule, noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), lymphocytic thyroiditis, and follicular carcinoma, Hurthle-cell carcinoma, and follicular and oxyphilic variant of papillary thyroid carcinoma. The purpose of this study was to determine the incidence of heterogenous lesions from the Bethesda category IV in thyroid ultrasound-guided FNAB.

Material and Methods: We searched the hospital database for the period 2023-2025 and, out of all ultrasound-guided FNAB reports, we culled Bethesda category IV results.

Results: Out of the 1671 ultrasound-guided FNAB, category IV was observed in 0.59% of cases ($n = 10$). Bethesda category IV was observed in 6 patients (16.7% male [$n = 1$] and 83.3% female [$n = 5$], aged 59 ± 17.92 years [37-83]). Eighty percent of the aspirated lesions ($n = 8$) were focal hypoechoic lesions, and 20% ($n = 2$) were focal normoechoic lesions; the lesion diameter was 12.4 ± 3.29 mm (10-50 mm). Thyrocytes of oxyphilic cell morphology were found in 40% of cases ($n = 4$), small follicular structures were found in 20% of cases ($n = 2$), microfollicular in 20% of cases ($n = 2$), and colloid in 30% of cases ($n = 3$).

Conclusions: Suspected follicular thyroid neoplasm is a relatively rare cytological diagnosis and is characterized by relatively high heterogenicity.

Abstract citation ID: lvag096.551

P426 - ECE_3821 - Epigenetic silencing of RASSF1A, MGMT and NALCN in plasma cfDNA of sporadic medullary thyroid carcinoma patients

George Simeakis[1], Konstantina Tekou[2], Elina Lagopodi[2], Maria Boudina[3], Georgios Christantoniou[3], Alexandra Chrisoulidou[3], Pantelis Constantoulakis[4], Konstantinos Chanopoulos[1], Maria Alevizaki[5], Kyriakos Vamvakidis[6], Athina Markou[2] and Evi Lianidou[2]

[1]*Thyroid Cancer Outpatient's Clinic, Endocrine Dept., 401 General Military Hospital of Athens, Athens, Greece;* [2]*Analysis of Circulating Tumor Cells (ACTC) Lab, Dept of Chemistry, National and Kapodistrian University of Athens, Athens, Greece;* [3]*Endocrine Dept., Theagenio Cancer Hospital, Thessaloniki, Greece;* [4]*Genotypos S.A, Athens, Greece;* [5]*National and Kapodistrian University of Athens, Athens, Greece;* [6]*Dept of Endocrine Surgery, Henry Dunant Hospital Center, Athens, Greece*

Objectives: Distant metastases (DM) and/or biochemical persistent disease (BPD) in MTC, adversely affect disease prognosis, with calcitonin and CEA doubling-times serving as the main prognostic indicators. The role of epigenetic modifications in thyroid cancer is under investigation. Liquid-biopsy, particularly through cell-free DNA (cfDNA) analysis, is a non-invasive tool providing real-time monitoring of disease progression and information on tumor biology. We aimed to evaluate whether DNA methylation of selected tumor suppressor genes in plasma-cfDNA provides prognostic information in sporadic medullary thyroid carcinoma (spMTC) patients.

Methods: The methylation status of three selected gene promoters (*RASSF1A, MGMT* and *NALCN*) was examined by highly specific and sensitive real-time methylation specific PCR assays in: (a) 60 peripheral blood (PB) samples of 24 spMTC patients with DM and/or BPD, collected at different time-points every 3-6 months, depending on disease progression, (b) 14 healthy donor (HD) samples. PB samples were processed for cfDNA extraction using the Qiagen Circulating Nucleic Acid Kit. Sodium-Bisulfite conversion of cfDNA was performed using the EZ DNA-Methylation-Kit. Methylation-Specific PCR was further performed using gene-specific primers that selectively amplified methylated sequences.

Results: In the 60 spMTC plasma-cfDNA samples DNA promoter was highly methylated in 11/60 (18.3%) for *RASSF1A*, 6/60

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(10.0%) for *MGMT* and 3/60 (5.0%) for *NALCN*. In the 24 patients studied, DNA promoter was highly methylated in 14/24 (58.3%) for *RASSF1A*, 5/24 (20.8%) for *MGMT* and 3/24 (12.5%) for *NALCN*. When we analyzed patients with **DM ($n = 14$) vs BPD ($n = 10$)**, DNA promoter was highly methylated in 8/14 (57.1%) vs 3/10 (30.0%) for *RASSF1A*, 4/14 (28.6%) vs 1/10 (10.0%) for *MGMT* and 3/14 (21.4%) vs 0/10 (0.0%) for *NALCN*. Comparing methylation status of the three selected tumor suppressor genes in patients with **DM vs BPD**, we found that 10/14 (71.4%) DM vs 3/10 (30.0%) BPD patients, $P < .05$, were characterized by significantly higher percentage of DNA methylation in at least one of the tumor suppressor genes studied. Notably, in 5/14 (35.7%) DM vs 1/10 (10.0%) BPD patients, DNA promoter methylation was detected concomitantly in two tumor suppressor genes. No methylation for any of the three genes was detected in all 14 HD samples.

Conclusions: DNA methylation status was significantly higher in spMTC patients with DM vs BPD possibly implicating a role of DNA methylation of tumor suppressor genes in the progression and metastatic potential of spMTC. Larger patients' series and comparison with the methylation status of the primary tumor are required to validate these results.

Abstract citation ID: lvag096.552

P427 - ECE_3323 - Thyroid Eye Disease Following Immunomodulatory Therapy for Multiple Sclerosis: A Case Series

Sandhi Nyunt[1,2], Mohammud Musleh[3,4], Claire Feeny[2], Ahmad Aziz[3,4], Vassiliki Bravis[2], Richard Nicholas[5], Karim Meeran[1,2] and Vickie Lee[3,4]

[1]Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom; [2]Department of Endocrinology, Imperial College Healthcare NHS Trust, London, United Kingdom; [3]Oculoplastic and Adnexal Service, Western Eye Hospital, Imperial College NHS Foundation Trust, London, United Kingdom; [4]Imperial College Ophthalmology Research Group (ICORG), London, United Kingdom; [5]Department of Neurology, Imperial College Healthcare NHS Trust, London, United Kingdom

Background: Immunomodulatory therapies for multiple sclerosis (MS), particularly immune reconstitution therapy, are associated with secondary autoimmune diseases, including autoimmune thyroid disease such as Graves' disease. However, the development of clinically significant thyroid eye disease (TED) following these therapies remains under-reported and poorly characterised. Alemtuzumab-induced immune reconstitution can trigger thyroid autoantibodies and orbital autoimmunity, providing a mechanistic basis for therapy-associated TED.

Methods: We conducted a retrospective case series of patients with MS who developed TED following exposure to immunomodulatory therapy. Patients were identified from a specialist thyroid eye disease multidisciplinary clinic at Imperial College Healthcare NHS Trust. Clinical data collected included patient demographics, thyroid and TED status with relevant investigations and management strategies and MS-related clinical features and treatments.

Results: Six patients with MS who developed TED following immunomodulatory therapy were identified: alemtuzumab ($n = 4$), natalizumab ($n = 1$) and interferon-based therapy with intravenous methylprednisolone and cyclophosphamide ($n = 1$). All patients were euthyroid with no prior history of Graves' disease or TED before initiation of immunotherapy. Smoking status was available for all patients; one was a current smoker, two were ex-smokers and the remainder were never-smokers.

TED developed after treatment exposure in all cases. Among alemtuzumab-treated patients, TED occurred at a median of 36 months following therapy (range 24-48 months). All patients were diagnosed with Graves' disease with positive thyrotropin receptor antibodies; four had suppressed TSH levels (<0.001 mU/L) at TED diagnosis.

At presentation, TED severity according to EUGOGO criteria ranged from mild to severe, with one patient classified as mild, four as moderate and one as severe. During follow-up, disease progression was observed, with peak EUGOGO severity reaching severe disease in four patients while one patient remained moderate and one mild. TED-directed immunosuppression included intravenous methylprednisolone ($n = 2$) and local triamcinolone ($n = 1$). Three patients underwent rehabilitative interventions, including extraocular muscle botulinum toxin injection, strabismus surgery, orbital decompression or eyelid surgery. Thyroid management included antithyroid drugs ($n = 3$) or thyroidectomy ($n = 3$).

Conclusions: This case series highlights that patients treated with immunomodulatory therapies for MS, particularly immune reconstitution therapy with alemtuzumab, may be predisposed to clinically significant TED in addition to secondary thyroid autoimmunity. From an endocrinology perspective, these findings support the need for prolonged thyroid and ocular surveillance for at least 3-5 years following treatment, with prompt assessment of ocular symptoms and timely referral to specialist multidisciplinary centres.

Abstract citation ID: lvag096.553

P428 - ECE_2815 - Clustering and response prediction in differentiated thyroid cancer: insights from the Hungarian thyroid cancer register

Celia Blasszauer[1] and Emese Mezosi[2,3]

[1]Budapest, Hungary; [2]PTE AOK, Pécs, Hungary; [3]Ist Department of Internal Medicine, University of Pecs, Pecs, Hungary

Differentiated thyroid cancer (DTC) is the most common endocrine malignancy, showing generally favorable prognoses but variable clinical presentations.

We analyzed anonymized data from the Hungarian Thyroid Cancer Register collected over 2023-2024. The cohort included 833 patients diagnosed with DTC. To uncover patient subgroups, unsupervised K-means clustering was implemented in Python, comparing predicted outcomes with recorded clinical responses. Results revealed four distinct clusters corresponding to varied outcome profiles.

Cluster 1 comprises younger patients with predominantly structural thyroid disease, characterized by nodular goiter and low systemic comorbidity burden. **Cluster 2** represented the lowest-risk phenotype, consisting of middle-aged patients with minimal symptom burden and the lowest prevalence of metabolic and cardiovascular comorbidities. **Cluster 3** reflected an older, metabolically burdened phenotype with high rates of diabetes, hyperlipidemia, and cardiovascular disease but without

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

enrichment for aggressive tumor features. In contrast, **Cluster 4** represented a small but clinically severe subgroup, characterized by advanced age, high comorbidity burden, increased lymph-node–related symptoms, and enrichment for advanced stage and metastatic disease.

Clinical stage distribution differed markedly across clusters, with Clusters 1 and 2 predominantly composed of early-stage disease, Cluster 3 showing intermediate stage distribution, and Cluster 4 enriched for advanced clinical stages. Treatment response also varied by cluster, with Clusters 1 and 2 demonstrating the highest rates of favorable response, Cluster 3 showing generally preserved response despite higher comorbidity burden, and Cluster 4 exhibiting the poorest response profile.

This study underscores the value of merging real-world registry data with machine learning for personalized DTC management. By associating demographics, clinical features, morphology, and comorbidities with treatment responses, this dual-layer analysis advances segment-level risk stratification and supports tailored clinical decision-making.

Abstract citation ID: lvag096.554

P429 - ECE_2074 - Efficacy and safety of RFA therapy in patients with benign thyroid nodules compared to other modalities

Roni Mechorish[1], Moshe Yehuda[1,2], Gideon Bachar[1,2], Ilan Shimon[1,3], Eyal Robenshtok[1,3] and Hadar Duskin-Bitan[1,3]

[1]*Gray Faculty of Medicine, Tel Aviv University, Petah Tiqva, Israel;* [2]*Department of Otolaryngology, Head and Neck Surgery, Rabin Medical Center, Petah Tiqva, Israel;* [3]*Rabin Medical Center, Endocrinology & Metabolism Institute, Petah Tiqva, Israel*

Background: Lobectomy had been a standard treatment for large and/or functioning thyroid nodules for many years, but may lead to postoperative hypothyroidism and visible scarring. Radiofrequency ablation (RFA) offers a minimally invasive alternative with preserving normal of thyroid tissue. Comparative outcome data from Israel remain limited.

Methods: A retrospective cohort study was conducted at Rabin Medical Center (2020-2025) including 206 adults with benign thyroid nodules: 116 treated with RFA and 90 with lobectomy. Demographic variables, thyroid function (TSH, FT4, FT3), need for chronic LT4 or antithyroid therapy, nodule volume change, and adverse events were assessed. The primary outcome was maintenance of euthyroidism; secondary outcomes included volume reduction and safety.

Results: Patients treated with RFA were younger (mean 48.8 vs 57.9 years) and predominantly female (106/116 vs 67/90). RFA preserved thyroid function in almost all cases, with 0/116 requiring chronic levothyroxine, compared to 15/90 (17%) after lobectomy. RFA achieved a mean nodule volume reduction of $66 \pm 7\%$, while no comparable data was available after lobectomy due to complete lobe excision. Early voice-related symptoms occurred in 14/90 (15.6%) after lobectomy vs 8/116 (6.9%) after RFA, and permanent vocal cord paralysis in two lobectomy patients (2.2%) and one RFA patient (0.9%). Postoperative swallowing discomfort was reported in 5/90 (5.6%) vs 4/116 (3.4%), respectively. RFA did not create a scar.

Conclusions: In this cohort, RFA provided a practical and safe alternative to lobectomy, maintaining euthyroidism, achieving substantial volume reduction, and resulting in fewer long-term hormone requirements and fewer local complications, without surgical scarring. These findings support the integration of RFA into routine practice for selected patients with benign thyroid nodules.

Abstract citation ID: lvag096.555

P431 - ECE_2913 - Hashimoto's Thyroiditis natural history—a single centre prospective study

Arianna Benedetti[1], Giulia Di Dalmazi[2], Tommaso Luciano[1], Noemi Mariello[1], Giorgia Rapagnetta[1], Ines Bucci[3] and Giorgio Napolitano[1]

[1]*Università "G. D'Annunzio" Chieti-Pescara, Chieti, Italy;* [2]*UOC Endocrinologia e Malattie Metaboliche, ASL Pescara, Pescara, Italy;* [3]*Chieti, Italy*

Background: Hashimoto's Thyroiditis (HT) is a common autoimmune disease characterized by lymphocytic infiltration of the thyroid gland, presence of thyroid-specific circulating autoantibodies (anti-Tg and anti-TPO) and varying degrees of thyroid dysfunction. Most patients present a normal thyroid function at diagnosis, and not all of them will progress to hypothyroidism: most studies reveal a progression rate to hypothyroidism of 5-15% within 5-10 years since diagnosis. We aimed to establish the prevalence of thyroid disfunction in patients with HT at diagnosis and during follow-up, defining the mean time to its onset, possible prognostic factors and impact on quality of life (QoL).

Methods: We designed a single centre prospective study including 178 adult patients who referred to our Endocrinology unit with a new diagnosis of HT, followed every 6 months. For each visit, we collected information about their anamnesis and QoL evaluated with the ThyPRO-39it questionnaire and performed thyroid gland ultrasound and blood tests regarding thyroid function. Median follow-up duration was 4.9 years (2020-2025).

Results: At diagnosis, 123 patients (69.1%) were euthyroid, 4 (2.3%) were hyperthyroid and 51 (28.6%) were hypothyroid. 16 of 123 (13%) initially euthyroid patients developed hypothyroidism during the study follow-up, with a mean time to progression of 19 ($\pm$21) months and a high interindividual variability. Patients who progressed to hypothyroidism showed significantly higher baseline TSH levels compared with those without progression (2.98 ± 0.86 vs 2.02 ± 1.06 respectively, *P*-value <.001). No significant differences were observed between groups with respect to age, sex, familial history of autoimmune thyroid disease, presence of other autoimmune disorders, FT4 levels, anti-thyroid antibodies, thyroid volume, the presence of thyroid nodules, or the ultrasound pattern of thyroid. A multivariate analysis with Cox regression model revealed that TSH was the only independent prognostic factor of progression to hypothyroidism (HR 1.99, *P*-value <.001). QoL, evaluated at 6 and 36 months since HT diagnosis, resulted compromised in all patients affected by HT irrespective of thyroid function, with the only exception of cosmetic complaints scale, significantly more compromised in patients with hyperthyroidism at the 6-month evaluation (*P*-value .01).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: HT is a common autoimmune disorder with important implications in QoL and a heterogeneous clinical course, with different possible effects on thyroid function. In our study, consistent with current literature, baseline TSH levels emerged as the only independent prognostic factor the development of hypothyroidism, potentially representing a discriminant to personalize follow-up timing in patients with HT.

Abstract citation ID: lvag096.556

P432 - ECE_2246 - Investigating the effects of maternal thyroid hormones on offspring cardiometabolic risk factors in adulthood: an intergenerational Mendelian randomization study

Marion Denos[1], Laxmi Bhatta[1], Marco Medici[2], Alexander Teumer[3], Ben Brumpton[1] and Bjørn Olav Åsvold[1]
[1]Trondheim, Norway; [2]Radboud University Medical Center, Nijmegen, The Netherlands; [3]University Medicine Greifswald, Greifswald, Germany

Background: Epidemiological studies reported that maternal thyroid function in pregnancy may have lasting effects on the offspring. However, only a very few studies investigated these lasting effects on cardiometabolic outcomes in offspring.

Objectives: This study used an instrumental variable framework as an alternative approach to investigate the effects of maternal thyroid hormones on offspring cardiometabolic risk factors related to body composition, blood pressure, glucose and lipid levels in adulthood.

Methods: We performed a two-sample intergenerational Mendelian randomization (MR) using genetic instruments selected from recent genome-wide association studies (GWAS) of thyroid hormones in up to 271 040 individuals of European ancestry, including thyrotropin (TSH) (259 single nucleotide polymorphisms (SNPs)), free thyroxine (FT4) (85 SNPs) and triiodothyronine (T3) (62 SNPs). SNP-outcome associations were obtained from adjusted GWAS (parental genotype adjusted for offspring genotype) of adult cardiovascular outcomes in three European cohorts (n = up to 564 765). Outcomes in this MR analysis were offspring body mass index, waist-to-hip ratio, systolic and diastolic blood pressure, blood glucose, HbA1c, C-reactive protein, total cholesterol, low- and high-density lipoprotein cholesterol, and triglycerides, measured at 24-62 years of age.

Results: We found no strong evidence of an effect of genetically predicted variation in maternal thyroid function on offspring cardiometabolic outcomes. In adjusted MR analyses, higher maternal TSH levels were associated with lower levels of triglycerides and diastolic and systolic blood pressure in adult offspring (mean differences in standard deviation (SD) units per one SD higher maternal TSH: triglycerides −0.05, 95% CI −0.09 to −0.01; diastolic blood pressure −0.05, 95% CI −0.09 to −0.01; systolic blood pressure −0.04, 95% CI −0.07 to 0.00), but these results were not robust to adjustment for multiple testing and not consistently supported by sensitivity analyses. Moreover, genetically predicted maternal FT4 and FT3 levels were not related to cardiometabolic outcomes in offspring.

Conclusions: Overall, our findings using available genetic instruments suggest that maternal thyroid hormones levels have little influence on offspring cardiometabolic risk factors in adulthood.

Abstract citation ID: lvag096.557

P434 - ECE_1052 - Thyroid storm—a rare presentation of subacute thyroiditis

Kevin Kwek, Hui Chia Wee and Htoo Htoo Mar
Endocrinology, Khoo Teck Puat Hospital, Singapore

Thyroid storm is a severe multi-system presentation of thyrotoxicosis, most common in patients with Graves disease. Severe subacute thyroiditis typically causes a self-limited short duration of hyperthyroidism and significant morbidity is typically rare. We present an unusual case of subacute thyroiditis presenting as thyroid storm.

A 66-year-old female was admitted via the Emergency Department to our institution after a pair of mechanical falls precipitated by generalized weakness without focal neurological symptoms. She had significant history of Type 2 Diabetes Mellitus, Hypertension, Dyslipidemia and Non-alcoholic Fatty Liver Disease. She had been suffering from fever, diarrhea and coryzal symptoms for several days prior to admission. On initial evaluation, she was severely dehydrated, pyrexic and lethargic. Evaluation of vital signs revealed sinus tachycardic (heart rate 120-140bpm) without hypotension. A thyroid function test performed for evaluation of tachycardia revealed severe primary hypothyroidism with free thyroxine (fT4) 96.6 pmol/L (RR 12-22) and TSH 0.015 mIU/L (RR 0.27-4.2).

As the calculated Burch-Warforsky Point Scale (BWPS) was 80pts, we made a diagnosis of thyroid storm. She was treated emergently with carbimazole 30mg twice daily, Lugol's iodine at 10 drops (65mg of inorganic iodine) thrice daily and intravenous hydrocortisone at 100mg thrice daily. The likely precipitant was a urinary tract infection, for which she received intravenous antibiotics.

Table 1 Further biochemistry

Test	Result	Reference range
fT4	97.6 pmol/L	12-22
TSH	0.015 pmol/L	0.27-4.2
Free triiodothyronine (fT3)	5.5 pmol/L	3.1-6.8
Thyrotropin receptor antibody	negative	
Thyroid stimulating immunoglobulin	negative	
Anti-thyroid peroxidase antibody	negative	
Anti-thyroglobulin antibody	negative	

The negative antibody screen and absence of thyroid eye disease, goitre and pretibial myxedema led us to question the presumptive diagnosis of Graves disease. In addition, the markedly raised fT4:fT3 ratio of 17.75 favoured thyroiditis, though non-thyroidal illness from infection would confound this interpretation. Thyroid ultrasonography demonstrated heterogenous echogenicity without increased internal vascularity and small subcentimetre nodules, which favoured thyroiditis.

Due to the severity of the initial presentation, carbimazole therapy was continued for 1 week. However, despite clinical

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

improvement, fT4 levels remained persistently elevated at 39.4 pmol/L. A radioiodine uptake scan was performed and demonstrated diffusely reduced tracer uptake in both thyroid lobes, confirming the diagnosis of thyroiditis. Thus, Carbimazole was ceased and her fT4 levels subsequently normalized without treatment.

This case highlights that subacute thyroiditis, while typically biochemically mild, can present explosively and cause significant morbidity. While subacute thyroiditis remains a rare cause, it should be considered when the clinical picture is inconsistent with Graves disease.

Abstract citation ID: lvag096.558

P435 - ECE_1997 - Multimodal management of ectopic lingual thyroid: surgical excision and radioactive iodine ablation

Praneet Bolusani[1], Aled Rees[2], David Scott-Coombes[2], John Rees[2] and Fizzah Iqbal[2]
[1]*Gloucestershire Hospitals NHS Trust, Gloucester, United Kingdom;* [2]*University Hospital of Wales, Cardiff, United Kingdom*

Introduction: Lingual thyroid represents the most common form of ectopic thyroid tissue and results from abnormal embryological migration of the thyroid gland. It can present in adulthood secondary to compressive symptoms or hypothyroidism, in the absence of normally located thyroid tissue. We present a case of dual ectopic thyroid tissue causing significant compressive symptoms, requiring multidisciplinary management with combination of surgical excision and radioactive iodine ablation.

Case: 52-year-old female presented with a 1-year history of dry cough associated with eating and drinking, with a globus sensation. She also reported several months of inability using her voice over prolonged periods. Past medical history included bilateral sensorineural hearing loss. Her work as an aviation safety trainer was affected, prompting investigation. Ultrasound scan of the neck demonstrated absence of thyroid tissue in the normal anatomical location. Subsequent MRI neck and thyroid uptake scan confirmed absence of normal functioning thyroid tissue, with two adjacent rounded masses seen at the tongue base. A 35mm anterior nodule towards the floor of mouth was mildly iodine-avid while a smaller 22mm posterior nodule was intensely avid. TSH was normal at 3.52 with a FT4 of 15.7. Following multidisciplinary discussion, surgical resection of the larger nodule, felt to be the main contributor to her compressive symptoms, was performed. Histopathology showed a multinodular goitre. CT-neck with contrast at 6 months demonstrated residual nodule at the tongue base. After discussion with the patient, radioactive iodine (RAI) treatment was undertaken. A 1-year post-RAI ultrasound neck showed size reduction from 22x20x23mm to 11x11x18mm. The patient reported full resolution of her symptoms and is now maintained on replacement dose levothyroxine.

Conclusion/Discussion: Lingual thyroid is a rare oropharyngeal entity resulting from failure of thyroid descent to its normal position during embryogenesis. It is more common in females and frequently associated with hypothyroidism. Patients may present with compressive symptoms including dysphagia, dysphonia, and upper airway obstruction. Management is individualised and based on symptom burden, size and thyroid function. While asymptomatic patients may be managed conservatively, the presence of compressive/voice-related symptoms warrants intervention. I-123 uptake scanning is a valuable diagnostic tool for confirming ectopic functioning thyroid tissue and guiding management.

This case highlights the complexity of dual ectopic lingual thyroid tissue and demonstrates the effectiveness of a multidisciplinary-guided combined surgical and RAI approach. Initial surgical resection relieved compressive symptoms, while subsequent RAI successfully reduced residual disease and avoided further invasive surgery, achieving symptom resolution and disease control.

Abstract citation ID: lvag096.559

P436 - ECE_2418 - When radioiodine uptake misleads: severe thyrotoxicosis from a long-standing multinodular goiter

Humera Tabassum[1,2,3], Evelyn Morales[1,2,3], Sathya Jyothinagaram[1,2] and Karyne Vinales[1,2]
[1]*Endocrinology, University of Arizona College of Medicine, Phoenix, United States;* [2]*Phoenix VA Healthcare System, Phoenix, United States;* [3]*Banner—University Medical Center Phoenix, Endocrinology, Medicine, Phoenix, United States*

Introduction: Subclinical hyperthyroidism due to multinodular goiter is often indolent and may remain untreated for years. Progression to severe thyrotoxicosis with neurological manifestations and delayed biochemical response to antithyroid therapy is rare, particularly with persistently negative radioiodine uptake.

Case Presentation: A 72-year-old male with a long-standing multinodular goiter incidentally identified on computed tomography in 2012 and a 10-year history of untreated subclinical hyperthyroidism was followed conservatively, as he remained asymptomatic and declined treatment. Thyroid radioiodine uptake scans performed in 2012, 2017, 2019, and 2024 consistently demonstrated absent uptake. Due to the markedly enlarged thyroid, pulmonary function testing revealed a moderately severe obstructive ventilatory defect, with diminished mid–lung volume expiratory flows, inspiratory limb flattening on flow-volume loops, and forced expiratory volume in one second (FEV1) of 57% predicted.

The patient later presented to the emergency department with acute encephalopathy. Laboratory evaluation revealed undetectable thyroid-stimulating hormone with elevated free triiodothyronine (5.8 pg/mL) and free thyroxine (3.56 ng/dL). Thyroid-stimulating immunoglobulin, TSH receptor antibodies, and thyroid peroxidase antibodies were negative, consistent with prior testing. Extensive evaluation for infectious, metabolic, and structural causes of encephalopathy was unrevealing.

The patient was initiated on methimazole 20 mg three times daily for four weeks without clinical or biochemical improvement and was subsequently transitioned to propylthiouracil 400 mg every eight hours, again without early response. Despite continuous inpatient therapy, thyroid hormone levels remained elevated, with free thyroxine measuring 2.32 ng/dL after nearly eight weeks. Biochemical euthyroidism was achieved only after more than ten weeks of antithyroid therapy, coinciding with complete resolution of encephalopathy. The patient is planned for definitive treatment with radioactive iodine.

Discussion: This case represents Jod-Basedow–independent decompensation of a long-standing autonomous multinodular goiter. Chronic autonomy and prolonged TSH suppression lead to reduced sodium-iodide symporter expression and inefficient

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

iodine trapping, explaining persistently negative radioiodine uptake despite large intrathyroidal hormone stores. Acute physiologic stress likely precipitated excessive hormone release, resulting in severe thyrotoxicosis and encephalopathy. Apparent resistance to antithyroid drugs reflects continued release of preformed hormone rather than increased synthesis.

Conclusions: This case highlights a rare but important mechanism of thyrotoxicosis in which long-standing autonomous multinodular goiter produces severe hormone excess despite absent radioiodine uptake. Recognizing this dissociation between iodine trapping and hormone output is critical to avoid misdiagnosis and delayed definitive therapy.

Abstract citation ID: lvag096.560

P437 - ECE_1239 - Preoperative use of potassium iodide (KI) in poorly controlled thyrotoxicosis: an audit of safety and efficacy

Helen Loo, Christine May and Helen Turner
Oxford University Hospital, Endocrinology, Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, United Kingdom

Background: The use of KI or Lugol's iodine solution as a preoperative treatment for patients with poorly controlled thyrotoxicosis who are intolerant or unresponsive to antithyroid drugs (ATDs) is well-documented but rarely systematically evaluated. This audit assesses the implementation and outcomes of outpatient KI therapy in patients at Oxford University Hospitals (OUH) requiring thyroidectomy due to inability to tolerate or poorly controlled thyrotoxicosis with ATD therapy.

Methods: Following registration as an audit, and patient selection from the endocrinology database, a 6-year retrospective data collection included: indication for KI treatment, thyroid biochemical changes with KI, patient outcomes, and tolerability.

Results: $N = 18$ patients (14/18 female 77.8%), mean age 48 years (31-72), $n = 3$ smokers, received iodine therapy before thyroidectomy. Graves' disease was the diagnosis for 100%; 5/18 (27.8%) had Thyroid eye disease. Indications for treatment were intolerance $n = 7$ (39%), LFT abnormality $n = 2$, neutropenia $n = 7$ (39%), cardiac indication $n = 2$

Thirteen patients received potassium iodide (65mg TDS), 4 received Potassium iodide (60mg TDS) (doses varying due to drug availability) and 1 patient was treated with Lugol's solution due to lactose intolerance. The treatment was well tolerated. 1 patient had delayed surgery due to contracting COVID post commencement of KI, with no rebound thyrotoxicosis after 7 pre-surgery days. 17 patients had KI for 10 days pre surgery, and 1 patient with fT3 < 8.4 pmol/L only required 7 days of KI therapy. Pre-treatment fT4 mean 31.8 pmol/L (range 23.2-58.3, (upper limit of normal 19 pmol/L)) and fT3 mean 17.38 pmol/L (range 8.4- 30.72, (upper limit of normal 5.4 pmol/L)). Thyroid function was monitored at 2-4-day intervals to ensure improvement. Thyroid function one day prior to surgery had fallen to fT4 mean 18.4 pmol/L (range 14.4-24.4) and fT3 mean 6.5 pmol/L (range 4.3-11). There were no perioperative complications eg thyroid storm, excess bleeding, or arrythmia, and KI was well tolerated by all.

Conclusions: This audit supports the efficacy and safety of preoperative outpatient iodine therapy in patients with uncontrolled thyrotoxicosis with appropriate monitoring. Patients with milder fT3 and fT4 elevation could be considered for a shorter treatment course. Logistical planning regarding date of planned surgery between medical and surgical teams is vital.

Abstract citation ID: lvag096.561

P440 - LBA_ECE_1022 - Evaluation of muscle quality and strength in type 2 diabetes using handgrip strength and triceps muscle ultrasound

Sabri Engin Altıntop[1], Irem Sonmezoglu Kutuk[1], Refika Yorulmaz Kaya[1], Mahinur Cerit[2], Mehmet Muhittin Yalcin[1], Altinova Alev[1], Mujde Akturk[1], Fusun Toruner[1], Ayhan Karakoc[1] and Ethem Turgay Cerit[1]
[1]Department of Endocrinology and Metabolism, Gazi University Faculty of Medicine, Ankara, Türkiye; [2]Department of Radiology, Gazi University Faculty of Medicine, Ankara, Türkiye

Background: Type 2 diabetes mellitus (T2DM) is associated with reduced skeletal muscle mass and function, a condition increasingly referred to as diabetic sarcopenia. These alterations highlight the importance of early assessment of muscle strength and quality in individuals with diabetes. This study aimed to evaluate handgrip strength and ultrasonographic characteristics of the triceps muscle in individuals with T2DM and to examine their associations with anthropometric parameters, body composition, and physical activity.

Methods: This cross-sectional study included 120 participants aged 18-65 years, comprising 60 individuals with T2DM and 60 healthy controls matched for age, sex, and body mass index (BMI). Body composition was assessed using a Tanita bioelectrical impedance analysis device, and physical activity was evaluated using the Rapid Assessment of Physical Activity (RAPA) questionnaire. Handgrip strength was measured from the dominant hand using a digital dynamometer. The triceps muscle of the dominant arm was evaluated by ultrasonography, and muscle thickness, subcutaneous fat thickness, muscle-to-fat ratio, and muscle echogenicity (an indirect indicator of muscle quality) were recorded.

Results: The median age was 55 years, and each group included 36 women and 24 men. Triceps muscle thickness correlated with arm muscle mass measured by bioelectrical impedance analysis ($P < .001$). Handgrip strength was lower in individuals with T2DM than in healthy controls (24.47 [13.56] kg vs 27.40 [10.60] kg; $P = .019$), whereas triceps muscle echogenicity was higher in the T2DM group ($P = .003$). Triceps muscle thickness and muscle-to-fat ratio did not differ between groups ($P > .05$). In sex-specific analyses, women with T2DM had lower handgrip strength (20.60 [5.88] kg vs 24.95 [4.05] kg; $P < .001$) and higher triceps muscle echogenicity ($P = .019$) than healthy women. In men, handgrip strength was similar between groups ($P = .797$), whereas triceps muscle echogenicity was higher in those with T2DM ($P = .044$). Treatment with SGLT2 inhibitors was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

associated with lower handgrip strength ($P = .034$) and higher triceps muscle echogenicity ($P = .003$). ROC analysis showed that diabetes duration predicted low handgrip strength (AUC = 0.75), with a cut-off of 7.5 years.

Conclusions: Our findings indicate that individuals with T2DM exhibit impairments in muscle quality (increased echogenicity) and muscle function (reduced handgrip strength) even without loss of muscle mass, with these alterations being more pronounced in women. These findings suggest that assessing diabetic sarcopenia should include muscle quality and function, not muscle mass alone.

Abstract citation ID: lvag096.562

P442 - LBA_ECE_1217 - Thyroid hormone alterations reshape gut microbial ecosystems in a rat model

Alara Ataacar Aydınoğlu[1], Akif Enes Arikan[2], Osman Ugur Sezerman[3], Tayyip Karaman[3], Samed Ozer[4] and İnan Anaforoglu[5]

[1]Acibadem Mehmet Ali Aydinlar University, Internal Medicine, Istanbul, Türkiye; [2]Acibadem Mehmet Ali Aydinlar University, General Surgery, Istanbul, Türkiye; [3]Department of Biostatistics and Medical Informatics, Acibadem Mehmet Ali Aydinlar University, Istanbul, Türkiye; [4]Acibadem Mehmet Ali Aydinlar University, Laboratory Animal Application and Research Center, Physiology, Istanbul, Türkiye; [5]Endocrinology and Metabolism, Internal Medicine, Acibadem Mehmet Ali Aydinlar University, Istanbul, Türkiye

Introduction: Thyroid dysfunctions profoundly affect multiple physiological systems. Growing evidence highlights a bidirectional interaction between gut microbiota and thyroid function, conceptualized as the "gut–thyroid axis." Dysbiosis may influence hormonal homeostasis through increased intestinal permeability and altered immune regulation while thyroid hormones themselves may reshape microbial communities. Yet, the mechanisms underlying this interaction remain unclear. A subset of patients with thyroid disorders continues to experience persistent symptoms such as fatigue, weight gain and impaired quality of life despite achieving biochemical euthyroidism. This clinical discordance raises the possibility that factors beyond circulating thyroid hormone levels, including alterations in gut microbiota, may contribute to the persistence of these symptoms.

Objective: This study aimed to investigate the effects of thyroid dysfunction, induced either chemically (levothyroxine, methimazole) or surgically (subtotal thyroidectomy), on gut microbiota composition in a rat model.

Methods: Twenty-five male Wistar Albino rats were allocated into control, hyperthyroidism (HE), hypothyroidism (HO), sham-operated (SHAM) and thyroidectomy (SHO) groups. Fecal samples were collected at baseline, weeks 4 and 7. Serum TSH and free T4 levels were measured at weeks 4 and 7. Microbial composition and diversity were assessed using 16S rRNA sequencing and bioinformatics analysis.

Results: Thyroid dysfunction induced significant alterations in microbial composition. HE rats exhibited increased *Oscillospiracea* and *Spirochaetaceae*, along with depletion of *Lactobacillus*. HO groups showed enrichment of anaerobic taxa such as *Desulfobacterota* and *Spirochaetota* (Table 1), whereas SHO groups were characterized by increased abundance of *Muribaculaceae* and *Desulfovibrionaceae* (Table 2). Alpha diversity increased over time, suggesting adaptive restructuring of the microbial ecosystem, while beta diversity analyses revealed temporal shifts in community composition. These microbial alterations occurred in parallel with changes in thyroid hormone levels and body weight dynamics, indicating a coordinated interaction between endocrine status and microbial ecology.

Conclusions: Specific taxa including *Lactobacillus*, *Campylobacterota* and *Desulfobacterota* may represent microbial signatures of thyroid dysfunction. These findings provide experimental support for the gut–thyroid axis and suggest that thyroid hormones may act as key ecological regulators of the intestinal microbiome. Importantly, the observed microbial shifts may offer a potential biological explanation for persistent metabolic symptoms and impaired quality of life reported in some patients despite achieving biochemical euthyroidism. These results highlight the need to consider microbiota-targeted approaches as potential adjunctive strategies in the management of thyroid disorders.

Table 1

Taxa/Phylum	HE-G1_mean	HO-G1_mean	HE-G2_mean	HO-G2_mean	HE-G3_mean	HO-G3_mean
Actinobacteriota	1.287	0.7925	0.3227	0.2289	0.1115	0.0376
Bacteroidota	67.0385	44.8389	54.9996	57.4919	53.5977	47.2246
Caldatribacteriota	0.4945	0.0015	0.743	0	0.2236	0
Campylobacterota	0.0248	0.0969	1.0201	0.2254	1.0731	0.4904
Chloroflexi	0	0.0008	0.0803	0	0	0
Cyanobacteria	0.029	0.034	0.8987	0.3396	0.6489	0.6731
Deferribacterota	0	0.0008	0.0941	0.0227	0.0684	0.0128
Desulfobacterota	0	0.1304	0.0691	1.2693	0.1347	1.3241
Elusimicrobiota	0.0207	0	0.1664	0.0277	0.0684	0.053
Euryarchaeota	28.9685	0.0075	37.9602	0.161	40.106	0.0909
Fibrobacterota	0	0	0.0011	0.0135	0	0.0077
Firmicutes	0	51.2023	0.0015	34.9272	0	43.6105
Fusobacteriota	0.1432	0	0.2264	0	0.3695	0.0007
Patescibacteria	0.0217	0.9417	1.9227	0.3133	2.9172	1.095
Proteobacteria	0.0012	1.2128	0.0553	1.3279	0.1285	1.3037
Spirochaetota	0.2519	0.7009	0.0012	3.6168	0.0136	3.9277
Thermoplasmatota		0.001		0.0315		0.1434

Table 2

Taxa/Family	SHAM-G1_mean	SHO-G1_mean	SHAM-G2_mean	SHO-G2_mean	SHAM-G3_mean	SHO-G3_mean
Prevotellaceae	52.7946	66.1255	51.0967	27.0935	20.6665	52.1887
Lachnospiraceae	11.5329	7.4383	6.5377	21.4889	23.6099	9.5264
Muribaculaceae	5.2176	5.3	9.7231	13.1270	8.6325	12.9846
Desulfovibrionaceae	0.1264	0.2180	0.3044	2.6545	0.6513	1.0036

Keywords dysbiosis, gut–thyroid axis, hypothyroidism, hyperthyroidism, microbiota, thyroidectomy

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.563

P443 - LBA_ECE_1020 - Causal analysis of traditional and environmental risk factors for long-term development of type 2 diabetes using a conditional survival Bayesian network

Jiyoung Choi and Mansuk Oh
Ewha Womans University, Statistics, Seoul, South Korea

Background: Traditional metabolic and lifestyle factors and ambient air pollutants are established contributors to type 2 diabetes (T2D), yet their joint causal structure and individual versus interacting interventional effects remain poorly characterized in long-term population studies.

Methods: We analyzed 11-year follow-up data from 2102 adults free of T2D at baseline in the Ansan cohort of the Korean Genome and Epidemiology Study (KoGES). A Conditional Survival Bayesian Network (CSBN)—integrating survival analysis with Bayesian network modeling—was applied to accommodate censored data, reconstruct the causal structure among demographic, lifestyle, metabolic, and air pollution variables, and quantify individual and joint interventional effects on T2D incidence.

Results: The CSBN revealed a holistic causal network distinguishing direct and indirect pathways from likely confounding associations. Obesity exerted the largest individual causal effect, approximately doubling 11-year T2D risk relative to normal weight. Elevated alanine aminotransferase (ALT) and older age increased risk by 40-50%, while family history of T2D, dyslipidemia, overweight, $PM_{2.5}$ and gaseous pollutants showed intermediate effects. Synergistic interactions were identified predominantly among metabolic factors: ALT combined with family history, dyslipidemia, or obesity displayed strong additive interactions. Air pollutants, by contrast, influenced T2D risk independently rather than through interactions with metabolic variables.

Conclusions: These findings support integrated public health strategies addressing multiple risk factors simultaneously. The CSBN framework provides a powerful tool for explicitly modeling causal interactions, informing targeted preventive interventions and efficient resource allocation for T2D prevention.

Keywords type 2 diabetes, air pollution, Bayesian network, causal inference, survival analysis, KoGES

Abstract citation ID: lvag096.564

P444 - LBA_ECE_1458 - Toward risk-adapted management of testicular lesions: a data-driven imaging framework derived from 20 years of clinical practice

Marta Tenuta[1,2], Francesco Carlomagno[1], Franz Sesti[1], Francesco Angelini[1], Giulia Pellegrini[1], Daniele Apostoli[1], Gabriele Savarese[3], Giorgio Franco[3], Lucia Manganaro[4], Fabio Magliocca[4], Daniele Gianfrilli[1], Andrea Isidori[1] and Carlotta Pozza[1]
[1]*Sapienza University, Experimental Medicine, Roma, Italy;* [2]*Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy;* [3]*Maternal and Child Health and Urological Sciences, Sapienza University, Roma, Italy;* [4]*Radiological, Oncological and Pathological Sciences, Sapienza University, Roma, Italy*

Background: Intratesticular lesions represent a heterogeneous group of neoplastic and non-neoplastic conditions, increasingly detected due to widespread use of high-resolution ultrasound. While ultrasound is highly sensitive, lesion characterization remains challenging, often leading to uncertainty-driven management and potential overtreatment. This study aimed to describe real-world management and develop an imaging-based, risk-adapted diagnostic framework for intratesticular lesions.

Methods: We conducted a single-center observational cohort study including 750 consecutive patients with intratesticular lesions evaluated between January 2005 and December 2025. Clinical, imaging, and follow-up data were prospectively collected. Management strategies included active surveillance (AS), testis-sparing surgery (TSS), or total orchiectomy (TO). Histopathology or ≥18 months of imaging stability served as reference standards. A stepwise diagnostic framework was derived a posteriori, integrating lesion size, ultrasound features, and second-level imaging such as contrast-enhanced ultrasound (CEUS) and MRI. Logistic regression, ROC analysis, and bootstrap validation were used for model development and performance assessment.

Results: Among 750 lesions, 415 (55.3%) were malignant. TO was performed in 57.6% of cases, TSS in 12.4%, and AS in 30%. Malignancy was confirmed in 94.7% of TO specimens. All malignant lesions under AS showed interval growth, whereas benign lesions remained stable or regressed.

Lesion size demonstrated excellent discrimination for malignancy (AUC 0.92), with <0.5 cm identifying a low-risk group (malignancy 5.2%) and ≥1.8 cm a high-risk group (PPV 94.6%). Intermediate-size lesions (0.5-1.8 cm, malignancy 45.3%) were further stratified using a five-feature ultrasound-based score (T-Les-SCORE), incorporating vascularization, calcifications, margins, echogenicity, and multifocality. The combined score (0-9) achieved good discrimination (AUC 0.902) and defined low- (≤3), intermediate- (4-5), and high-risk (≥6) categories.

Clinical modifiers such as prior germ cell tumor and testicular microlithiasis improved model performance (AUC 0.929), while positive tumor markers acted as an absolute indication for surgery.

In intermediate-risk lesions, CEUS showed good diagnostic performance (AUC 0.789), capturing most residual diagnostic information. MRI demonstrated similar performance (AUC 0.793) and provided additional reassurance in selected cases with non-suspicious CEUS, although findings were exploratory. Sequential imaging reduced malignancy prevalence from 55.3% overall to 0% in lesions with both negative CEUS and MRI.

Conclusions: This study proposes a pragmatic, stepwise imaging framework integrating lesion size, structured ultrasound assessment, and selective second-level imaging. The model enables risk-adapted management, potentially reducing unnecessary orchiectomy while maintaining oncological safety.

Abstract citation ID: lvag096.565

P445 - LBA_ECE_1014 - Real-world disease burden and care gaps in chronic hypoparathyroidism: results from the multicentre Greek OPA registry

Rodis Paparodis[1,2,3], Ioannis Androulakis[1], Nicholas Angelopoulos[1], Andreas Rizoulis[1,4], Anastasios Boniakos[1], Petros Varnavas[1], Panagiotis Mylonas[1], Dimos Florakis[1],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Stylianos Fountoulakis[1], Dimitrios Askitis[1], Maria Tsaroucha[1], Christianna Stylianidou[1], Athanasios Tsekouras[1], Emmanouil Choustoulakis[1], Christos Andronis[1], Valentina Petkova[1], Garyfallia Tzifa[1], Dimitra Zianni[1], Ermioni Tseniklidi[1], George Simeakis[1,5], Areti Korakovouni[1], Vasilis Gioxaris[1], Sofia Tsirona[1,6], Christina Pamporaki[1,7], Ploutarchos Tzoulis[1,8], Ilias Perogamvros[1,9], Dimitrios Papadogias[1], Panagiotis Spyropoulos[1], Eleni Laspa[1], Maria Karaflou[1], Danae Delivanis[1], Sarantis Livadas[1,10], Nicolaos Valvis[1], Angeliki Laina[1], Antonios Xydakis[1], Konstantinos Manolopoulos[1], Paraskevi Mentzelopoulou[1], Dimitrios Papadimitriou[1,11], Eleni Patrianakou Xanthakou[1], Eva Kassi[12] and Juan Carlos Jaume[2,3]

[1]Hellenic Endocrine Network, Athens, Greece; [2]Loyola University, Maywood, IL, United States; [3]Edward Hines Jr VA Hospital, Hines, IL, United States; [4]Iaso General Hospital, Endocrinology, Diabetes and Metabolism, Larisa, Greece; [5]Thyroid Cancer Outpatient's Clinic, Endocrine Dept., 401 General Military Hospital of Athens, Athens, Greece; [6]Endocrinology, Diabetes and Metabolism, Euroclinic Hospital, Athens, Greece; [7]Carl Gustav Carus at TU Dresden, Endocrinology, University Hospital, Dresden, Germany; [8]University College, Medicine, London, United Kingdom; [9]Diabetes, Endocrinology & Gastroenterology, University of Manchester, Manchester, United Kingdom; [10]Athens Medical Center, Endocrinology, Diabetes and Metabolism, Athens, Greece; [11]Pediatric Endocrinology, Pediatrics, University of Thessaly, Larisa, Greece; [12]LAIKO General Hospital of Athens, National and Kapodistrian University of Athens, Endocrine, Propaedeutic Internal Medicine, Athens, Greece

Background: Chronic hypoparathyroidism is a rare endocrine disorder associated with biochemical instability, renal complications, and impaired quality of life. Real-world evidence describing disease burden and management patterns outside centralized registries remains limited. We aimed to characterize clinical features, biochemical control, monitoring practices, and treatment gaps in a nationwide multicentre cohort.

Methods: The OPA study is a retrospective multicentre registry conducted across 41 endocrinology clinics in Greece. Adult patients with chronic hypoparathyroidism (>12 months disease duration) were identified through combined ICD-10 diagnostic codes and active vitamin D prescription records, followed by manual chart verification. Demographic, biochemical, treatment, and complication data were extracted from medical records. Multivariable logistic regression analyses were performed to identify predictors of suboptimal biochemical control, care gaps, and renal impairment.

Results: A total of 522 patients were included; 83.1% were female and median disease duration was 8.0 years (IQR 5.0-15.0). Post-surgical disease accounted for 95% of cases. Optimal biochemical disease control was achieved in 54.8% of patients with complete datasets, while 45.2% had suboptimal control and 6.7% had persistent hypocalcaemia. Hypercalciuria occurred in 37.0% of assessed patients, and nephrolithiasis and nephrocalcinosis were observed in 17.0% and 5.2%, respectively. Overall, 80.8% of patients exhibited at least one predefined care gap related to biochemical targets, monitoring practices, or treatment optimization. Although 45.8% of patients met predefined eligibility criteria for PTH replacement therapy, only 8.2% were receiving PTH treatment. In multivariable analyses, younger age was associated with suboptimal biochemical control, longer disease duration predicted care gaps, and renal impairment was associated with older age and cumulative disease duration.

Conclusions: In this large real-world multicentre cohort, chronic hypoparathyroidism remained associated with substantial biochemical instability, renal complications, and gaps in recommended monitoring despite specialist care. The low utilization of PTH replacement therapy among eligible patients highlights potential barriers to implementation of guideline-recommended management.

Abstract citation ID: lvag096.566

P447 - LBA_ECE_1469 - From valve to algorithm: first report of advanced hybrid closed-loop insulin delivery during major cardiac surgery

Martha Scherer[1], Michael Uth[1], Serghei Cebotari[1] and Maria Tichomirowa[2]

[1]Institut national de chirurgie cardiaque et de cardiologie interventionnelle, Luxembourg; [2]Endocrinology, Centre Hospitalier du Nord, Ettelbrück, Luxembourg

Background: Management of glycemia during major cardiac surgery remains challenging, particularly in elderly patients with long-standing type 2 diabetes and high glycemic variability. While intravenous insulin infusion is standard, the intraoperative use of advanced hybrid closed-loop (AHCL) systems has not been reported in this setting.

Case Presentation: We report the first use of an AHCL system during major cardiac surgery in a 79-year-old woman with type 2 diabetes and acute heart failure following unsuccessful MitraClip therapy. Due to intolerance to injectable GLP-1 receptor agonists and suboptimal glycemic control, she was initiated on an AHCL system (MiniMed™ 780G with Simplera Sync sensor).

The patient underwent elective mitral valve replacement. Total anesthesia time was 5 h 30 min, including 4 h 30 min of surgery and 2 h 10 min of cardiopulmonary bypass. During the entire procedure, the patient received continuous norepinephrine for hemodynamic support. The AHCL system was maintained in SmartGuard™ mode throughout.

Results: Intraoperative glycemic control was excellent, with time in range (70-180 mg/dL) of 90% and no time below range. Simplera sensor values showed strong concordance with arterial blood glucose measurements (Mean arterial glucose was 158.7 ± 7.6 mg/dL). While a parallel FreeStyle Libre 3 Plus sensor displayed signal disturbances during electrocautery use, the Simplera sensor remained stable and unaffected.

Conclusions: This case demonstrates the feasibility, safety, and robustness of AHCL systems during prolonged cardiac surgery, even under cardiopulmonary bypass and continuous inotropic support with levosimendan. AHCL may represent a promising alternative to conventional insulin protocols in complex perioperative settings.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.567

P448 - LBA_ECE_1352 - Lean Young-Onset Diabetes in Bangladesh: Distinct Clinical and Metabolic Features Beyond Classical Type 2 Diabetes

Nusrat Sultana, Mashfiqul Hasan, Kishore Shil, Sayad Abdus-Salam, Koushik Ashraf, Abdullah Bhuiyan and Muhammad Hasanat
Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh

Background: Young-onset diabetes in South Asians manifests frequently in lean individuals. However, the metabolic triggers of this phenotype remain poorly characterized.

Objective: This study aimed to evaluate the metabolic profiles in lean, non-autoimmune young-onset diabetes mellitus (DM) in a Bangladeshi cohort.

Methods: This cross-sectional study enrolled 373 participants, aged 18 to 34 years, from the Young Diabetes Clinic of the Department of Endocrinology at Bangladesh Medical University, Dhaka, Bangladesh, during the period of 2023 and 2024. Before enrollment, those with positive islet autoantibodies, low C-peptide, pancreatic pathology, and monogenic variants were excluded. β-cell function (HOMA2-B) and insulin resistance (HOMA2-IR) were quantified using the HOMA2 C-peptide calculator. Participants were categorized into four groups based on glycemic status and body mass index (BMI): lean DM ($n = 53$), obese DM ($n = 125$), lean non-DM ($n = 78$), and obese non-DM ($n = 117$).

Results: Lean DM participants were comparable to other groups in age, sex, and family history, though smoking was more prevalent than in lean controls ($P < .05$). Prevalence of central obesity and blood pressure levels of lean DM were similar to those of lean controls, but the lipid profile was comparable to that of obese DM. The median HbA1c was higher in lean DM than in obese DM (11.6% vs 8.5%; $P < .001$), while their median HOMA2-B was lowest across all other groups ($P < .01$). The HOMA2−IR in lean DM was lower than in obese DM but significantly higher than in lean controls and mirrored the resistance seen in the obese non-DM group ($P < .001$).

Conclusions: Lean young-onset diabetes in Bangladesh seems to represent a distinct phenotype with disproportionate insulin secretory defect and only modest insulin resistance and metabolic dysfunction. These features do not align well with the classic type 2 diabetes spectrum, suggesting the need for more tailored screening approaches and a reconsideration of its classification to support more appropriate management.

Keywords lean diabetes, young-onset diabetes, beta-cell function, insulin resistance

Abstract citation ID: lvag096.568

P449 - LBA_ECE_1231 - Does the use of reflex testing for thyroid function tests (TFTs) –only testing FT4 when TSH is out of range—effect the prescribing of levothyroxine (LT4)? an England wide investigation

Adrian Heald[1], Mike Stedman[2], Peter Taylor[3], Suhani Bahl[3], Anish Patil[1], Nadia Chaudhury[4], Robert Kemp[1], Rajshekhar Mudaliar[1], Rupinder Kochhar[1], Lakdasa Premawardhana[3], David Halsall[5], Ian Halsall[5], David Holland[6], Antonio Bianco[7], Onyebuchi Okosieme[3] and Colin Dayan[8]
[1]Endocrinology, Salford Royal Hospital, Salford, United Kingdom; [2]Res Consortium, Andover, United Kingdom; [3]University of Cardiff, Cardiff, United Kingdom; [4]University of Oxford, Oxford, United Kingdom; [5]Addenbrookes Hospital, Cambridge, United Kingdom; [6]The Benchmarking Partnership, Keele, United Kingdom; [7]University of Texas, Galveston, United States; [8]University of Birmingham, Birmingham, United Kingdom

Objective: There has been a significant growth in LT4 prescribing over the last 20 years, most of which has been of lower dose tablets. Most decisions about initiation and dosing are based levels of TSH and FT4 measured in requested TFTs. We report here an exploratory exercise to determine if there is any difference at general-practice level in the way that the amount of TFT data being presented affects the amount/doses of LT4 prescribed

Methods: Data for total number of TSH (1.179million) and FT4 (0.680million) tests in each of 763 GP practices was made available. The number of total FT4 as %total TSH was taken as amount reflex testing. Practices were split into 3-reflex classes by FT4 as % of TSH results in each practice, with High Reflex (<20%FT4+TSH), Moderate (20%-79%) and Low (90+%). The actual monthly amount of LT4 prescribed was extracted from publicly reported annual prescribing data. Data in 300 of the 763 GP practices where both prescribed patient demographic and prescribing data were available were applied to each practice population split by age group/sex to calculate the expected number of prescriptions/total mcg/ total number of tablets for LT4, % of actual vs expected standardised for the practice population size/sex/age mix.

Results: The laboratory number of TFT tests carried out in 2023 was used for 731-general practices with over 2000-registered patients each. The table below reflects the levels of prescribing relative to expected for those practices with different levels of reflex testing. Total number of prescriptions analysed was 3.51million.

Reflex level of FT4% TSH	Number of practices (% total)	TFT ratio FT4/ TSH	LT4 prescriptions actual/ expected	LT4 mcg actual/ expected
High reflex (<20%)	274 (37.5%)	13.7%	90.9%	106.2%
Moderate reflex (20%-89%)	224 (30.6%)	47.3%	96.7%	99.9%
Low reflex (≥90%)	233 (31.9%)	98.3%	98.4%	94.1%

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

This shows that when reflex testing is high ie often TSH alone, fewer prescriptions are being written, but the total mcg LT4 are higher, so on average each prescription is for a higher dose.

Conclusions: Our findings suggest that general practices that are provided with less data (high reflex: TSH alone) are prescribing more LT4 to fewer patients than general practices that receive both FT4+TSH values. Thus, the level of information being provided might be being reflected into their prescribing decisions. We suggest that consideration be given to providing both TSH and FT4 levels to clinicians to enable the most appropriate initiation/adjustment of LT4 dose.

Abstract citation ID: lvag096.569

P450 - LBA_ECE_1110 - Evaluation of a nutraceutical based on white mulberry leaves, fenugreek, niacin, chrome, zinc and a probiotic for reducing insulin resistance in patients with prediabetes: the NoDiab study

Francisco Javier Martinez-Martin[1,2], Sara Andrada-Diaz[3], Agnieszka Kuzior[2], Ana Maria Sanchez Garcia[2], Juan Fernandez-Jimenez[2], Irene Hernandez-Hernandez[1,2], Facundo Marcelo Guerrero-Kesselman[2], Borja Santana-Ojeda[1], Inmaculada Molinero-Marcos[1] and Claudia Arnas-Leon[1,2]

[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain; [3]Bioksan Naturalmente Juntos, Medical Advisory, Las Palmas de Gran Canaria, Spain

Introduction and Objectives: In the adult Spanish population the prevalence of prediabetes has been estimated at 15%, with an annual diabetes incidence of 1.16% (approximately 386 000 individuals). While metformin, glitazones, GLP-1RAs and SGLT2is may reduce this risk, none is currently approved for this indication. Acarbose, an α-glucosidase inhibitor, reduces the risk of progression to T2DM (STOP-NIDDM trial). White mulberry (Morus Alba) leaves contain 1-deoxynojirimycin, a potent α-glucosidase inhibitor. A nutraceutical based on a standardized white mulberry leaf extract, also containing fenugreek, inulin, *Lactiplantibacillus plantarum* A14, chromium, zinc and niacin has been developed for the treatment of prediabetes. We conducted an open-label trial (NoDiab) to evaluate the tolerability and efficacy of this nutraceutical, using the HOMA2-IR index (a validated predictor of T2DM development) as the primary outcome.

Methods: Adult subjects with prediabetes were recruited, excluding those with morbid obesity, serious concomitant diseases, alcoholism, substance abuse, and current or planned pregnancy. After informed consent, baseline anthropometry and laboratory tests, they were instructed to take one pill of the nutraceutical daily before lunch with a glass of water. Follow- up visits are scheduled at 3-4 and 6-7 months. In addition to changes in the HOMA2-IR, secondary endpoints were HOMA2-β, 10-year cardiovascular risk (SCORE2), lipid profile, systolic BP, BMI, fasting glucose and insulin, HbA1c, albuminuria, liver fibrosis risk (FIB-4 index) and tolerability (questionnaire).

Results: In 113 subjects (71 women, age 56.4 ± 6.7 years), HOMA2-IR decreased from 1.659 ± 0.721 to 1.269 ± 0.581 ($P < .001$) while HOMA2-β remained unchanged; SCORE2 decreased from to 4.23 ± 1.98 to 3.58 ± 1.76% ($P < .001$); non-HDLc from 161.5 ± 31.2 to 145.1 ± 20.9 mg/dL ($P < .001$); systolic BP from 138.8 ± 13.6 to 133.1 ± 11.2 mmHg ($P < .001$); fasting glucose from 107.5 ± 10.8 to 98.5 ± 8.9 mg/dL ($P < .001$); fasting insulin from 12.6 ± 6.1 to 9.7 ± 4.4 μU/ml ($P < .001$); HbA1c from 6.06 ± 0.24 to 5.83 ± 0.18% ($P < .001$); albuminuria from 28.4 ± 15.2 to 21.5 ± 14.3 mg/g Cr ($P = .035$); C-reactive protein from 3.66 ± 1.97 to 2.89 ± 1.27 mg/dL ($P < .001$); FIB-4 index from 1.42 ± 0.25 to 1.22 ± 0.24 ($P = .003$). Weight reduction was non-significant. No serious tolerability issues were reported, and no patient withdrew from the study due to adverse effects.

Conclusions: In the open-label NoDiab study, this nutraceutical produced a significant reduction in insulin resistance (−22.5%), along with improvements in the cardiovascular risk profile of prediabetic subjects (15.4% reduction in SCORE2, 9.9% in non-HDL cholesterol and 5.7 mmHg in systolic BP), with excellent tolerability. Prediabetes is primarily managed through lifestyle modifications, but their effectiveness is limited and no pharmacological options are currently approved; this nutraceutical may help fill this therapeutic gap.

Abstract citation ID: lvag096.570

P451 - LBA_ECE_1255 - Assessment of adrenal vein sampling selectivity by plasma metanephrine in primary aldosteronism with and without mild autonomous cortisol secretion

Tatiana Kokorina, Nadezhda Platonova, Ivan Sitkin, Vitalii Ioutsi, Khamzat Magomedov, Kseniya Komshilova, Ekaterina Troshina, Galina Melnichenko and Natalia Mokrysheva

Endocrinology Research Centre, Moscow, Russia

Introduction: Adrenal vein sampling (AVS) is the gold standard for subtype diagnosis in primary aldosteronism (PA). However, cortisol-based assessment of selectivity may be unreliable in patients with mild autonomous cortisol secretion (MACS), potentially leading to misinterpretation of AVS results. Plasma metanephrine has been proposed as a more stable marker of adrenal vein cannulation.

Aim: To evaluate cortisol-based selectivity and the additional value of metanephrine during unstimulated AVS in patients with PA, both with and without MACS.

Methods: We retrospectively analysed 90 sequential unstimulated AVS procedures performed by a single operator in 83 patients with confirmed PA in a tertiary referral centre between October 2024 and March 2026. All patients underwent systematic screening for MACS with 1-mg overnight dexamethasone suppression (DST). MACS was defined as post-dexamethasone serum cortisol >50 nmol/L. Cannulation success was defined as a cortisol selectivity index >3 and a metanephrine selectivity index >12.

Results: Forty patients (48.2%) were classified as MACS. The cannulation success rate defined by cortisol was lower in patients with MACS than in those without MACS (56% vs 73%). Application of a metanephrine-based selectivity index >12

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

increased the overall cannulation success rate to 92.2%. High success rates were observed both in patients with MACS (91.1%) and without MACS (93.3%), corresponding to absolute increases of 35% and 20%, respectively.

Table 1 Patient characteristics

Variable	MACS ($n = 40$)	No MACS ($n = 43$)	*P*-value
Age, years	56.5 [48; 63.5]	48 [43; 54]	.002
BMI, kg/m^2	29.5 [25.7; 34.1]	28.3 [24.4; 34.4]	.845
Aldosterone, pmol/L	1022.5 [634; 2144.9]	1000 [614; 2080]	.743
Renin, mU/L	0.84 [0.5; 4.35]	0.8 [0.5; 1.6]	.321
Serum potassium, mmol/L	4.2 [3.58; 4.62]	3.96 [3.67; 4.35]	.346
Serum creatinine, µmol/L	84.6 [65.6; 113.1]	69.2 [64.7; 81.7]	.102
SBP, mmHg	157 [145; 175]	158 [140; 170]	.599
DBP, mmHg	90 [84; 102.5]	100 [85; 107]	.671
Antihypertensive drugs, *n*	3 [2; 4]	3 [2; 4]	.134

Conclusions: Cortisol-based assessment of AVS selectivity appears less effective in patients with PA and MACS, likely due to cortisol co-secretion. Metanephrine may be a more suitable marker for evaluating AVS selectivity in patients with PA and concomitant cortisol secretion.

Abstract citation ID: lvag096.571

P452 - LBA_ECE_1067 - Targeted metabolomics to distinguish primary from endocrine hypertension: results from the prospective ENSAT-HT study

Parminder Reel[1], Smarti Reel[1], Laurence Amar[2,3], Benjamin Pariente[3], Jaap Deinum[4], Henricus Johannes Louis Maria Timmers[5], Cornelia Prehn[6], Jerzy Adamski[6,7,8], Filippo Ceccato[9], Silvia Monticone[10], Fabrizio Buffolo[10], Paolo Mulatero[10], Mirko Peitzsch[11], Christian Cole[1], Isabel Stüfchen[12], Holger Schneider[12,13], Martin Reincke[12], Gian Paolo Rossi[14], Livia Lenzini[14], Teresa Cosentino[2], Guillaume Assie[15,16,17], Anne Blanchard[18], Maria-Christina Zennaro[2,19], Emily Jefferson[1], Felix Beuschlein[12,20] and Zoran Erlic[20]

[1]Division of Population Health and Genomics, School of Medicine, University of Dundee, Dundee, United Kingdom; [2]Université de Paris, PARCC, INSERM, Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Unité Hypertension artérielle, Paris, France; [3]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Unité Hypertension artérielle, Paris, France; [4]Department of Medicine, Section of Vascular Medicine, Radboud University Medical Center, Nijmegen, The Netherlands; [5]Department of Medicine, Section of Endocrinology, Radboud University Medical Center, Nijmegen, The Netherlands; [6]Research Unit Molecular Endocrinology and Metabolism, Genome Analysis Center, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany; [7]Lehrstuhl für Experimentelle Genetik, Technische Universität München, Freising-Weihenstephan, Germany; [8]Department of Biochemistry, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; [9]UOC Endocrinologia, Dipartimento di Medicina DIMED, Azienda Ospedaliera-Università di Padova, Padova, Italy; [10]Division of Internal Medicine and Hypertension Unit, Department of Medical Sciences, University of Torino, Torino, Italy; [11]Institute of Clinical Chemistry and Laboratory Medicine, Universitätsklinikum Carl Gustav Carus, Dresden, Germany; [12]Medizinische Klinik und Poliklinik IV, LMU Klinikum, LMU München, München, Germany; [13]Division of Vascular Medicine, Department of Medicine IV, LMU University Hospital, München, Germany; [14]Department of Medicine-DIMED, Specialized Center of Excellence for Hypertension of the European Society of Hypertension and Emergency Medicine Unit, Padova, Italy; [15]Université de Paris, Institut Cochin, INSERM, CNRS, Paris, France; [16]Department of Endocrinology, Center for Rare Adrenal Diseases, AP-HP, Hôpital Cochin, Paris, France; [17]Department of Endocrinology, Center for Rare Adrenal Diseases, Assistance Publique–Hôpitaux de Paris, Hôpital Cochin, Paris, France; [18]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Centre d'Investigations Cliniques, Paris, France; [19]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Service de Génétique, Paris, France; [20]Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich (USZ) and University of Zurich (UZH), Zurich, Switzerland

Background: Arterial hypertension can be considered a global epidemic, and despite increased disease awareness and the availability of effective treatment options, global control rates remain unsatisfactory. Early identification of endocrine hypertension (EHT), including primary aldosteronism (PA), pheochromocytoma/paraganglioma (PPGL), and Cushing syndrome (CS), is essential for patient-tailored management, as these conditions are potentially curable and require disease-specific treatment strategies. However, current diagnostic pathways are complex and resource-intensive. We previously demonstrated promising results using targeted metabolomics (TM) to distinguish primary hypertension (PHT) from EHT in a retrospective cohort. The aim of this prospective multicenter study was to further examine the diagnostic performance and reproducibility of our previous findings.

Methods: In this prospective study, patients with PHT and EHT were recruited from seven European centers within the ENSAT-HT consortium. Targeted metabolomics profiling was performed on plasma samples using liquid chromatography–mass spectrometry. Discriminatory metabolites were identified using two complementary analytical strategies: a conventional statistical approach based on sequential univariate and multivariate analyses and a machine learning approach using random forest models.

Results: From July 2016 till March 2020 a total of 1050 patients were recruited (474 PHT: mean age 49 years, 46.2% female; 576 EHT: mean age 50 years, 41.4% female), including 495 PA, 38 PPGL, and 43 CS patients. Among 155 metabolites and 22 metabolic indices analyzed, the conventional statistical approach identified 66 discriminatory metabolites (14 of 31 previously identified) and 14 metabolic indices (4 of 7 previously identified). The machine learning approach identified 19 discriminatory

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

metabolites (4 of 15 previously identified) and 9 metabolic indices (3 of 8 previously identified). The discriminative performance of the top 15 metabolites (C10, C12, C14:1, C18:2, C2, lysoPCaC17:0, PCaaC32:2, PCaaC34:1, PCaaC34:2, PCaaC34:3, PCaaC36:1, PCaaC36:2, PCaaC36:3, Serotonin, Taurine) identified by the conventional approach (AUC 0.764) and the 19 metabolites (Ac-Orn, C10, C12, C14:1, C18:1, C18:2, C2, Glu, lysoPCaC17:0, PCaa32:2, PCaa34:1, PCaa34:2, PCaaC34:3, PCaaC36:1, PCaaC36:2, PCaaC36:3, PCaeC36:3, Serotonine, Taurine) identified by the machine learning approach (AUC 0.72) was comparable between methods but lower than observed in the previous retrospective study (AUC 0.86 and 0.83, respectively).

Conclusions: Targeted metabolomics demonstrated moderate discriminatory performance in this large prospective multicenter cohort of hypertensive patients. However, only a subset of previously identified metabolites and metabolic indices was reproducibly confirmed. Understanding the sources of these differences will be essential before targeted metabolomics can be implemented in routine clinical practice.

Abstract citation ID: lvag096.572

P453 - LBA_ECE_1004 - Multi-Omics identifies STK11-Driven Signalling Shift in sparsely granulated somatotropinomas

Pinaki Dutta[1], Vaishali Kaur[1], Debajyoti Chatterjee[2], Apinderpreet Singh[3], Maryada Sharma[4] and Ashutosh Rai[5]
[1]Postgraduate Institute Of Medical Education And Research Chandigarh, Endocrinology, Chandīgarh, India; [2]Postgraduate Institute Of Medical Education And Research Chandigarh, Histopathology, Chandīgarh, India; [3]Postgraduate Institute Of Medical Education And Research Chandigarh, Neurosurgery, Chandīgarh, India; [4]Postgraduate Institute Of Medical Education And Research Chandigarh, ENT, Chandīgarh, India; [5]Panjab University, Biochemistry, Chandīgarh, India

Background: Somatotropinomas are divided into sparsely (SG) and densely granulated (DG) based on granularity. SG exhibits aggressive clinical behaviour (presentation at younger age, high proportion of invasiveness, resistance to treatments and recurrence compared to DG). We hypothesized that proteomic and phosphoproteomic differences underpin this heterogeneity.

Methods: High-throughput mass spectrometry-based proteomics and phosphoproteomics analysis was performed on SG ($n = 4$) and DG ($n = 4$) tumours. Gene ontology and pathway enrichment done using Fun Rich. Candidates (AMPKβ S108, mTOR, ULK1 S638, MAPT T548, and TSC1 S1080) of significantly enriched STK11 pathway (cut-off = 1.5-fold-change) were considered for validation by immunohistochemistry (IHC) ($n = 33$; SG = 25, DG = 8) on tissue microarray in an independent cohort. Functional assays on GH3 cell lines and primary culture ($n = 9$) treated with selective inhibitors included proliferation, apoptosis, and phosphorylation of downstream substrates. Public transcriptomic datasets were re-analysed for independent validation.

Results: We identified 788 proteins and 5081 phosphopeptides differentially regulated between SG and DG tumours (FDR < 0.05). Phosphoproteomic shifts enriched for metabolic regulation indicated increased activity of the STK11 pathway (90 proteins over-phosphorylated) in SG tumours ($P < .0001$). There was increased expression of STK11 ($P = .007$) in SG compared to DG tumours, along with enhanced expression of its regulatory adaptor STRAD ($P = .003$). Mass spectrometry showed significantly higher phosphorylation of AMPKβ S108, ULK1 S638, TSC1 S1080, and MAPT (Tau) T548 in SG tumours. Validation by IHC showed strong cytoplasmic and nuclear staining of TSC1 S1080 ($P = .009$), ULK1 S638 ($P = .006$), AMPKβ S108 ($P = .0005$), and MAPT (Tau) T548 ($P = .01$) predominantly in SG tumours compared to DG. Functional relevance of STK11/AMPK signalling was assessed using GH3 cell lines and primary somatotropinoma cultures treated with selective inhibitors. Treatment with Rapamycin, HY-16966 and Dorsomorphin resulted in significant decrease in cell viability in SG tumours ($P < .0001$) and GH3 cells ($P < .0001$). No haemolysis was observed at 1 μM of these inhibitors suggesting safety for normal cells. We observed significant decrease in GH levels ($P < .05$) at 1 μM concentration of these inhibitors. Inhibitor treatment reduced downstream phosphorylation of TSC S1080 ($P = .003$), ULK1 S638 ($P = .004$), and AMPKβ S108 ($P = .01$), supporting a functional role for STK11 signalling in tumour cell survival and growth. Our in-house proteomics data and publicly available transcriptomic datasets showed decreased expression of STK11 pathway proteins (MEF2C, FGFR3, TBC1D4, SPP1, SORBS1, mTOR, MAPT).

Conclusions: Multi-omics analysis reveals distinct STK11-driven signalling in sparsely-granulated somatotropinomas, with consistent validation by orthogonal methods. AMPK, mTOR, and ULK1 emerge as candidate therapeutic targets for subtype-directed tumour management.

Abstract citation ID: lvag096.573

P454 - LBA_ECE_1115 - Follicular fluid steroidomic signatures as predictors of oocyte competence and IVF outcomes

Tinatin Kutchukhidze
University of Oxford, Oxford, United Kingdom

Background: Oocyte competence is a key determinant of IVF. Accurate prediction of oocyte competence remains a major challenge in IVF, with 40-50% of morphologically normal oocytes failing to produce high-quality embryos. Follicular fluid steroidomics offers a window into the oocyte microenvironment. Follicular fluid, as the oocyte's immediate microinvironment, contains steroid hormones, growth factors, and metabolites that directly influence maturation and embryonic potential. Steroidal hormones such as estradiol, progesterone, testosterone, androstenediole, and cortisol have been linked to follicle size, oocyte maturation, and fertilization in small-scale studies (<50 00cyte). Advances in LC-MS/MS-based steriodiomics now allow simultaneous high-sensitivity quantification of multiple steroid metabolites, offering the potential to define predictive

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hormonal signatures. A large-scale, systematic evaluation is needed to translate these laboratory findings into clinical IVF practice.

Objectives: Map the steroidomic profile of follicular fluid in a large IVF cohort and identify predictive hormonal signatures for oocyte competence and IVF outcomes.

Methods: In this prospective observational study, 120 women undergoing IVF/ICSI at a tertiary reproductive center contributed follicular fluid from 842 dominant follicles (>18 mm). LC-MS/MC quantified 15 steroid hormones and metabolites, including estradiol, progesterone, testosterone, androstenedione, DHEA, and cortisol. Oocyte competence was defined as mature (MII vs MI/GV), fertilization(2PN formation), and embryo quality(blastocyte grading on day 5). Clinical endpoints included implantation and clinical pregnancy rates. Multivariate logistic regression identified independent steroidomic predictors, while ROC curves evaluated predictive performance. Subgroup analyses examined ratios such as estradiol-totestosterone, reflecting the estrogen/androgen balance within the follicular microenvironment.

Results: Higher estradiol and progesterone levels were strongly associated with MII oocyte ($P < .001$). elevated androstenedione and testosterone correlated negatively with fertilization ($P = .003$). a distinct steroidomic signature, featuring a high estradiol-to testosterone ratio and optimal progesterone, predicted high-quality blastocyst formation (AUC = .81). Cortisol elevation was linked to poorer embryo quality and lower implantation rates ($P < .01$). In multivariate models, estradiol/testosterone ratio and progesterone remained independent predictors of oocyte competence and clinical pregnancy(adjusted OR 2.4,95% CL 1.6-3.8)

Conclusions: follicular fluid steroidomic profiling provides a robust, biologically meaningful predictor of oocyte competence and IVF outcomes. The intrafollicular balance between estrogens and androgens emerges as a key determinant of developmental potential. Applying biomarkers in embryology practice could enhance oocyte selection, optimize stimulation protocols, personalize IVF strategies, and make a transformative step in precision reproductive endocrinology.

Abstract citation ID: lvag096.574

P455 - LBA_ECE_1092 - Metyrapone treatment improves the pro-inflammatory profile in patients with mild autonomous cortisol secretion

Anna Tosin[1], Sebastian Wrighton[2], Helena Niziolek[1], Clemens Baumgartner[1], Paul Fellinger[1], Luise Bellach[1], Alexandra Kautzky-Willer[1], Michael Krebs[1], Michael Leutner[1], Winfried Pickl[2] and Peter Wolf[1]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria; [2]Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Institute of Immunology, Vienna, Austria

Research Question: Hypercortisolism is associated with a low-grade inflammatory state; however, evidence in patients with mild autonomous cortisol secretion (MACS) remains limited. This study aims to compare disease-specific shifts of inflammatory cytokine profiles between patients with MACS to patients with non-functional adrenal adenoma (NFA) and to investigate the effects of medical treatment with metyrapone.

Methods and Material: Patients with MACS ($n = 25$, 21 females) were compared to patients with NFA ($n = 25$, 21 females) of comparable age (63 (55-67) vs 61 (54-68) years) and BMI (27 (24.2-30.5) vs 28.5 (27.5-32.2) kg/m^2). A sub-cohort of 14 MACS patients was prospectively re-evaluated following 12 weeks of treatment with evening doses of metyrapone (500 mg at 6 PM & 250 mg at 10 PM) as part of an exploratory secondary analysis of the AdrenalCLOCK study. Leukocytes, lymphocytes, and neutrophils were assessed and individual ratios were calculated. Cytokine levels were measured using a 37-plex Luminex bead-based assay. Mann-Whitney U tests were applied for intergroup cross-sectional analysis. Wilcoxon signed-rank tests were performed for outcome comparison after medical treatment in MACS patients.

Results: Treatment with metyrapone led to a significant improvement in the neutrophil-to-lymphocyte ratio (2.22(1.67-2.77) vs 2.14 (1.37-2.60) $P < .001$), accompanied by significant alterations in 15 cytokines, including CD40L, EGF, FLT-3L, G-CSF, GROa, IFNg, IL 1RA, IL-4, IL-9, IL-12p40, IL-17A, TGFa and TNFb. Statistically, follow-up examination after metyrapone treatment revealed the most pronounced decreases in IL-15 ($P = .0009$) and IL-18 ($P = .001$), cytokines that play key roles in NK-cell homeostasis and activation, respectively. Comparison between patients with MACS and NFA revealed no significant differences between groups.

Conclusions: Treatment with evening doses of metyrapone attenuates the pro-inflammatory immune profile in MACS. Whether this immune modulation contributes to improvement of the adverse cardiometabolic risk profile observed in these patients will require further investigation.

Abstract citation ID: lvag096.575

P457 - LBA_ECE_1018 - Telomere length in untreated congenital isolated growth hormone deficiency

Angela Leal[1], Júnia Ribeiro De Oliveira Longo Schweizer[2], Rodrigo Calado[3], Martin Bidlingmaier[2], Roberto Salvatori[4], Barbara Santana[3], Jan Frystyk[5], Fabricia Alvisi[1], Viviane Almeida[1], Elenilde G. Santos[1], Keila R. Villar-Gouy[1], Enaldo Melo[1], Nathalie Santana[1], Francisco Pereira[1], Carla R. P. Oliveira[1], Luciana Pedral S. D. Leite[1], Francisco de Paula[3], Angela Silva[1], Margaret Castro[3] and Manuel H. Aguiar Oliveira[1]

[1]Hospital Universitário, Endocrinology, Medicine, Aracaju, Brazil; [2]Department of Medicine IV, Ludwig Maximilian University of Munich, Munich, Germany; [3]University of Sao Paulo Ribeirao Preto Medical School, Ribeirao Preto, Brazil; [4]Johns Hopkins, Endocrinology, Baltimore, United States; [5]University of Southern Denmark, Odense, Denmark

Background: Accelerated telomere shortening has been associated with biological aging and influence of the GH-IGF-I axis has

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

been implicated in this process. The Itabaianinha cohort in Brazil presents with severe isolated congenital GH deficiency (IGHD) due to a homozygous mutation in the GHRH receptor gene (*GHRHR*). Affected individuals exhibit severe short stature, central obesity, and hypercholesterolemia, but do not show premature atherosclerosis and maintain a normal life expectancy, with brain aging consistent with chronological age. The objective of this study was to evaluate the leukocyte telomere length (LTL) in these IGHD individuals.

Methods: We assessed LTL in 36 IGHD subjects with homozygous *GHRHR* c.57+1G→A mutation, and 36 controls homozygous for the wild type allele. Serum IGF-I, IGF-II, and biochemical parameters were measured. LTL was measured by quantitative polymerase chain reaction using telomere-to-single copy gene (T/S) ratio.

Results: IGHD individuals had markedly reduced height and body weight compared with controls (height: 1.3 (0.1) vs 1.7 (0.1) m; weight: 43.1 (7.3) vs 70.8 (11.2) kg; $P < .0001$ for both), while BMI was similar (27.2 (7.0) vs 27.1 (4.8) kg/m^2; $P = .942$). IGF-I (ng/mL) and IGF-II (ng/mL) were profoundly reduced in IGHD (IGF-I: 11.0 (5.5) vs 144.5 (70.5); IGF-II: 327.0 (122.5) vs 896.5 (363.0), respectively; $P < 0.0001$ for both). IGHD subjects exhibited undetectable or extremely low IGF-I concentrations, while IGF-II levels were approximately 2.5-fold lower than in controls. The T/S ratio did not differ significantly between IGHD and controls (0.8 (0.6) vs 0.9 (0.4); $P = .593$). A modest positive correlation was found between the T/S ratio and IGF-II ($r = 0.376$; $P = .045$), whereas no significant correlations were observed between the T/S ratio and IGF-I or HOMA-IR.

Conclusion: Lifelong untreated IGHD is not associated with alterations in leukocyte telomere length. These findings are consistent with the normal longevity and normal brain aging observed in this IGHD cohort.

Abstract citation ID: lvag096.576

P458 - LBA_ECE_1238 - Prevalence, vascular risk factors and complications of metabolic syndrome in a population of people living with type 1 diabetes: results from the French SFDT1 cohort

Adrien Burel[1], Agathe Guenego[1], Morgane Mauger[1], Marine Briand[1], Solène Eon[1], Pierre-Yves Benhamou[2], Banu Isabela[3], Marie Lepage[4], Pierre Gourdy[5], Laurence Salle[6], Jean-Pierre Riveline[7], Emmanuel Cosson[8], Guy Fagherazzi[9] and Patricia Vaduva[1]

[1]Diabetes, Endocrinology and Nutrition, Rennes University Hospital, Rennes, France; [2]Endocrinology, Diabetes and Nutrition, Grenoble University Hospital, Grenoble, France; [3]Endocrinology and Diabetes, Saint-Joseph Hospital, Paris, France; [4]Endocrinology—CARDEO Department, Boulogne-sur-mer Hospital, Boulogne-sur-mer, France; [5]Toulouse University Hospital, Diabetes, Toulouse, France; [6]Diabetes and Endocrinology, Limoges University Hospital, Limoges, France; [7]Endocrinology and Diabetes, Lariboisière Hospital, Paris, France; [8]Endocrinology, Diabetes and Nutrition, Avicenne—Bobigny University Hospital, Bobigny, France; [9]Department of Precision Health, Luxembourg Institute of Health, Luxembourg, Luxembourg

Background and aims: Type 1 diabetes (T1D) is increasingly associated with features of insulin resistance and obesity, a phenotype known as "double diabetes". This study aimed to evaluate the prevalence of metabolic syndrome (MetS) features and its associated vascular complications, while assessing the utilization patterns of non-insulin adjunct therapies in a large real-world cohort.

Methods: We conducted a retrospective observational study of 2043 adult patients with T1D (pwT1D) from the French SFDT1 national cohort. MetS was defined according to IDF/AHA criteria. Dyslipidemia and hypertension were assessed using ESC/EAS 2023 guidelines. Logistic regression models were used to identify factors associated with chronic complications and the prescription of adjunct therapies.

Results: In the whole population, the median age and duration of T1D were 38 years [28-51 years] and 21 years [12-32 years], respectively. MetS, MASLD (FLI>60) and insulin resistance (eGDR<7.5 mg/kg/min) affected 32%, 18.9% and 32% of the population, respectively. Dyslipidemia, hypertension, and obesity were present in 50.7%, 20.3%, and 19.2% of the participants, respectively. Suboptimal management was frequent: 81.4% had inadequately treated dyslipidemia and 11.7% had inadequately managed or undiagnosed hypertension. Longer diabetes duration (OR = 1.05; $P < .01$), retinopathy (OR = 1.85; $P = .0017$), and nephropathy (OR = 1.77; $P = .0158$) were linked to higher risks of untreated dyslipidemia. Complications rates were: 37.2% of retinopathy, 15% of nephropathy, and 4.7% of major adverse cardiovascular events. Patients accumulating both hypertension and dyslipidemia exhibited critical complication rates (71.4% of retinopathy and 45.3% of nephropathy). Adjunct non-insulin therapies were prescribed, off-label, to 5.6% of patients (Metformin:3.7%; GLP-1R agonists:2.5%; SGLT2 inhibitors:0.1%). Multivariable analyses revealed that prescription of these therapies was significantly associated with a 42% reduction in the risk of uncontrolled hypertension (OR = 0.58; $P = .0464$). Conversely, longer diabetes duration (years) (OR = 1.05; $P < .01$), retinopathy (OR = 1.85; $P = .0017$), and nephropathy (OR = 1.77; $P = .0158$) were linked to higher risks of untreated dyslipidemia. Prescription of these agents was primarily driven by BMI (kg/m^2) (OR = 1.20) and the presence of hypertension (OR = 2.34) rather than glycemic levels. Eating disorders (SCOFF score ≥ 2) were reported in 31.9% of participants, with no significant association with adjunct therapy use.

Conclusion: Double diabetes affects one-third of the T1D population and is a major driver of micro/macrovascular complications. Despite a high prevalence of metabolic risk in our cohort of pwT1D, we observed a marginal use of currently off-label adjunct non-insulin therapies. These findings underscore the need for efficacy and safety trials, as well as updated clinical guidelines to integrate metabolic management beyond insulin therapy in T1D.

Abstract citation ID: lvag096.577

P459 - LBA_ECE_1387 - Liver fibrosis enhances risk stratification beyond cardiovascular–kidney–metabolic staging

Weinan Xie[1,2], Zhujun Sheng[3] and Xiyan Zhao[3]

[1]Beijing, China; [2]Beijing University of Chinese Medicine, Beijing, China; [3]Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: The cardiovascular–kidney–metabolic (CKM) framework has recently been proposed to improve integrated risk stratification across metabolic, renal, and cardiovascular domains. However, liver fibrosis, a key manifestation of systemic metabolic dysfunction, is not incorporated into current CKM staging. Its potential incremental value in risk prediction remains unclear.

Methods: We conducted a population-based analysis using data from the National Health and Nutrition Examination Survey (NHANES) 2017-2018 cycle, including participants with available vibration-controlled transient elastography data. Liver fibrosis was assessed using liver stiffness measurement (LSM). CKM stages were defined based on metabolic risk factors, diabetes, chronic kidney disease, and cardiovascular disease. All-cause mortality was ascertained through linkage with the National Death Index. Cox proportional hazards models were used to evaluate the association between liver fibrosis and mortality. The incremental predictive value of liver fibrosis beyond CKM staging was assessed using discrimination and reclassification metrics, including C-statistics, net reclassification improvement (NRI), and integrated discrimination improvement (IDI).

Results: Liver fibrosis was associated with increased risk of all-cause mortality independent of CKM stage and conventional risk factors. Incorporation of liver fibrosis into the CKM framework improved risk discrimination and reclassification performance compared with CKM staging alone. These associations were consistent across different CKM strata.

Conclusions: Liver fibrosis may provide additional prognostic information beyond the current CKM framework. Integrating hepatic fibrosis into cardiometabolic risk stratification models may enhance identification of individuals at high risk of adverse outcomes.

Abstract citation ID: lvag096.578

P460 - LBA_ECE_1332 - Preserved muscle mass does not reflect functional status in patients with acromegaly in remission: the role of muscle quality

Ayşe Merve Ok Kurt[1,2], Ümmü Mutlu[1], Fatih Bektaş[1,3], Hulya Hacisahinogullari[1], Gulsah Yenidunya Yalin[1], Tuğba Erdoğan[4], Gulistan Bahat[4], Nurdan Gul[1], Ayse Kubat Uzum[1] and Ozlem Soyluk Selcukbiricik[1]

[1]Endocrinology and Metabolism, Istanbul University Istanbul Faculty of Medicine, Istanbul, Türkiye; [2]Endocrinology and Metabolism, Kocaeli City Hospital, Kocaeli, Türkiye; [3]Endocrinology and Metabolism, Bağcılar Training and Research Hospital, İstanbul, Türkiye; [4]Geriatrics, Internal Medicine, Istanbul University Istanbul Faculty of Medicine, İstanbul, Türkiye

Background: Acromegaly is characterized by excess growth hormone (GH), leading to significant alterations in body composition, including increases in body size, skeletal muscle and fat mass. Despite increased muscle mass, muscle strength and quality may not be preserved, and data on their clinical impact remain limited. It is unclear whether these alterations persist and affect physical performance after biochemical remission.

Objective: To evaluate alterations in body composition and their impact on muscle mass, muscle strength, and muscle quality, and to identify impaired physical performance in patients with acromegaly in remission.

Methods: This cross-sectional study included 81 patients with acromegaly in remission (41 women, 40 men). Body composition and muscle mass parameters, including skeletal muscle mass (SMM) and SMM indices adjusted for body mass index, weight, and height^2 [SMMI (BMI), SMMI (weight), SMMI (height^2)], and muscle quality indices (MQI), were assessed with BIA. MQIs were calculated as handgrip strength divided by SMM and SMMI parameters. Muscle strength was evaluated using handgrip dynamometry, with low muscle strength defined as <20 kg in women and <35 kg in men. Parameters were classified according to sex-specific cut-off values derived from the Turkish population (Bahat et al.). Physical performance impairment was defined as reduced performance in either the chair stand test or 4-meter walking speed test. ROC curve analysis was performed.

Results: The study population had a mean age of 49.2 ± 10.9 years, with a median follow-up of 109 (73-157) months. Impaired physical performance was identified in 6 patients (7.4%).

Handgrip strength was lower in patients with impaired physical performance (26.3 ± 3.6 vs 42.4 ± 12.6 kg, $P < .001$); however, low handgrip strength was observed in only three patients, none of whom were in the impaired group. SMM and SMMI (height^2) did not differ ($P = .185$; $P = .878$), SMMI (BMI) (0.83 ± 0.18 vs 1.18 ± 0.28, $P < .001$) and SMMI (weight) (35.2 [29.4-37.9] vs 40.6 [36.7-43.9], $P = .014$) were lower in patients with impaired performance.

MQI-SMM and MQI-SMMI (height^2) were lower in patients with impaired performance (0.88 ± 0.13 vs 1.22 ± 0.21; 2.19 ± 0.26 vs 3.6 ± 0.89, respectively; both $P < .001$). In contrast, MQI-SMMI (BMI) and MQI-SMMI (weight) did not differ ($P = .513$; $P = .138$).

MQI-SMMI (height^2) showed the highest discriminative performance (AUC: 0.973), followed by MQI-SMM (0.940) and handgrip strength (0.920).

Conclusions: Even in remission, acromegaly may remain associated with impaired physical performance. Despite increased muscle mass, functional impairment may persist and be masked. Therefore, patients with acromegaly should be evaluated for muscle function and quality during follow-up.

Abstract citation ID: lvag096.579

P461 - LBA_ECE_1060 - Functional characterization of a non-canonical SDHD splice-site variant (c.314+4A > G) in a family with thyroid and carotid paragangliomas

Grigoris Effraimidis[1,2], Varvara Trachana[1], Evmorfia Tzagkaraki[3], Emmanouela Linardaki[3], Dimitris Valakos[4], Giannis Vatsellas[4], Georgios Kyriakopoulos[5], Constantine Stratakis[3,6,7] and Katerina Saltiki[8]

[1]Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece; [2]Department of Endocrinology and Metabolic Diseases, University General Hospital of Larissa, Larissa, Greece; [3]Institute of Molecular Biology and Biotechnology of the Foundation for Research and Technology Hellas (IMBB-FORTH), Heraklion, Greece; [4]Greek Genome Center, Biomedical Research Foundation, Academy of Athens, Athens, Greece; [5]Department of Pathology, Evangelismos Hospital, Department of Biological Chemistry, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [6]Pediatrics, University of Athens Medical School, Athens, Greece; [7]Hospital for Endocrine Surgery Research Center, HCA Florida Healthcare, HCA Healthcare Research Institute,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Tampa, Florida, United States; [8]Endocrine Unit, Department of Clinical Therapeutics, National and Kapodistrian University, Athens, Greece

Background: Thyroid paragangliomas (TPGLs) are exceptionally rare (<0.1% of thyroid neoplasms, ~0.5% of all paragangliomas) and frequently occur within hereditary head and neck paraganglioma syndromes. While hereditary paragangliomas are frequently linked to *SDHD* germline variants, intronic splice-site alterations are scarcely reported in TPGLs. We describe the clinical and functional characterization of a TPGL associated with a novel intronic *SDHD* variant.

Methods: We investigated a family of a 36-year-old woman with intrathyroidal TPGL and bilateral carotid body paragangliomas in her father and brother, all carrying a heterozygous intronic *SDHD* variant, c.314+4A > G (NM_003002.5). Germline testing was performed by next-generation sequencing, followed by in-depth RNA sequencing on whole blood to assess splicing and allele-specific expression. RNA-seq libraries were prepared with a directional protocol and sequenced on an Illumina NextSeq 2000 (~80 M 150-bp paired-end reads/sample), aligned with HISAT2, quantified with HTSeq, and analyzed with DESeq2; splice junctions were visualized by sashimi plots in IGV.

Results: The *SDHD* c.314+4A > G variant lies within the intron 3 donor site and is absent from gnomAD and the Leiden University Medical Center SDHD gene variant database; SpliceAI predicts splice disruption (Δ score 0.81). RNA-seq demonstrated two competing exon 3→4 junctions in both carriers: a canonical junction from the wild-type allele and a cryptic junction 4 bp downstream, attributable to the mutant allele. In the proband and her brother, aberrant junctions accounted for approximately half of all exon 3→4 splice events, consistent with a "leaky" splice-site defect and predicted frameshift with premature termination. Despite sharing the same variant, overall *SDHD* expression was lower in the proband than in her brother, consistent with allele-specific transcript imbalance and possible haploinsufficiency. Co-segregation of c.314+4A > G with thyroid and bilateral carotid body paragangliomas across three paternally related relatives supports its role in a hereditary SDHD-associated paraganglioma syndrome.

Conclusions: This study provides direct RNA-level evidence that the intronic *SDHD* c.314+4A > G variant causes aberrant splicing and supports reclassification from VUS to likely pathogenic under ACMG/AMP criteria (PS3, PM2, PP3, segregation). These findings expand the spectrum of splice-disrupting *SDHD* c.314 variants implicated in hereditary head and neck paragangliomas, highlight TPGL as part of this spectrum, and underscore the value of RNA-based assays in interpreting non-canonical splice-site changes.

Abstract citation ID: lvag096.580

P462 - LBA_ECE_1305 - Combined Effect of Osilodrostat and Mitotane in Adrenocortical Carcinoma 3D models

Fabiola Vaglica[1], Laura Tomasello[1], Mattia Biondo[2], Giuseppe Siragusa[2], Giorgio Arnaldi[1], Giuseppe Pizzolanti[1,3] and Valentina Guarnotta[1]

[1]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy; [2]Department of Biological, Chemical and Pharmaceutical Sciences and Technologies (STEBICEF), University of Palermo, Palermo, Italy; [3]ATeN Center, Palermo, Italy

Systemic treatment of adrenocortical carcinoma (ACC) relies on mitotane. Osilodrostat, an 11β-hydroxylase inhibitor used to treat Cushing's syndrome, is also used to manage the ACC-associated hypercortisolism. Currently, the combination of osilodrostat and mitotane remains poorly investigated, even though it represents a treatment strategy in ACC with combined hypercortisolism. We assessed the effects of osilodrostat and mitotane, both individually and in combination, using the NCI-H295R cell line in two-dimensional (2D) cultures and three-dimensional (3D) spheroid models, which more closely recapitulate the *in vivo* tumour microenvironment. Osilodrostat showed no significant cytotoxicity in either the 2D or 3D models (IC_{50} > 100 μM). By contrast, mitotane reduced cell viability in a dose-dependent way, with IC_{50} values of 25.92 μM in 2D and 44.98 μM in 3D, indicating lower sensitivity in the 3D context. Drug interaction was studied using a dose-dose matrix and the Highest Single Agent (HSA) model. In 3D models, the drug combination produced greater inhibition of cell viability than mitotane alone; at 50 μM mitotane, inhibition increased from 21.84% (alone) to 42.89% (combined with 100 μM osilodrostat). The HSA analysis showed a mean synergy score of 5.97 ($P = 1.35 \times 10^{-6}$), reaching a maximum score of 18.12 for the combination of 50 μM mitotane and 100 μM osilodrostat. Morphological analysis also showed a significant reduction in spheroid area after the administration of the drug combination compared to mitotane alone at 50 μM (−45.6% vs −21.2%; $P = .0076$). Moreover, calcein AM/DAPI fluorescent staining revealed a significant increase in the ratio of non-viable to viable cells (MFIb/g from 0.84 with the combination to 1.79 with 50 μM of mitotane; $P < .0001$). Cell counting confirmed a 72% reduction in viability with the combination, compared with a 46% reduction observed with 50 μM mitotane alone. Docking analysis of CYP11B1 identified a primary catalytic site (C1) for both compounds. However, they displayed distinct orientations and steric incompatibilities that precluded simultaneous binding to the same site. Sequential docking revealed an alternative, lower-affinity cavity (C4) for mitotane when osilodrostat occupied C1, suggesting a potential concentration-dependent multi-site effect. Overall, osilodrostat does not exert a direct cytotoxic effect but significantly enhances mitotane's adrenolytic activity in 3D ACC models. These findings provide a preclinical rationale for combination strategies and support further translational and clinical studies integrating steroidogenesis inhibition with adrenolytic therapy in ACC.

Abstract citation ID: lvag096.581

P463 - LBA_ECE_1389 - High-resolution metabolomics reveals a BMI-independent metabolic signature in polycystic ovary syndrome

Utku Maraşlı[1], Seren Aksun[2], Sevilay Erdoğan Kablan[3], Emirhan Nemutlu[4] and Bulent Yildiz[5]

[1]Department of Internal Medicine, Hacettepe University Faculty of Medicine, ANKARA, Türkiye; [2]Division of Endocrinology, Hacettepe University Faculty of Medicine, ANKARA, Türkiye; [3]ANKARA, Türkiye; [4]Department of Analytical Chemistry, Hacettepe University Faculty of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Pharmacy, ANKARA, Türkiye; [5]Division of Endocrinology and Metabolism, Hacettepe University School of Medicine, Division of Endocrinology and Metabolism, ANKARA, Türkiye

Background: Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder with metabolic alterations not fully explained by obesity or androgen excess.

Objective: To define a plasma metabolomic signature of PCOS independent of BMI and to evaluate associations with measures of androgen excess.

Methods: Forty women with PCOS (mean age: 22.9 ± 2.7 years; mean BMI: 23.4 ± 4.6 kg/m^2) and 40 age- and BMI-matched healthy controls underwent standardized clinical, biochemical, and hormonal assessment. Plasma metabolomic profiling was performed using integrated GC–MS and LC–MS platforms. Data were analyzed using principal component analysis (PCA), partial least squares–discriminant analysis (PLS-DA) with cross-validation and permutation testing, false discovery rate (FDR)-adjusted univariate analysis, receiver operating characteristic (ROC) analysis, pathway enrichment (MetaboAnalyst), and Spearman correlations with clinical parameters.

Results: PCA and PLS-DA demonstrated clear separation of PCOS and control groups. PLS-DA achieved high discrimination (accuracy = 0.95, $R^2 = 0.92$, $Q^2 = 0.78$) and was validated by permutation testing ($P = .002$). Thirty-one metabolites were significantly altered after FDR correction.

Threitol, a four-carbon sugar alcohol, emerged as the top discriminatory metabolite (fold change = 5.86, FDR = 3.59×10^{-14}), achieving near-perfect discrimination between PCOS and controls (multivariate ROC AUC = 0.993; 95% CI: 0.962-1.000), highlighting its potential as a novel metabolic marker.

Pathway analysis revealed significant perturbations in branched-chain amino acid (BCAA: valine, leucine, isoleucine)) biosynthesis ($P = 5.49\times10^{-5}$, FDR = 0.004), alanine–aspartate–glutamate metabolism (a central amino acid–energy pathway) ($P = 1.56\times10^{-4}$, FDR = 0.006), and the citrate cycle ($P = .00103$, FDR = 0.028), indicating disrupted core energy metabolism.

Threitol correlated inversely with total testosterone (r = −0.46), free androgen index (r = −0.56), and anti-Müllerian hormone (AMH) (all $P < .001$). Palmitoylcarnitine correlated positively with total testosterone (r = 0.35, $P = .001$). Other key metabolites, including BCAA and energy metabolites, showed no significant association with androgen or insulin resistance measures.

Conclusions: High-resolution metabolomics identifies a robust, BMI-independent metabolic signature in PCOS characterized by BCAA and energy metabolism alterations. Selected metabolites show targeted associations with androgen levels, supporting refined metabolic phenotyping in PCOS.

Abstract citation ID: lvag096.582

P464 - LBA_ECE_1425 - Prognostic value of site-specific methylation of G0S2 gene in low-risk patients with adrenocortical carcinoma

Arianna Propato[1], Anna Aurora Dedonno[1], Giulia Cantini[1], Julia Penitenti[1], Chiara Lepri[1,2], Tonino Ercolino[1], Guido Di Dalmazi[3], Antonio De Leo[3], Lorenzo Zanatta[1], Gabriella Nesi[4], Letizia Canu[1] and Michaela Luconi[1,5]

[1]Florence, Italy; [2]Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy; [3]Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy; [4]University of Florence, Health Sciences, Florence, Italy; [5]University of Florence, Experimental and Clinical Biomedical Sciences, Florence, Italy

Adrenocortical cancer is a rare malignancy, characterized by a high heterogeneity of the tumor mass and aggressiveness in the advanced infiltrating and metastatic stages (ENSAT stage III and IV). However, even cancers with the low staging (ENSAT I and II) characterized by low risk of recurrence can display poor prognosis. Therefore, there is a pressing need for novel markers to improve patients' molecular characterization in view of applying personalized and precision medicine approaches to the disease.

In this small pilot study, we developed a novel method to quantify the percentage of specific CpG methylation in the promoter of G0S2 gene (Met-G0S2), previously identified as a good marker of gene hypermethylation signature (CIMP high) associated with ACC poor outcome. Met-G0S2 levels were significantly higher and more heterogenous in the tumor samples from 35 patients with diagnosis of ACC compared with the 10 normal adrenals analyzed ($P < .01$). MetG0S2 did not correlate with ENSAT tumor stages. When focusing on ACCs classified at low ENSAT stage I and II, high MetG0S2 percentage (cut-off corresponding to the 80th percentile of MetG0S2 percentage distribution in ACC) was able to identify those patients characterized by a significantly lower overall and progression free survival (Kaplan-Meier survival curve log-rank = 0.013 and 0.038, respectively). In a Cox regression multivariable survival-risk analysis adjusted for tumor resection margin status and cortisol secretion as confounding factors, only Met-G0S2 percentage maintained statistical significance of the risk of tumor progression (Hazard Ratio[95%CI] = 21.4[1.5-310.0], $P = .025$, $n = 20$). Finally, ACCs stratification according to Met-G0S2 showed a statistically significant difference in G0S2 expression evaluated by qRT-PCR ($P = .036$) and in Ki67% ($P = .024$), respectively lower and higher in high Met-G0S2 tumors.

In conclusion, these preliminary data suggest MetG0S2 as a potential molecular marker able to identify a subgroup of patients with poor prognosis among ACC patients classified at poor risk on the base of stage I/II, enabling a more refined profiling of the tumors and improvement of patients' clinical management.

Abstract citation ID: lvag096.583

P465 - LBA_ECE_1235 - Skeletal and renal complications in patients with X-linked rickets: patterns related to age at diagnosis and treatment exposure

Anna Skowrońska-Szcześniak[1] and Michal Popow[2]

[1]Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland; [2]Warsaw, Poland

Background: X–linked hypophosphataemic rickets (XLH) is a hereditary disorder characterized by FGF23–mediated renal phosphate wasting and impaired bone mineralization. Despite treatment, long–term skeletal and renal complications remain a significant clinical concern.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Aim: To evaluate the prevalence of skeletal and renal complications in adulth patients with XLH and explore their relationship with age at diagnosis and treatment exposure.

Methods: We conducted a retrospective single–centre analysis of 26 patients with XLH. Clinical data included age at diagnosis, treatment duration, and the presence of fractures and renal complications (nephrocalcinosis and/or nephrolithiasis). Patients were stratified according to age at diagnosis (≤4 years vs >4 years).

Results: The median age at diagnosis was 3 years, with most patients diagnosed in early childhood, although delayed diagnosis was observed in a subset. Fractures were present in 46% of patients, while renal complications were observed in 85%. Patients diagnosed after the age of 4 years tended to have a higher prevalence of fractures (50% vs 37.5%). In contrast, renal complications were highly prevalent regardless of age at diagnosis (100% vs 75%). No clear association was observed between treatment duration and the presence of renal complications. Male patients tended to have a higher rate of skeletal complications, although this finding should be interpreted with caution due to the small sample size.

Conclusions: In our centre, skeletal and renal complications are highly prevalent in adult patients with XLH and may reflect different underlying mechanisms. While skeletal complications appear to be associated with delayed diagnosis, renal complications are common and are not clearly explained by treatment duration alone, suggesting a potential contribution of disease-related factors. These findings highlight the complexity of disease burden in XLH and the need for optimized management strategies.

Abstract citation ID: lvag096.584

P466 - LBA_ECE_1294 - Artificial intelligence on opportunistic Pet/CT scans for predicting vertebral fracture risk in men undergoing androgen deprivation therapy for prostate cancer

Maria Francesca Birtolo[1,2], Riccardo Levi[1,3], Cristina Garibbo[1], Tommaso Lania[1], Andrea Lania[1,2], Letterio Politi[1,3] and Gherardo Mazziotti[1,2]
[1]*Department of Biomedical Sciences, Humanitas University, Pieve-Emanuele (Milan), Italy;* [2]*Endocrinology, Diabetology and Andrology Unit, Metabolic Bone Diseases and Osteoporosis Section, Humanitas Research Hospital, Rozzano (Milan), Italy;* [3]*Neuroradiology Unit, Humanitas Research Hospital, Rozzano, Italy*

Purpose: Predicting fracture risk in men undergoing androgen deprivation therapy (ADT) for prostate cancer is challenging, as bone mineral density may not be a reliable tool in this context. We recently demonstrated the high potential of a radiomics-based machine learning model for identifying women at high fracture risk during hormone deprivation therapy for breast cancer. This study aims to test the same approach in men undergoing ADT.

Methods: one hundred and ninety-nine men (median age 79 years; IQR 73-84) who were exposed to ADT (median duration: 24 months, IQR 11-48) for prostate cancer were included. Radiomics analyses were performed on CT images co-registered with PSMA PET scans, which were performed for tumour staging. Non-fractured and non-metastatic vertebrae (C1–L5) were automatically segmented using a convolutional neural network to extract radiomics features (RFs). Each feature was tested for its ability to predict vertebral fractures (VFs), as assessed by a longitudinal morphometric approach during ADT. Predictive models were built using a machine learning pipeline based on Random Forest classifier model, including automatic feature selection on training sets. These models were then tested using cross-validation to assess their ability to predict VFs.

Results: During ADT, new VFs were diagnosed in 28 men (14.1%) in association with lower L1-L4 T-score ($P = .0158$), and higher FRAX score for hip and major fractures ($P < .001$ and $P = .006$, respectively). In the univariate analysis, 50 out of 107 feature values calculated from unfractured vertebrae were found to be significantly associated with VFs. Significant differences were found between men with and without VFs in terms of first, second and shape-based features. Fifteen RFs were selected as the most important for developing the machine learning model. In the clinical model, the two most important features for predicting VFs in the Random forest model were age and the duration of ADT exposure. The ML model based on RFs showed a high ability to predict VFs (accuracy 0.783, ROC 0.735, sensitivity 0.519, specificty 0.827), outperforming that based on clinical features (accuracy 0.672, ROC 0.650, sensitivity 0.519, specifity 0.698). The RF "first order 10 Percentile" was the most relevant feature in the model, suggesting that a reduction in the lower bound of intensity values is positively associated with the development of VFs ($P = .0023$).

Conclusions: The radiomics-based ML model showed high potential in identifying men at high fracture risk during ADT for prostate cancer.

Abstract citation ID: lvag096.585

P467 - LBA_ECE_1195 - Improved detection of advanced fibrosis using a metabolically informed model in the MASLD era: comparison with FIB-4

Meliha Melin Uygur[1], Volkan Yazman[1], Ayse Nur Gul[1], Ismail Keskin[1], Özgür Uygur[2] and Caglayan Keklikkiran[3]
[1]*Department of Endocrinology and Metabolism, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize Merkez, Türkiye;* [2]*Department of Geomatic Engineering, Faculty of Civil Engineering, Yildiz Teknik Universitesi, İstanbul, Türkiye;* [3]*Faculty of Medicine, Department of Radiology, Recep Tayyip Erdoğan University, Rize, Türkiye*

Background: The transition from nonalcoholic fatty liver disease (NAFLD) to metabolic dysfunction–associated steatotic liver disease (MASLD) reflects a paradigm shift emphasizing the central role of metabolic dysfunction in liver disease progression. While non-invasive scores such as FIB-4 are widely used for risk stratification, their performance may be suboptimal in metabolically high-risk populations. We aimed to develop and evaluate a

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

metabolically informed model for predicting advanced fibrosis and to compare its performance with FIB-4.

Methods: In this cross-sectional study, we included 346 adults with body mass index (BMI) ≥25 kg/m^2 who underwent liver stiffness assessment using transient elastography. Advanced fibrosis was defined according to established liver stiffness measurement thresholds. Multivariable logistic regression analysis was performed to identify independent predictors of advanced fibrosis, including liver enzymes, fasting glucose, and prediabetes/diabetes status. Model performance was assessed using receiver operating characteristic (ROC) analysis and compared with FIB-4. Risk stratification performance was evaluated across predefined low-, intermediate-, and high-risk categories.

Results: Advanced fibrosis was identified in a subset of patients characterized by a high metabolic burden. In multivariable analysis, prediabetes/diabetes emerged as the strongest independent predictor of advanced fibrosis (OR 4.18, 95% CI 1.87-9.36, $P < .001$). Additional independent predictors included AST (OR 1.09), GGT (OR 1.01), and fasting glucose (OR 1.01), while ALT showed an inverse association (OR 0.96). Notably, BMI was not associated with advanced fibrosis ($P = .355$). The proposed model demonstrated superior discriminative ability compared to FIB-4 (AUC 0.816 vs 0.711). Furthermore, the model improved risk stratification, with a lower prevalence of advanced fibrosis in the low-risk group (3.8% vs 15.3%) and better separation across intermediate and high-risk categories.

Conclusions: In patients with overweight or obesity, advanced fibrosis is primarily driven by metabolic dysfunction rather than adiposity itself. A metabolically informed model incorporating glycemic status and liver enzymes outperforms FIB-4 in both discrimination and risk stratification. These findings support the conceptual shift from NAFLD to MASLD and highlight the importance of integrating metabolic parameters into fibrosis risk assessment.

Figure 1

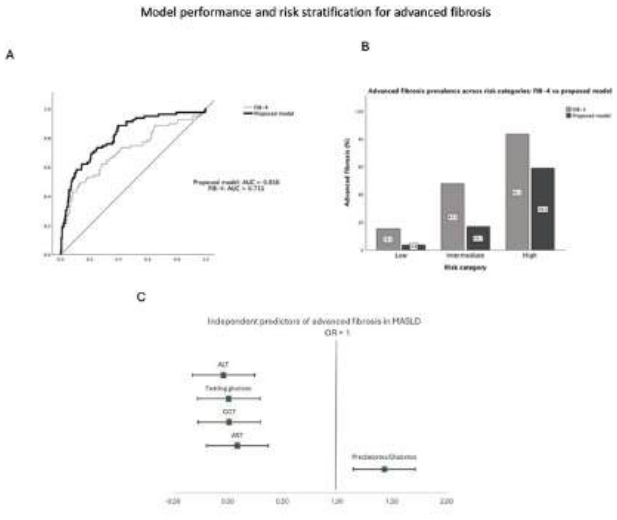


Figure 1. Model performance and predictors of advanced fibrosis in MASLD.
(A) ROC curve comparison showing improved discrimination of the proposed model compared to FIB-4
(B) Prevalence of advanced fibrosis across risk categories demonstrating improved stratification by the proposed model.
(C) Forest plot of multivariable logistic regression identifying independent predictors of advanced fibrosis.

Abstract citation ID: lvag096.586

P468 - LBA_ECE_1424 - Peptides mimicking transmembrane helices modulate Follicle-stimulating hormone receptor oligomerisation, signalling, and follicle growth

Ruijuan Xu[1], Thomas Hopkins[1], Chrisel D'souza[1], Peter McCormick[2] and Kim Jonas[1]
[1]King's College London, London, United Kingdom; [2]University of Liverpool, Liverpool, United Kingdom

Introduction: Follicle-stimulating hormone receptor (FSHR) is a G protein-coupled receptor (GPCR) expressed in ovarian granulosa cells, where it regulates follicle growth, development and oestradiol production[1]. While the physiological importance of FSHR is clear, the mechanisms specifying its pleiotropic signalling outcomes remain elusive. FSHR has been shown to form oligomers, a structural arrangement known to govern the trafficking and signalling profiles of GPCRs[2]. Transmembrane (TM) mimicking peptides can insert into the lipid bilayer and interfere with these TM–TM interactions[3]. Therefore, targeting FSHR oligomerisation represents a novel pharmacological strategy distinct from conventional agonism or antagonism.

Aim: To design FSHR targeting transmembrane (TM) mimetic peptides and assess their effects on FSH/FSHR-dependent signalling, oligomerisation, and follicle growth.

Methods: FSHR TM peptides were designed and synthesised based on TM regions: TM1, TM3, TM4, TM6, and TM7. To test their ability to impact FSH/FSHR functions, HEK293 cells expressing mFSHR were used impact on FSHR signalling as follows: cAMP via Glosensor™ live kinetic assay, Western blotting for phospho-ERK/AKT/CREB, HTRF for IP1 generation. FSHR oligomerisation was assessed by NanoBiT® complementation. The effect of TM peptides on FSH/FSHR-dependent follicle growth was assessed in isolated murine pre-antral follicles.

Results and Discussion: Individual FSHR-targeting peptides had no effect on FSH-dependent signalling. However, combinations of TM peptides produced distinct modulatory effects. TM1,7 and TM1,3,4,6,7 reduced FSH-dependent cAMP production, whereas TM1,3 selectively decreased FSH-dependent ERK phosphorylation, and TM1,7 enhanced IP1 production. NanoBiT complementation assays showed that TM1,3 and TM1,3,4,6,7 increased FSHR oligomerisation. In isolated murine follicle cultures, TM1,7 attenuated FSH-dependent follicle growth, consistent with its inhibitory effect on cAMP signalling. Taken together, these findings suggest that distinct FSHR oligomeric complexes mediate different aspects of FSH signalling and function. Targeting specific FSHR oligomers with TM-mimetic peptides may therefore represent a novel strategy for selective ovarian FSHR modulation.

References

1. Simoni M, Gromoll J, Nieschlag E. The follicle-stimulating hormone receptor: biochemistry, molecular biology, physiology, and pathophysiology. *Endocr Rev*. 1997;18:739-73. doi: 10.1210/edrv.18.6.0320.
2. Agwuegbo UC, Jonas KC. Molecular and functional insights into gonadotropin hormone receptor dimerization and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

oligomerization. *Minerva Ginecol*. 2018;70:539-548. doi: 10.23736/S0026-4784.18.04287-9.
3. Tarasova NI, Rice WG, Michejda CJ. Inhibition of G-protein-coupled receptor function by disruption of transmembrane domain interactions. *J Biol Chem*. 1999;274:34911-5. doi: 10.1074/jbc.274.49.34911.

Abstract citation ID: lvag096.587

P469 - LBA_ECE_1347 - Low-dose atomoxetine improves brain fatigue syndrome in women with Hashimoto's thyroiditis: a pilot study

Rana Almudhammed[1,2]
[1]*department of Biochemistry and Internal Medicine, Diyala College of Medicine, private Clinic, BAGHDAD, Iraq;* [2]*department of Biochemistry and Internal Medicine, Diyala College of Medicine, Diyala, Iraq*

Background: A subset of young women with Hashimoto's Thyroiditis (HT) report persistent brain fatigue and cognitive slowing despite achieving biochemical euthyroidism (TSH < 4 mIU/L) on levothyroxine. Symptoms including cognitive slowing, emotional lability, sensory and emotional sensitivity, drained mental energy, brain fog, inability to maintain focus, and a long recovery time after mental effort are extremely common among women with hypothyroidism despite achieving biochemical euthyroidism. We hypothesize this is driven by autoimmune-related microglial neuroinflammation rather than residual hypothyroidism. This study evaluates the use of low-dose atomoxetine (10 mg) in addressing brain fatigue syndrome.

Methods: We evaluated 50 women (aged 25-35) with HT who reported persistent mental fatigue, impaired attention, and prolonged cognitive recovery times. To isolate autoimmune-related fatigue, we applied strict exclusion criteria: BMI > 27, prediabetes/diabetes (HbA1c > 5.7%, fasting glucose > 100 mg/dL), premature ovarian insufficiency, iron or B12 deficiency, and psychiatric comorbidities (anxiety/depression). Patients over 35 were excluded to rule out perimenopausal symptom overlap. Baseline and 12-week fatigue levels were measured using the Mental Fatigue Scale (MFS). Patients received atomoxetine 10 mg daily alongside their standard levothyroxine. Atomoxetine increases norepinephrine in the prefrontal cortex. Recent research suggests that norepinephrine isn't just a neurotransmitter; it is a potent immunosuppressor within the Central Nervous System (CNS). Norepinephrine acts on beta-adrenoceptors on microglial cells and astrocytes. High levels of norepinephrine suppress the production of pro-inflammatory cytokines.

Results: At baseline, the cohort exhibited clinically significant mental fatigue with a mean MFS score of 22.8 (SD ± 4.1). After 12 weeks of the combined intervention, the mean MFS score decreased to 16.4 (SD ± 4.5). This reduction achieved statistical significance ($P = .014$). Patients reported noticeable clinical improvements, primarily in attention span and recovery time after cognitive exertion. The intervention was well tolerated, with few patients discontinuing the trial due to adverse effects, and thyroid function tests remained stable.

Conclusions: The combination of low-dose atomoxetine and levothyroxine provides a clinically meaningful reduction in persistent mental fatigue for euthyroid women with HT. These preliminary findings support the theory that targeted neuro-inflammatory modulation may benefit patients whose cognitive symptoms do not respond to standard thyroxine replacement.

Abstract citation ID: lvag096.588

P470 - LBA_ECE_1453 - Is preoperative alpha-blockade still necessary? initial experience from a newly established adrenal center

Dmitrii Buzanakov[1], Pier Alesina[2], Anke Meyer[1], Serge Tahl[3], Peter Goretzki[1] and Polina Knyazeva[1]
[1]*Helios University Hospital Wuppertal, Department of Endocrine Surgery, Wuppertal, Germany;* [2]*Evang. Kliniken Essen-Mitte, University of Duisburg-Essen, Essen, Germany;* [3]*Department of Anesthesiology, Helios University Hospital Wuppertal, Wuppertal, Germany*

Introduction: Catecholamine-secreting tumors have traditionally been managed with preoperative alpha-adrenergic blockade. Recently, the necessity of this standard approach has been increasingly debated. In this study, we present our initial experience demonstrating the feasibility of performing surgery for such tumors without preoperative alpha-blockade.

Materials and Methods: From May 2022 to September 2025, 17 patients (13 female, 4 male; mean age 58 ± 15 years) with catecholamine-producing tumors (14 pheochromocytomas and 3 paragangliomas) underwent surgery at a center without previous specialization in adrenal surgery. Standard anesthesiological management included general anesthesia, insertion of a central venous catheter, and placement of an arterial line, with Urapidil used as the main antihypertensive agent. Preoperative alpha-blockade was not applied, except in one case where it had been initiated prior to referral.

Results: Most patients were symptomatic: 14 patients had arterial hypertension, and 3 patients had diabetes mellitus. The median duration of surgery was 40 minutes (range: 20-240 minutes). One patient with a 10 cm paraganglioma underwent primary open surgery. In one additional case, conversion from laparoscopic to open surgery was required due to strong tumor adherence to the liver and a tumor size of 13 cm. The remaining 14 procedures were performed using minimally invasive techniques, including one laparoscopic adrenalectomy (combined with distal pancreatectomy) and 13 retroperitoneoscopic operations. Partial adrenalectomy was performed in 6 patients. The mean tumor size was 5.1 ± 3.4 cm (median 4 cm; range 2-13 cm). The median maximal systolic arterial pressure was 190 mmHg (range: 130-210 mmHg). Two patients developed atrial fibrillation, which resolved spontaneously. Two patients who underwent open surgery were admitted to the intensive care unit for 1 day. The median postoperative hospital stay was 2 days (range: 2-8 days). No major complications or mortality were observed.

Conclusions: Our preliminary findings suggest that omitting preoperative alpha-blockade in surgery for catecholamine-secreting tumors is feasible and safe. Targeted training of the anesthesiology team, standardized perioperative management, and close interdisciplinary coordination are essential for achieving favorable outcomes.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.589

P471 - LBA_ECE_1019 - Quantitative proteomic profiling of adrenal tumors identifies key drivers of malignancy

Anna Angelousi[1], Georgia Rouni[2], Martha Nikopaschou[2], Gregory Kaltsas[3], Georgios Kyriakopoulos[4], Athina Markou[5], Nicolas Nicolaides[6] and Martina Samiotaki[2]

[1]First Departmenet of Internal Medicine, Unit of Endcorinology, National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece; [2]BSRC Alexander Fleming, Athens, Greece; [3]First Propaideutic Departement of Internal Medicine, National and Kapodistrian University of Athens, Athens, Greece; [4]Evaggelismos Hospital, Athens, Greece; [5]Department of Endocrinology, Genennimatas General Hospital, Athens, Greece; [6]University of Cyprus, Nicosia, Greece

Background: Adrenocortical carcinoma (ACC) is a rare but aggressive neoplasm, for which early diagnosis and differentiation from adrenocortical adenoma (ACA) is crucial for subsequent treatment and prognosis.The aim of the study was to identify proteomic markers that differentiate ACC, ACA, and normal adrenal tissue based on analysis of archival adrenal tissue sections preserved as formalin-fixed paraffin-embedded (FFPE) samples.

Methods: A total of 24 FFPE tissues were included from 9 patients with ACC (median age of 55.5 years), 9 patients with ACA (median age of 60.5 years), and 6 patients with normal adrenal glands (controls), based on histological evaluation. All ACA cases ($n = 9$), as well as 4/9 ACC tumors, were secretory. The majority of ACC cases ($n = 7/9$) were stage III/IV according to ENSAT, with a median Ki-67 proliferation index of 29%, and were metastatic. Tissue was collected by scraping from microscope slides, and proteins were extracted using repeated cycles of heating and sonication in a 4% SDS lysis buffer. Digestion was performed using the SP3 method, and quantification was carried out by LC–MS/MS using Data-Independent Acquisition. Data processing was performed using DIA-NN (library-free), followed by statistical analysis and pathway enrichment.

Results: More than 6000 proteins were quantified from FFPE material. ACC samples showed increased signaling of insulin-like growth factor 2 (IGF2) along with reduced expression of the following mitochondrial membrane and steroidogenesis-related proteins: Ferredoxin Reductase (FDXR), 11-beta-hydroxylase (CYP11B1), and Glycosylphosphatidylinositol Specific Phospholipase D1 (GPLD1). Secretogranin-1 and Chromogranin-A, proteins associated with hormone storage and secretion, were decreased in ACC. In addition, enrichment of the Nucleotide Excision Repair pathway was observed, consistent with increased cellular proliferation.

Conclusions: DIA-based proteomic analysis of FFPE tissues reveals distinct molecular signatures that differentiate ACC from ACA and normal adrenal tissue. Alterations in the IGF2 axis, steroidogenesis, and DNA repair mechanisms may serve as useful diagnostic and biological markers for understanding adrenal tumorigenesis

Abstract citation ID: lvag096.590

P473 - LBA_ECE_1355 - Gestational diabetes and adverse neonatal outcomes: evidence from a prospective cohort study

Tania Tofail, Nusrat Sultana, Prodipta Chowdhury, Tahmina Ferdousi, Nazia Akter, Solaiman Hossain and Muhammad Hasanat

Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh

Background: Gestational diabetes mellitus (GDM) is a major contributor to adverse perinatal outcomes, yet evidence from South Asian populations using contemporary diagnostic criteria remains limited. This study evaluated maternal and neonatal outcomes among women with GDM compared with those with normal glucose tolerance (NGT) in a tertiary care setting in Bangladesh.

Methods: A prospective cohort study was conducted among pregnant women attending the antenatal clinic of Bangladesh Medical University between May 2022 and January 2025. GDM was diagnosed using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. Women with singleton pregnancies were followed until delivery. Maternal and neonatal outcomes were assessed, and multivariable logistic regression was performed to evaluate the independent association between GDM and neonatal outcomes.

Results: Among 325 participants, women with GDM ($n = 178$) were older and had higher BMI, a greater family history of diabetes, and a higher prevalence of previous GDM than women with NGT (all $P < .01$). Hypothyroidism was more frequent in the GDM group (25.8% vs 15.0%; $P = .016$), while other maternal complications were similar. Neonates born to mothers with GDM had significantly higher rates of macrosomia (13.0% vs 1.4%; $P < .001$), jaundice (24.2% vs 11.6%; $P = .004$), fetal distress (14.0% vs 5.4%; $P = .011$), and hypoglycemia (9.0% vs 0.7%; $P < .001$). In multivariable logistic regression analysis, GDM remained independently associated with macrosomia (aOR 10.28, 95% CI 2.21-47.75), neonatal hypoglycemia (aOR 9.83, 95% CI 1.23-78.21) and neonatal jaundice (aOR 2.94, 95% CI 1.31-6.61).

Conclusions: GDM diagnosed using IADPSG criteria was independently associated with increased risks of macrosomia, neonatal hypoglycemia, jaundice, and fetal distress. These findings highlight the importance of early detection and optimal management of GDM to reduce preventable neonatal complications.

Keywords GDM, macrosomia, neonatal hypoglycemia, perinatal outcome

Abstract citation ID: lvag096.591

P475 - LBA_ECE_1057 - Clinical outcome and safety profile of combination therapy with low-dose semaglutide and metformin vs metformin alone in polycystic ovary syndrome with obesity

Hurjahan Banu[1] and Rafayel Islam[2]

[1]Endocrinology, Bangladesh Medical university, Dhaka, Bangladesh; [2]Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder where obesity exacerbates metabolic and androgenic features. The combination of low-dose semaglutide and metformin in South Asian women with PCOS and obesity may be an effective and safe treatment modality.

Objectives: To compare the effectiveness and safety of a combined low-dose semaglutide and metformin with metformin alone in women with PCOS and obesity.

Materials and Methods: This Phase II randomized controlled trial was conducted at the Department of Endocrinology at

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Bangladesh Medical University from January 11 to October 16, 2025. A total of 31 reproductive-aged Bangladeshi women with PCOS and obesity (BMI $\geq$ 27.5 kg/m^2) were randomly assigned to two groups. The metformin group ($n = 16$) received 1000 mg of metformin daily. The combination group ($n = 15$) received the same metformin dose plus subcutaneous semaglutide, starting at 0.25 mg weekly for 4 weeks, then increasing to 0.5 mg weekly for 12 weeks. Both groups received similar standardized lifestyle modifications. Clinical and metabolic data were collected at baseline and after 16 weeks, with interim evaluations at weeks 4, 8, and 12. Data analysis used paired and independent t-tests, Mann-Whitney U test, Chi-square test, and Fisher's Exact test, with a significance level set at $P < .05$.

Results: The combination therapy group achieved greater reduction in body weight (mean difference, MD = −4.6%, $P = .001$), waist circumference (MD = −5.7%, $P < .001$), hip circumference (MD = −3.2%, $P < .001$), waist-to-hip ratio (MD = −2.9%, $P = .028$) and diastolic blood pressure (MD = −6.8%, $P = .023$) compared to the metformin group. Changes in the modified Ferriman–Gallwey score and systolic blood pressure did not differ significantly between groups. Notably, 93.3% of combination-treated participants achieved clinically meaningful weight loss (≥5% from baseline), compared with only 43.8% receiving monotherapy ($P = .006$). Adverse events were primarily gastrointestinal, predominantly in the initial treatment weeks, and resolved completely.

Conclusions: Combining low-dose semaglutide with metformin substantially outperforms metformin monotherapy in managing obesity and associated clinical metabolic derangements in women with PCOS and obesity. The superior weight loss, enhanced mobilization of abdominal fat, and reduced diastolic blood pressure, combined with a favorable safety profile, establish this combination as a valuable therapeutic option for PCOS cases with obesity in Bangladesh.

Abstract citation ID: lvag096.592

P478 - LBA_ECE_1368 - Remodelling of GPCR expression in endometrial cancer highlights KISS1R as a candidate receptor

Ece Akgun, Niamh Sayers and Aylin Hanyaloglu
London, United Kingdom

Background: G protein-coupled receptors (GPCRs) are the largest family of cell-surface receptors and play central roles in mediating extracellular signaling, including hormonal, metabolic, and microenvironmental cues. Increasing evidence indicates that aberrant GPCR expression contributes to cancer-associated processes such as proliferation, invasion, immune modulation, and metabolic adaptation. Moreover, recent pan-cancer studies suggest that this is highly tissue-specific and may reveal clinically relevant signaling signatures. Endometrial cancer is characterised by strong hormonal regulation and a dynamic tumour microenvironment, both of which are likely to influence GPCR-mediated signalling. However, the global GPCR expression profile in endometrial cancer remains poorly defined, limiting our understanding of this disease.

Objective: The objective of this study is to define the differential expression profile of GPCRs in endometrial cancer based upon data generated by the TCGA Research Network.

Methods: In this study, we performed a comprehensive bioinformatic analysis of GPCR expression in endometrial cancer using publicly available RNA-sequencing data from The Cancer Genome Atlas Uterine Corpus Endometrial Carcinoma (TCGA-UCEC). All analyses were performed using R Statistical Software (v4.5.2.). A paired analysis was conducted on 23 primary endometrial adenocarcinoma tumors and matched adjacent healthy endometrium tissues. Raw count data were processed using edgeR package (v4.0) with TMM normalization and logCPM transformation, followed by differential expression analysis with Benjamini–Hochberg false discovery rate (FDR) correction. Guide to Pharmacology GPCR list (v2025.3) excluding olfactory receptors was used to curate the GPCR list.

Results: After filtering, 17432 genes were retained, of which 10224 were significantly differentially expressed (FDR < 0.05). Among 402 genes from the curated GPCR list, 149 GPCRs were significantly differentially expressed in the paired analysis (FDR < 0.05). Notably, the majority of differentially expressed GPCRs exhibited strong down-regulation with large effect sizes, whereas a smaller subset of receptors showed consistent up-regulation across patients. Among the most significantly upregulated receptors, KISS1R emerged as a top candidate (logFC ≈ 4.06, FDR ≈ 2.3×10^{-7}), alongside other GPCRs linked to diverse signaling pathways. Exploratory analysis stratified by tumour grade indicated a tendency for increased expression of selected GPCRs, including KISS1R, in higher-grade tumours, although this observation requires further validation.

Conclusions: Overall, these findings reveal a pronounced remodeling of the GPCR expression landscape in endometrial cancer, characterized by widespread receptor down-regulation and selective up-regulation of specific GPCRs. This study provides a systematic framework for understanding GPCR dysregulation and highlights candidate GPCRs for future functional and translational investigation.

Abstract citation ID: lvag096.593

P479 - LBA_ECE_1402 - Urinary aldosterone and related metabolites by LC-MS/MS for the screening and subtyping of primary aldosteronism

Alice Stephenson[1], Brian Keevil[1], David Marshall[1] and Emily Goodchild[2]
[1]*Manchester University NHS Foundation Trust, Manchester, United Kingdom;* [2]*St Bartholomew's Hospital, London, United Kingdom*

Introduction: Primary Aldosteronism (PA) is the most common cause of secondary hypertension and is associated with increased risk of morbidity and mortality when compared to primary hypertension. We have developed a LC-MS/MS method for the measurement of aldosterone, cortisol and related metabolites in early morning urine samples, with the aim of providing an alternative screening test for PA. This aims to streamline identification and subtyping of PA. This would be of particular value in patients with KCNJ5 mutations, allowing faster referrals for adrenalectomy and improved patient outcomes.

Method: Analysis of 18-hydroxycortisol (18-OHF), 18-oxocortisol (18-OXOF), aldosterone, cortisol, 18-hydroxycortisosterone and tetrahydroaldosterone was performed in a single LC-MS/MS method, following liquid-liquid extraction with ethyl acetate.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Correlation of urinary steroids was evaluated. Correlation of the hybrid steroids 18-OHF and 18-OXOF was compared between matched urine and serum samples from patients with PA ($n = 57$).

Results: Validation parameters were acceptable, with the method demonstrating good recovery and minimal matrix effects. Urinary tetrahydroaldosterone and aldosterone showed agreement in numerical values ($r = 0.7212$). A clear numerical correlation was observed between 18-OXOF concentrations in serum and urine ($r = 0.7765$). A correlation was also observed between serum 18-OXOF and 18-OHF and urine 18OHF:cortisol ratios ($r = 0.6023, 0.6715$).

Conclusions: We have developed an LC-MS/MS assay to measure aldosterone and related metabolites in early morning urine samples. This has clinical applications at providing a streamlined screening test for PA, which could allow for early identification of PA subtypes. We hope to develop our in-house method further and aim to implement this approach in the future diagnostic work-up of PA patients. The results of this investigation will be matched with patient genotypes in future.

Abstract citation ID: lvag096.594

P480 - LBA_ECE_1416 - Right molecule, wrong moment: timing-dependent consequences of calcitriol on follicular dynamics and oocyte maturation

Ali Zeyghami[1,2,3], Hamid Ahmadi[1], Timea Judith Csabai-Tanics[1,2,3] and Zoltan Bognar[1,2,3]

[1]Department of Medical Biology, University of pecs Medical School, Pécs, Hungary; [2]National Laboratory of Human Reproduction, University of Pécs, Pecs, Hungary; [3]Szentágothai Research Centre, Universsity of Pecs, Pécs, Hungary

Introduction: The ovarian follicle is a precisely regulated endocrine microenvironment in which granulosa cells coordinate hormonal signalling and oocyte development. Among its modulators, calcitriol (1,25-dihydroxyvitamin D_3)—the biologically active form of vitamin D—has emerged as a significant regulator of reproductive function, acting through the nuclear vitamin D receptor (VDR) expressed in granulosa cells and follicular tissue. VDR activation influences anti-Müllerian hormone (AMH), a glycoprotein governing primordial follicle recruitment and ovarian reserve. Equally central is the steroidogenic enzyme aromatase (CYP19A1), which drives androgen to estradiol conversion within granulosa cells—a process integral to oocyte quality. While the roles of these mediators in folliculogenesis are increasingly recognized, how the timing of calcitriol exposure relative to FSH stimulation shapes their downstream regulation remains an underexplored question in reproductive endocrinology.

Methods: Adult female CD-1 mice (8-12 weeks) underwent controlled ovarian stimulation with exogenous FSH, followed by hCG to trigger ovulation. A supra-physiological dose of calcitriol (100 ng, i.p.) was administered at one of three time points: two days prior to gonadotropin stimulation (Vit D −2), concurrently with FSH, or two days thereafter. A vehicle-treated cohort served as the reference control. Cumulus–oocyte complexes (COCs) were retrieved sixteen hours post-hCG and assessed for meiotic maturation. Ovarian tissue was processed for immunohistochemical localization of AMH and aromatase (CYP19A1) and protein extraction for quantitative expression analyses.

Results: Immunohistochemical assessment revealed differential AMH and aromatase (CYP19A1) expression patterns across experimental groups. The Vit D −2 group exhibited elevated AMH localization alongside reduced aromatase (CYP19A1) expression compared to other groups, while an opposing pattern—characterized by diminished AMH and enhanced aromatase localization—was observed in the Vit D +2 group. Western blot analysis provided quantitative corroboration of these findings, indicating that calcitriol exerts a timing-dependent influence on the endocrine profile of granulosa cells. Follicular distribution analysis in the Vit D −2 group further demonstrated a decline in primary follicle proportion alongside a relative expansion of the antral follicle pool.

Conclusions: These findings underscore calcitriol timing as a critical modulator of granulosa cell endocrine function, follicular dynamics, and meiotic competence. The bidirectional, timing-dependent shifts in AMH and aromatase expression—corroborated by Western blot—highlight a context-dependent mechanism of vitamin D signaling with meaningful implications for its precise use in assisted reproductive protocols.

Keywords anti-Müllerian hormone (AMH), aromatase, folliculogenesis, vitamin D (calcitriol)

Abstract citation ID: lvag096.595

P484 - LBA_ECE_1385 - Acromegaly-associated diabetes and cardiovascular risk: evidence from a Swedish nationwide matched-cohort study

Angelo Milioto[1,2], Oskar Ragnarsson[1,2], Annika Rosengren[3,4], Martin Adiels[5], Diego Ferone[6,7], Gudmundur Johannsson[1,2] and Daniela Esposito[1,2]

[1]Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [2]Department of Endocrinology, Sahlgrenska University Hospital, Gothenburg, Sweden; [3]Department of Molecular and Clinical Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [4]Department of Medicine, Geriatrics and Emergency Medicine, Sahlgrenska University Hospital/Östra, Gothenburg, Sweden; [5]University of Gothenburg, 5School of Public Health and Community Medicine, Institute of Medicine, Gothenburg, Sweden; [6]Endocrinology Unit, Department of Internal Medicine and Medical Specialties (DIMI), University of Genova, Centre of Excellence for Biomedical Research (CEBR), Genova, Italy; [7]Endocrinology Unit, IRCCS Ospedale Policlinico San Martino, Genova, Italy

Introduction: While type 2 diabetes (T2DM) is typically linked to obesity, acromegaly-associated diabetes mellitus (ACRO-DM) develops in patients with relatively lean phenotype due to their excess growth hormone exposure. The clinical impact of this distinct metabolic profile is not fully understood. This study aims to primarily investigate the burden of cardiovascular morbidity, alongside survival outcomes, in individuals with ACRO-DM compared to those with T2DM.

Methods: This population-based, matched-cohort study utilized Swedish national health registries. The study cohort consisted of patients with acromegaly identified in the National Patient

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Register (PNR) who had concurrent diabetes recorded in the National Diabetes Register (NDR) or were treated with an antidiabetic drug recorded in the National Drug Register. A T2DM reference group was extracted from the National Diabetes Register and matched 10:1 to the ACRO-DM subjects based on gender, age, calendar year and duration of diabetes. Data on cardiovascular diseases were extracted from PNR. The baseline was defined as the date of the first NDR entry or the initial prescription of an antidiabetic drug, whichever occurred first. Hazard ratios (HRs) have been adjusted for smoking, income and education.

Results: The study included 348 ACRO-DM patients and 3480 matched T2DM controls. Both cohorts had comparable baseline characteristics, including mean age (~60 years), glycemic control (HbA1c ~55 mmol/mol), diabetes duration (~3 years) and follow-up period (~9.3 years). At baseline, cardiovascular disease was more frequent in the ACRO-DM cohort compared to the T2DM controls (61.2% vs 43.2%), specifically for stroke, hypertension, heart failure and arrhythmia. During follow-up, longitudinal analyses showed that patients with ACRO-DM had higher risk of cardiovascular events than T2DM controls (HR 1.55; 95% CI, 1.24-1.94), pulmonary embolism (HR 3.26; 95% CI, 1.94-5.95), venous embolism (HR 2.27; 95% CI, 1.29-4.00) and arrhythmias (HR 1.48; 95% CI, 1.11-1.98). A sensitivity analysis showed that hydrocortisone replacement did not affect the risk of pulmonary or venous embolism in patients with ACRO-DM. Mortality did not significantly differ among the two groups, cardiovascular mortality (HR 1.12; 95% CI, 0.78-1.60) and all-cause mortality (HR 1.18; 95% CI, 0.96-1.46).

Conclusions: ACRO-DM is characterized by a higher cardiovascular disease burden than standard T2DM. Despite this increased cardiovascular morbidity, overall and cardiovascular mortality rates remain comparable between the two conditions.

Abstract citation ID: lvag096.596

P485 - LBA_ECE_1392 - The impact of pegvisomant on lipid metabolism in acromegaly: a systematic review and meta-analysis

Angelo Milioto[1,2], Federico Gatto[3,4], Christian Basile[5,6], Eva Hessman[7], Diego Ferone[3,4], Oskar Ragnarsson[1,2], Gudmundur Johannsson[1,2] and Daniela Esposito[1,2]
[1]*Department of Internal Medicine and Clinical Nutrition, University of Gothenburg, Institute of Medicine, Sahlgrenska Academy, Gothenburg, Sweden;* [2]*Department of Endocrinology, Sahlgrenska University Hospital, Gothenburg, Sweden;* [3]*Department of Internal Medicine and Medical Specialties (DIMI), University of Genova, Endocrinology Unit, School of Medical and Pharmaceutical Sciences, Genova, Italy;* [4]*Endocrinology Unit, IRCCS Ospedale Policlinico San Martino, Genova, Italy;* [5]*Department of Clinical Science and Education, Karolinska Institutet, Södersjukhuset, Stockholm, Sweden;* [6]*Heart Care Foundation, ANMCO Research Center, Florence, Italy;* [7]*University of Gothenburg, Biomedical Library, Gothenburg University Library, Gothenburg, Sweden*

Introduction: Acromegaly is characterized by altered lipid profile due to the effect that growth hormone (GH) has on lipid metabolism. Pegvisomant is a GH-receptor antagonist approved for the treatment of acromegaly that has demonstrated a favorable impact on glucose metabolism; however, data on its effect on lipid metabolism are limited. The aim of this study is to synthesize available evidence on the impact of pegvisomant on total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL) and triglycerides (TGL) in patients with acromegaly.

Methods: A database search of PubMed, Cochrane Central and Embase was conducted for studies on pegvisomant in acromegaly in May 2025 and updated in March 2026. Two reviewers performed an initial screening of titles and abstracts and examined the full texts of the selected articles. Retrospective and prospective studies assessing lipid metabolism in patients with acromegaly before and after treatment with pegvisomant were included. Extracted data were systematically synthesized. Study quality was independently assessed by two reviewers using the NHLBI Quality Assessment Tool. The protocol for this systematic review adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and was registered in PROSPERO (CRD420261344770). Results are reported as mean difference (MD) and 95% confidence interval (CI).

Results: In total, 2239 articles were identified. After title and abstract screening, 147 articles involving 343 patients were reviewed in full text and ten were included in the systematic review. In most cases, TC, LDL, HDL and TGL remained unchanged after treatment with pegvisomant. Six studies were included in the meta-analyses as 4 were excluded due to overlapping populations. Following pegvisomant treatment, pooled analysis of 5 studies (involving 248 patients) revealed that TC remained unchanged after treatment with pegvisomant (MD 0.03 mg/dL; 95% CI: −0.17 to 0.23). Likewise, LDL showed no significant change in pooled analysis of 4 studies involving 163 patients (MD 0.05 mg/dL; 95% CI: −0.29 to 0.39). Similarly, pooled analysis of 3 studies involving 141 patients demonstrated no significant change in HDL (MD −0.02 mg/dL; 95% CI: −0.06 to 0.03). In contrast, TGL increased after treatment with pegvisomant with an MD of 0.22 mg/dL (95% CI: 0.08 to 0.36), based on 3 studies involving 96 patients.

Conclusions: This is the first systematic review and meta-analysis evaluating the impact of pegvisomant on lipid metabolism. Meta-analysis demonstrated a significant increase in TGL, while TC, LDL, and HDL remained unchanged after pegvisomant treatment.

Abstract citation ID: lvag096.597

P486 - LBA_ECE_1303 - Baseline bone mineral density does not predict early skeletal recovery after parathyroidectomy: a real-world cohort study

Müge Yılmaz[1], Ece Seçgin Demir[1], Senem Boz Aksoy[2], Busra Kanbur[1], Mehmet Dönmez[2], Meryem Özoğlu[3], Hale Ay[3], Baver Kızartıcı[3], Ziya Mithat Bıyıklı[4], Naile Gokkaya[5], Serhat Özçelik[2] and Kadriye Aydin[6]
[1]*Department of Endocrinology and Metabolism, Endocrinology and Metabolism, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye;* [2]*Department of Endocrinology and Metabolism, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye;* [3]*Department of Endocrinology and Metabolism, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye;* [4]*Department of Endocrinology and Metabolism, Endocrinology and metabolism, University of Health*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Sciences, Kartal Dr. Lütfi Kırdar City Hospital, istanbul, Türkiye; [5]Department of Endocrinology and Metabolism, Endocrinology and metabolism, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye; [6]İstanbul, Türkiye

Background: Primary hyperparathyroidism (PHPT) is characterized by predominant cortical bone loss. Although bone mineral density (BMD) is expected to improve after parathyroidectomy, early postoperative changes and their relationship with baseline BMD and metabolic parameters remain unclear. This study aimed to evaluate the association between baseline regional BMD and early postoperative changes in BMD (ΔBMD) as the primary outcome, and to explore correlations with metabolic parameters as the secondary outcome in a real-world cohort.

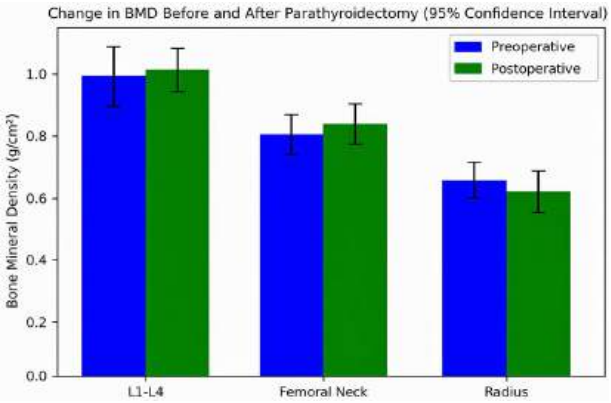
Methods: This retrospective study included patients who underwent parathyroidectomy for PHPT between 2014 and 2024. Patients with chronic kidney disease or multiglandular disease were excluded. Preoperative and first-year postoperative BMD (lumbar spine, femoral neck, distal radius) and biochemical parameters were analyzed. Changes in BMD (ΔBMD) and their associations were assessed using Spearman correlation analysis. A *P*-value <.05 was considered statistically significant.

Results: A total of 39 patients were included in the study. Preoperative PTH levels were 181.6 ± 114.6 pg/mL, serum calcium levels were 11.29 ± 0.64 mg/dL, and phosphorus levels were 2.66 ± 0.54 mg/dL. Preoperative BMD was 0.997 ± 0.24 g/cm^2 at the L1–L4 lumbar spine, 0.808 ± 0.15 g/cm^2 at the femoral neck, and 0.652 ± 0.11 g/cm^2 at the distal one-third radius. Parathyroidectomy resulted in significant increases in lumbar spine and femoral neck BMD ($P = .003$ and $P = .002$, respectively), whereas no significant change was observed at the distal radius ($P = .612$).

No significant association was found between baseline BMD and ΔBMD at any skeletal site (lumbar: r = −0.360, $P = .055$; femoral neck: r = −0.165, $P = .393$). Changes in PTH were also not associated with ΔBMD. In contrast, Δlumbar and Δfemoral neck BMD showed a moderate positive correlation (r = 0.394, $P = .034$).

Metabolic analysis revealed a significant negative correlation between insulin resistance and serum phosphorus levels (HOMA-IR: r = −0.490, $P = .004$).

Figure



Conclusions: In this cohort, early postoperative BMD improvement following parathyroidectomy occurred independently of baseline BMD, suggesting that initial skeletal status does not predict short-term bone recovery. These findings support a multifactorial regulation of early skeletal response beyond baseline bone mass. The lack of improvement at cortical sites is consistent with slower cortical bone remodeling. This may have implications for postoperative monitoring and risk stratification in PHPT patients.

Abstract citation ID: lvag096.598

P487 - LBA_ECE_1248 - Real-world efficacy and safety of mitotane monotherapy in the management of severe Cushing syndrome at a tertiary referral center

Xiang Zhou, Wan Su, Lian Duan, Huijuan Zhu and Lin Lu
Peking Union Medical College Hospital, Beijing, China

Objective: Mitotane is a potent steroidogenesis inhibitor; however, its use in severe Cushing syndrome (CS) is often limited by the delayed onset of action and side effects. This study was aimed to evaluate the real-world efficacy and safety of mitotane monotherapy in patients with challenging severe CS.

Design: Retrospective, single-center study.

Methods: We analyzed patients with severe CS treated with mitotane at Peking Union Medical College Hospital between January 2024 and January 2026. Mitotane was initiated at 500 mg twice daily and titrated based on tolerance and therapeutic response. Remission was defined as the normalization of 24-hour urinary free cortisol (24h-UFC). Clinical characteristics, treatment outcomes as well as frequency and severity of adverse events (AEs) were assessed.

Results: As of the data cut-off (4 March 2026), eighteen patients were included, with median baseline 24h-UFC 69-fold (IQR 18-115; range 5.5-303.4) the upper limit of normal (ULN). One patient died from cardiac arrest three days after initiation of mitotane and was excluded from efficacy analysis. Remission was achieved in twelve (70.6%) patients, after a median time of 42 d (IQR 24-96), with a mean mitotane dose of 1.56 ± 0.52 g/d. In the five patients who didn't achieve remission, their 24h-UFC decreased by 95.3% (IQR 85.5%-95.3%), dropping from 100.4-fold (IQR 87.6-140.5) to 4.8-fold (IQR 3.2-12.1) ULN, at a median mitotane dose of 1.25 g/d (IQR 0.8-2.0). Baseline lymphocyte percentage, CD 4+ lymphocyte count and potassium levels were significantly higher in the remission group compared to the non-remission group ($P < .05$). Common AEs included: liver enzyme abnormality (grade 1-2, $n = 9$; grade 3-4, $n = 7$), hyperlipidemia (grade 1-2, $n = 10$; grade 3-4, $n = 4$), gastrointestinal syndromes (grade 1-2, $n = 10$) and adrenal insufficiency (grade 1-2, $n = 6$). Notably, among seven patients with grade 3-4 liver enzyme abnormality, four exhibited isolated gamma-glutamyl transferase elevation while alanine aminotransferase, aspartate aminotransferase, and bilirubin levels were normal. Treatment discontinuation occurred in two patients due to severe hepatotoxicity.

Conclusions: Monotherapy of mitotane demonstrated substantial efficacy in controlling severe hypercortisolism with good tolerance, and the time to remission was comparable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

to other oral steroidogenesis inhibitors. This suggested the potential role of mitotane as a viable option for severe CS, particularly in regions where alternative steroidogenesis inhibitors are inaccessible.

Abstract citation ID: lvag096.599

P489 - LBA_ECE_1144 - Autoimmunity following subacute thyroiditis: thyroid autoantibody development and associated clinical factors

Murat Calapkulu, Murat Görgülü, İlknur Ozturk Unsal and Erman Cakal
Endocrinology and Metabolism, Ankara Etlik City Hospital, Ankara Etlik City Hospital, Ankara, Türkiye

Background: Subacute thyroiditis is a self-limited inflammatory thyroid disorder, most commonly following viral infections. Although thyroid function typically recovers, follicular destruction may trigger thyroid autoimmunity through antigen release. The development of thyroid autoantibodies and, in some cases, progression to chronic autoimmune thyroid disease have been reported; however, data on long-term autoantibody development and its determinants remain limited. This study aimed to investigate the incidence and predictors of thyroid autoantibody development during long-term follow-up in patients with subacute thyroiditis.

Methods: This study was designed as a retrospective cohort analysis. Medical records of 734 patients diagnosed with subacute thyroiditis at our center were retrospectively reviewed.. Patients with at least one year of follow-up and negative thyroid autoantibodies at diagnosis were included. Patients with positive thyroid autoantibodies at baseline or a prior diagnosis of hypothyroidism were excluded. A total of 73 patients met the inclusion criteria. Patients were divided into two groups based on the development of thyroid autoantibody positivity during follow-up, and demographic, laboratory, and treatment-related data were compared between groups.

Results: During follow-up, thyroid autoantibody positivity developed in 12 patients (16.4%). Anti–thyroid peroxidase antibody positivity was observed in 4 of 73 patients (5.5%), anti-thyroglobulin antibody positivity in 9 of 73 patients (12.3%), and TSH receptor antibody positivity in 3 of 61 patients (4.9%). The majority of patients remained autoantibody-negative throughout follow-up. Patients were divided into two groups based on the development of thyroid autoantibody positivity during follow-up. There were no significant differences between the groups in terms of age, gender, white blood cell count, neutrophil count, lymphocyte count, erythrocyte sedimentation rate, C-reactive protein levels, TSH, free T4, or free T3 levels. However, total thyroid volume was significantly higher in patients who developed thyroid autoantibody positivity compared with those who did not. No significant associations were observed between thyroid autoantibody development and thyroid functional status at diagnosis, ultrasonographic involvement pattern (unilateral or bilateral involvement), recurrence status, number of recurrences, or treatment modality, including nonsteroidal anti-inflammatory drugs and corticosteroid therapy.

Conclusions: Thyroid autoimmunity may develop in a considerable proportion of patients following subacute thyroiditis. While most demographic, biochemical, and clinical parameters were not associated with autoantibody development, increased thyroid volume emerged as a potential risk factor. These findings suggest that structural thyroid changes during the acute phase of subacute thyroiditis may contribute to subsequent autoimmune activation, highlighting the importance of long-term follow-up in patients with marked thyroid enlargement.

Keywords subacute thyroiditis, autoimmunity

Abstract citation ID: lvag096.600

P490 - LBA_ECE_1448 - Patterns of polyautoimmunity in patients with autoimmune thyroid diseases

Reti Zsuzsanna[1,2], Boglarka Kiss[3,4] and Alpar Kiss[5]
[1]*George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Endocrinology, Targu Mures, Romania;* [2]*Endocrinology, Mures County Hospital, Târgu Mureș, Romania;* [3]*University of Pecs, Pecs, Hungary;* [4]*University of Pecs, Oncology, Pecs, Hungary;* [5]*Codespring, Odorheiu Secuiesc, Romania*

Introduction: Autoimmune thyroid diseases (ATDs), Hashimoto's thyroiditis (HT) and Graves' disease (GD), often coexist with other autoimmune disorders. This study aimed to assess the frequency of these associations and to analyze their patterns in relation to the timing of disease onset.

Materials and Methods: In this retrospective study, we analyzed data from patients with ATD registered during a 10-month interval in our Endocrinology Department. The sole inclusion criteria were the presence of at least one additional confirmed autoimmune disease beside thyroid autoimmune disease. Data were analysed using network analysis in Python, and statistical evaluation was conducted using a binomial test. Triple associations were included in a weighted manner.

Results: A total of 780 patients were evaluated, of whom 130 met the inclusion criteria. Among these, 86.9% ($n = 113$) had HT and 13.1% ($n = 17$) had GD. Network analysis identified 28 autoimmune diseases, yielding 48 distinct combinations. In 84.6% of cases, two autoimmune conditions were present, while in 15.4% of cases, three or more conditions coexisted. Multiple associations involved 15 different conditions, most commonly vitiligo ($n = 7$) and type 1 diabetes (T1DM) ($n = 6$). T1DM was observed only with vitiligo and Addison's disease (AD), whereas vitiligo co-occurred with a different disorder in every case, showing the most diverse pattern. In multiple associations, systemic diseases other than vitiligo appeared only in the presence of other systemic diseases. When HT-associated comorbidities were categorized, binomial testing indicated that autoimmune conditions affecting the skin ($P = .00274$) and the nervous system ($P = .031$) were more likely to precede HT. In contrast, systemic ($P = .00015$) and gastrointestinal diseases ($P = .0059$) were more frequently observed following HT. These findings were also reflected in the most diverse multiple associations. In cases where HT and T1DM co-occurred ($n = 7$), neither condition showed temporal predominance. In contrast, among patients with concurrent AD and HT ($n = 13$), HT preceded AD in 7 cases, while both conditions were diagnosed simultaneously in the remaining 6 cases. All three conditions co-occurred in 4 cases. HT was most associated with rheumatoid arthritis ($n = 26$). GD was associated with 9 different diseases, most commonly psoriasis ($n = 5$), and appeared as a secondary

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

disease ($P = .007$).

Conclusions: HT demonstrated a relatively consistent temporal pattern depending on the associated comorbidity, whereas GD more frequently appeared as a secondary condition. Network analysis may help guide screening frequency in multisystem autoimmune disorders.

Abstract citation ID: lvag096.601

P491 - LBA_ECE_1191 - The influence of zinc administration on VEGF imunoexpression in lungs of diabetic rats

Cristina Gales[1], Carmen Lacramioara Zamfir[1], Gabriela Rusu-Zota[1], Mihai Nechifor[1] and Daniel Costel Gales[2]
[1]*Histology Department, University of Medicine and Pharmacy "Grigore T Popa" Iasi, Iasi, Romania;* [2]*Pedology Department, University of Life Sciences "Ion Ionescu de la Brad", Iasi, Romania*

Introduction: Diabetes mellitus is a systemic disorder associated with inflammation and oxidative stress, targeting kidney, lungs and the vascular system. Zinc is an essential microelement and an antioxidant which was found to be deficient in diabetes mellitus with poor glycemic control. Vascular endothelial growth factor (VEGF) plays a crucial role in angiogenesis and vascular homeostasis. The study investigates the influence of $ZnCl_2$ administration on lung diabetic lesions and VEGF expression.

Materials and Methods: The study was carried out on four groups of 6 adult male Wistar rats, for 8 weeks. The first group received only a 2 mL/kg/day saline solution daily. The second group received on the first day 65 mg/kg streptozotocin (STZ) i.p. in a single dose. The third group received $ZnCl_2$ 5 mg/kg/day i.p. daily. The fourth group received on the first day 60 mg/kg STZ i.p. in a single dose and $ZnCl_2$ 5 mg/kg/day daily. Diabetic rats had fasting blood glucose levels exceeding 250 mg/dL. After eight weeks all animals were anesthetized and were sacrificed. For each lung, 5 sections were stained with HE and Anti-VEGFA antibody (Abcam, 1:200 in PBST) and were examined using a Leica microscope. The extent of lung lesions (fibrosis and neutrophil infiltration) was evaluated semi-quantitative with the following score: 0 = none; 1 <0-25% of the lung (mild severity); 2 = 25-50% of the lung (moderate); 3 >50% of the lung (severe). We used IHC Profiler program for the automated scoring of the intensity and percentage of VEGF positive stained cells. The obtained data were statistically interpreted by ANOVA test.

Results: After 8 weeks the STZ group presented thickening of the alveolar and bronchiolar walls and septal, peribronchiolar and perivascular inflammatory infiltration; also a strong, positive VEGF cytoplasmic expression in the alveolar and bronchial epithelium. $ZnCl_2$ significantly reduced the extent of lung lesions score (2.27 ± 0.43 in the STZ group vs1.92 ± 0.28 in the STZ+ $ZnCl_2$ group, $P < .05$) and the percentage of moderate cytoplasmic stained cells (36.90 ± 4.81 in the STZ group, with a final positive staining score, vs 32.78 ± 3.14 in the STZ+ $ZnCl_2$ group, $P < .05$, with a final positive and low positive staining score).

Conclusions: The obtained results showed that $ZnCl_2$ significantly reduced diabetic lung inflammation and fibrosis and VEGF imunoexpression score. Zinc supplementation may be protective against lung lesions and VEGF-induced angiogenesis in diabetes.

Abstract citation ID: lvag096.602

P493 - LBA_ECE_1189 - Risk factors for post-transplant diabetes mellitus in heart transplant recipients: emphasis on postoperative glycemic control

Rui Zhang, Hongzhao You, Yingying Hu, Yanyan Chen, Jie Huang and Sheng Liu
National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Background and Aim: Post-transplant diabetes mellitus (PTDM) is a common metabolic complication after heart transplantation (HT), yet data on its risk factors, particularly the role of postoperative glycemic control, remain limited. This study aimed to identify predictors of PTDM in HT recipients, with a specific focus on postoperative mean blood glucose (MBG) levels.

Methods: This retrospective cohort study included 305 adult HT recipients without pre-existing diabetes who underwent transplantation at Fuwai Hospital (2015-2020). Patients were categorized by in-hospital MBG: strict (<7.8 mmol/L), moderate (7.8-10.0 mmol/L), or liberal (≥10.0 mmol/L) glycemic control. PTDM was diagnosed according to WHO/ADA criteria. Multivariable logistic regression and restricted cubic spline (RCS) analyses were used to evaluate associations.

Results: Over a 5-year follow-up, PTDM occurred in 130 patients (42.6%). Independent pre-transplant predictors included male sex (OR 2.77, 95% CI 1.34-5.71), higher preoperative HbA1c (OR 1.97, 95% CI 1.02-3.80), and elevated triglyceride levels (OR 2.36, 95% CI 1.26-4.40). RCS analysis showed a linear positive association between MBG and PTDM risk (P overall <.001). Higher MBG remained an independent predictor after multivariable adjustment (OR 1.55, 95% CI 1.16-2.06). Compared with moderate control, liberal glycemic control (MBG ≥10.0 mmol/L) was associated with a significantly increased PTDM risk (OR 2.30-3.39 across models, $P < .05$).

Conclusions: Male sex, adverse preoperative metabolic profiles, and poor postoperative glycemic control independently increase PTDM risk after HT. Liberal glycemic targets (≥10.0 mmol/L) should be avoided to reduce PTDM incidence in patients without pre-existing diabetes.

Abstract citation ID: lvag096.603

P494 - LBA_ECE_1396 - Long-term effects of a protein- and PUFA-rich diet on abdominal adipose tissue after 3 years: results of the NutriAct randomized controlled trial (NutriAct)

Nina Meyer[1,2], Brigitte Weiß[2,3], Charlotte Wernicke[2], Laura Pletsch-Borba[2], Thu Nguyen[2], Elisa Alvarez-Hernandez[2,3,4], Linna Li[2,3,4], Anne Pohrt[5], Michail Lazaratos[2,3], Jürgen MacHann[3,6], Christiana Gerbracht[2], Andreas Pfeiffer[2], Joachim Spranger[2,7] and Knut Mai[2,3,4]
[1]*Department of Endocrinology and Metabolism, Charité—Universitätsmedizin Berlin, Berlin, Germany;* [2]*NutriAct-Competence Cluster Nutrition Research, Berlin-Potsdam, Germany*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[3]German Center for Diabetes Research (DZD), München-Neuherberg, Germany; [4]Department of Human Nutrition, German Institute of Human Nutrition, Potsdam-Rehbruecke, Nuthetal, Germany; [5]Charité—Universitätsmedizin Berlin, Institute of Biometry and Clinical Epidemiology, Berlin, Germany; [6]Institute for Diabetes Research and Metabolic Diseases (IDM) of the Helmholtz Center Munich, Tübingen, Germany; [7]DZHK (German Centre for Cardiovascular Research), Berlin, Germany

Introduction: A reduced visceral and non-visceral adipose tissue (VAT, NVAT) content was reported after 12 months of an isocaloric diet high in proteins and unsaturated fatty acids within the randomized controlled trial NutriACT. This reduction was independent of body weight changes, primarily driven by higher dietary PUFA intake, and led to reduced LDL-cholesterol (LDL).

Objectives: We aimed to investigate whether reductions in VAT/NVAT and associated improvements in cardiometabolic risk markers can be sustained over 36 months and, if so, what factors contribute to this.

Methods: Participants in the intervention group (IG) followed a dietary pattern high in mono-/poly-UFA (15-20%E/10-15%E), plant protein (15-25%E) and fiber (≥30 g/day); the control group (CG) followed standard of care per the German Nutrition Society. MRI-based assessment of VAT/NVAT and metabolic phenotyping were performed at 0, 12 and 36 months. A subgroup of 320 subjects (50-79 years) with MRI data at baseline and at least one follow-up was analyzed. Linear mixed models assessed intervention effects on VAT and NVAT; mediation analyses identified contributing factors.

Results: Marked increases in protein and PUFA intake were achieved within 12 months and maintained through month 36. The intervention significantly affected VAT and NVAT over 3 years ($P = .038$, $P = .003$). In the IG, VAT decreased at 12 months ($P < .001$) but returned to near-baseline levels by 36 months (p t12–t36 = .004, t0–t36 = .919), while NVAT decreased at 12 months ($P = .009$) and remained below baseline at 36 months (p t0–t36 < .001). In the CG, VAT increased from 12 to 36 months ($P = .041$), and NVAT decreased at 12 months ($P < .001$) but stabilized thereafter. Protein and PUFA intake were inversely associated with both VAT and NVAT; fiber intake selectively affected VAT. Total and LDL-cholesterol improved significantly after 12 months in women in the IG but rebounded by 36 months. In men, both markers stabilized after an initial decrease without reaching significance versus baseline.

Conclusions: The intervention had a stronger, more sustained effect on NVAT than on VAT, with VAT returning to near-baseline levels by 36 months. Reductions in both depots were driven by protein and PUFA intake; fiber intake selectively affected VAT. Early cardiometabolic improvements were not maintained long-term, underscoring the need for longer dietary intervention trials to identify strategies for sustainable adipose tissue reduction.

Abstract citation ID: lvag096.604

P495 - LBA_ECE_1275 - ZIP9 links zinc homeostasis to neuroendocrine regulation of reproduction in zebrafish

Rui Wang[1], Ruijuan Xu[1], Rhiannon Boseley[2], Tina Geraki[2], Alexander Morrell[3], Alexander Griffiths[3], Robert Hindges[4], Kim Jonas[1] and Christer Hogstrand[5]

[1]Department of Women & Children's Health, King's College London, London, United Kingdom; [2]Diamond Light Source, Harwell Science and Innovation Campus, Didcot, United Kingdom; [3]London Metallomics Facility, King's College London, London, United Kingdom; [4]Centre for Developmental Neurobiology, King's College London, London, United Kingdom; [5]Department of Analytical, Environmental & Forensic Sciences, King's College London, London, United Kingdom

The zinc transporter ZIP9 has been proposed to function as a membrane androgen receptor; however, its role in endocrine regulation of reproduction remains unclear.

This study aimed to characterise the reproductive phenotype of ZIP9 deficiency in a vertebrate model and define the underlying endocrine and mechanistic basis.

A zebrafish *zip9* knockout line was generated using CRISPR/Cas9. Reproductive performance was assessed in incross and outcross mating pairs, and embryo development was monitored up to 24 hours post-fertilisation (hpf). Expression of key hypothalamic-pituitary-gonadal (HPG) axis genes was analysed by qPCR, and ovarian histology was performed. Metal distribution in larvae was analysed by laser ablation inductively coupled plasma time-of-flight mass spectrometry (LA-ICP-TOF-MS), followed by micro X-ray fluorescence (XRF) imaging and tomography of the head region.

Zip9 knockout zebrafish exhibited reduced growth. While courtship behaviour appeared normal, reproductive output was markedly impaired in females but not males. Crosses involving $zip9^{-/-}$ females showed significantly reduced spawning rates and egg numbers, irrespective of male genotype, whereas $zip9^{-/-}$ males reproduced normally. Female-specific infertility was further evidenced by 100% embryo mortality by 24 hpf, with embryos arrested at the 1-cell stage and reduced chorion size.

Histological analysis revealed ovarian disorganisation with accumulation of early-stage follicles, indicating disrupted folliculogenesis. qPCR analysis demonstrated pronounced, sex-specific dysregulation of HPG axis genes. Key neuroendocrine regulators (*kiss1, kiss2, gnrh2, gnrh3, fshb, lhb*) were suppressed in female brains but elevated in males, with downstream disruption of gonadal gene expression. In addition, hepatic expression of vitellogenin (*vtg*) and oestrogen receptor (*esr1*), essential for yolk formation, was reduced by more than 60%.

LA-ICP-TOF-MS revealed reduced zinc, copper and iron levels in *zip9*-deficient larvae. In wildtype larvae, zinc was enriched in a brain region corresponding to the hypothalamic-pituitary area; this localisation was absent in *zip9* mutants. XRF imaging and tomography confirmed the loss of this distinct zinc distribution, indicating disruption of zinc-dependent neuroendocrine signalling.

ZIP9 is a critical, female-specific regulator of reproductive function. Its loss disrupts ovarian development, impairs yolk formation, and results in complete embryo mortality. The associated sex-specific dysregulation of HPG axis genes, together with loss of zinc patterning in neuroendocrine regions, supports a model in which ZIP9 maintains hypothalamus-pituitary-gonad communication through regulation of zinc distribution, thereby enabling female fertility.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.605

P497 - LBA_ECE_1171 - A pilot trial for phytosomal silymarin plus N-acetyl L-cystein, vitamin E and myo-inositol in prediabetic patients with preclinical liver disease. Focus: risk of liver fibrosis and insulin resistance

Francisco Javier Martinez-Martin[1,2], Sara Andrada-Diaz[3], Borja Santana-Ojeda[1], Inmaculada Molinero-Marcos[1], Claudia Arnas-Leon[1,2], Ricardo Jose de Leon-Durango[1], Alba Hernandez-Lazaro[4], Agnieszka Kuzior[2], Maria del Pino Perez-García[5] and Carmen Acosta-Calero[6]

[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain; [3]Bioksan Naturalmente Juntos, Medical Advisory, Las Palmas de Gran Canaria, Spain; [4]Servei d'Endocrinologia i Nutricio, Sabadell, Parc Taulí Hospital Universitari, Barcelona, Spain; [5]Centro de Salud San Gregorio, Family & Community Medicine, Telde, Las Palmas, Spain; [6]Hospital Universitario de Gran Canaria Doctor Negrin, Cardiology, Las Palmas de Gran Canaria, Spain

Introduction: Silymarin is an extract of the milk thistle (Sylibum marianum) seeds, containing a mixture of flavonolignans (silybinin, isosilybinin, silycristin, silydianin, and others), useful in the treatment of toxic liver damage and as adjunctive therapy in chronic hepatitis and cirrhosis. Recent studies have shown potential benefits of silymarin in the treatment of diabetes mellitus and metabolic liver disease. We conducted a study on the effect of silymarin on insulin sensitivity in prediabetic patients with preclinical liver disease.

Methods: For this open, uncontrolled trial, patients 40-75 years old of both sexes with prediabetes and moderately elevated transaminases or GGT (<3×ULN) were assigned for treatment twice a day for 3 months with a capsule containing SILIPHOS® 180 mg (standardized phytosomal silymarin) plus N-acetyl L-cystein 150 mg, alpha-tocopherol 116 mg (vitamin E) and myo-inositol 50 mg. The main endpoint was the change in the FIB-4 score for the risk of liver fibrosis. Secondary endpoints: change in the HOMA2-IR index (https://dtu.ox.ac.uk/homacalculator), fasting glucose, insulin, HbA1C, and the change of status from prediabetes to normoglycemia or diabetes mellitus. Tertiary endpoints: changes in AST, ALT and GGT. Additional endpoints: changes in BMI, lipid profile, blood pressure and heart rate. Security endpoints: Reported adverse effects and compliance (by questionnaire).

Results: 12 patients were recruited (67% women, age 51.6 ± 8.3 years, BMI 31.2 ± 5.6 kg/m^2). The FIB-4 score was significantly reduced from 1.58 ± 0.56 to 1.25 ± 0.48 ($P = .021$, paired t-test).The HOMA-2 index was significantly reduced from 3.51 ± 0.57 to 2.95 ± 0.46 ($P = .028$, paired t-test). Fasting insulin, but not fasting glucose or HbA1C, was also significantly reduced. 2 patients changed status to normoglycemia but none progressed to diabetes mellitus. AST, ALT and GGT were significantly reduced. BMI, lipid profile, blood pressure and heart rate did not change significantly, but there was a trend for reduced triglycerides and increased HDL-cholesterol. The mean reported compliance was 88% and no serious side effects were reported; no patient withdrew from the study.

Conclusions: The combination (extracts of Silybum marianum, plus N-acetyl L-cystein, alpha-tocopherol and myo-inositol) was well tolerated and able to ameliorate the FIB-4 index and the HOMA-2 IR index of prediabetic patients with preclinical liver damage. Their fasting insulin and the liver enzyme profile was also improved. This combination could be expected to reduce the long term risk of progression to clinical metabolic liver disease and type 2 diabetes in these patients. The limitations of this pilot trial are obvious, but a full-scale trial seems warranted.

Abstract citation ID: lvag096.606

P498 - LBA_ECE_1477 - Very low-dose cyproterone acetate (12.5 mg/day) is effective and well tolerated without increasing hypertension risk in young transgender women

Ricardo Jose de Leon-Durango[1], Inmaculada Molinero-Marcos[1], Borja Santana-Ojeda[1], Claudia Arnas-Leon[1,2], Agnieszka Kuzior[1,2], Irene Hernandez-Hernandez[1,2], Carmen Acosta-Calero[1,3], Alba Hernandez-Lazaro[1,4], Jennifer Maria Perez-Rivero[5] and Francisco Javier Martinez-Martin[1,2]

[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain; [3]Cardiology, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [4]Servei d'Endocrinologia i Nutricio, Parc Taulí Hospital Universitari, Sabadell, Barcelona, Spain; [5]Centro de Salud de Escaleritas, Las Palmas, Spain

Background and Objective: Cyproterone acetate (CPA) is associated with significant adverse effects, including hyperprolactinemia, weight gain, depression, thromboembolic risk, hepatotoxicity, and meningioma, yet its optimal dose remains undefined. CPA has also been linked to an increased risk of hypertension, even at doses as low as 25 mg/day. We aimed to evaluate whether a very low dose of CPA (12.5 mg/day) is effective as an antiandrogen, assess its safety profile, and determine its association with hypertension.

Methods: Transgender women under 30 years of age without prior orchiectomy were offered CPA at 12.5 mg/day instead of the classical standard 50-100 mg/day, in combination with individually titrated estradiol. The CPA dose was increased to 25 mg/day (and up to 50 mg/day if needed) in cases of plasma testosterone >2 nmol/L or clinical hyperandrogenism.

Body weight, blood pressure, AST, ALT, GGT, prolactin, FSH, LH, estradiol, and testosterone were monitored. A historical control group treated with standard-dose CPA (50-100 mg/day) plus estradiol was used for comparison. Hypertension was defined according to current European Society of Hypertension guidelines. All participants provided informed consent.

Results: A total of 198 patients were enrolled, with a median follow-up of 4.9 years. 159 (80.3%) remained on CPA 12.5 mg/day, 15 (7.6%) required escalation to 25 mg/day, and 6 (3.0%) to 50 mg/day; 16 (8.1%) discontinued due to gender-affirming surgery and 2 (1.0%) were lost to follow-up. No serious adverse events or treatment discontinuations due to side effects were observed.

The historical control group included 100 patients with comparable baseline characteristics. Suppression of testosterone, LH, and FSH was effective and comparable between groups. A moderate increase in prolactin was observed (25.2 ± 12.5 to 39 ± 24.2 ng/mL, $P = .003$).

No significant changes in liver enzymes, blood pressure, or body weight were observed in the study group, whereas these

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

parameters increased significantly in the control group. The incidence of hypertension was significantly lower in the low-dose group (4 vs 18 patients, *P*-value = .000002, Odds-Ratio = 0.1032, 95% CI: 0.0357-0.2984).

Conclusions: Very low-dose CPA (12.5 mg/day) was effective and well tolerated as an antiandrogen in most young transgender women. While higher doses are associated with a dose-dependent increase in hypertension risk, this lower dose appears safer. Further studies are needed to confirm these findings.

Abstract citation ID: lvag096.607

P499 - LBA_ECE_1127 - Mopal-27 attenuates hepatic fibrosis through FGF-21–mediated endocrine signaling

Hye In An and Hyo-Jong Lee
Sungkyunkwan University, School of Pharmacy, Suwon-si, Gyeonggi-do, South Korea

Fibroblast growth factor-21 (FGF-21) is a liver-derived endocrine hormone that plays a central role in systemic metabolic stress adaptation and hepatic homeostasis. Increasing evidence indicates that FGF-21 exerts protective effects against chronic liver injury and fibrogenesis, key processes driving the progression of hepatic fibrosis. Hepatic fibrosis, characterized by excessive extracellular matrix deposition, represents a critical pathological stage leading to cirrhosis and liver failure. However, the antifibrotic potential of Mopal-27, a plant-derived alkaloid isolated from *Loganiaceae* seeds, and its relevance to endocrine-mediated metabolic regulation remain unclear.

In this study, Mopal-27 suppressed α-smooth muscle actin (α-SMA) expression in human hepatic stellate cells (LX-2), indicating inhibition of stellate cell activation. In a thioacetamide (TAA)-induced mouse model of hepatic fibrosis, Mopal-27 administration markedly attenuated fibrotic pathology, accompanied by reduced expression of fibrosis-associated markers including α-SMA, vimentin, and collagen type I. In parallel, inflammatory responses were diminished, as evidenced by decreased levels of IL-6 and TNF-α and reduced infiltration of F4/80-positive macrophages in liver tissue. Notably, Mopal-27 treatment induced a dose-dependent increase in hepatic FGF-21 expression.

Collectively, these findings suggest that Mopal-27 alleviates hepatic fibrosis by suppressing stellate cell activation and inflammatory responses, potentially through induction of FGF-21–mediated endocrine signaling pathways. These results highlight Mopal-27 as a promising therapeutic candidate targeting the metabolic–endocrine axis in fibrotic liver disease.

Abstract citation ID: lvag096.608

P500 - LBA_ECE_1111 - Evaluation of the association between metabolic and hepatic markers and diabetic retinopathy in patients with type 2 diabetes mellitus

Irem Sonmezoglu Kutuk[1], Sena Cetin[2], Benay Karabulut[3], Sabri Engin Altıntop[4], Huseyin Baran Ozdemir[3] and Altinova Alev[1]
[1]*Department of Internal Medicine, Division of Endocrinology and Metabolism, Gazi University Faculty of Medicine, Ankara, Türkiye;* [2]*Department of Internal Medicine, Gazi University Faculty of Medicine, Ankara, Türkiye;* [3]*Department of Ophthalmology, Gazi University Faculty of Medicine, Ankara, Türkiye;* [4]*Ankara, Türkiye*

Objective: In recent years, non-invasive hepatic injury markers associated with metabolic dysfunction-associated fatty liver disease (MAFLD) have been suggested to reflect systemic inflammation and metabolic burden, and therefore may have a role in predicting diabetic microvascular complications. In this study, we aimed to evaluate the relationship between hepatic injury and fibrosis markers as well as atherogenic lipid indices with the presence and severity of diabetic retinopathy in patients with type 2 diabetes mellitus.

Methods: A total of 209 patients with type 2 diabetes mellitus were included in the study. Diabetic retinopathy was classified based on ophthalmological evaluation as no retinopathy, non-proliferative diabetic retinopathy (NPDR), and proliferative diabetic retinopathy (PDR). Metabolic and hepatic markers evaluated included LDL/HDL cholesterol ratio, non-HDL cholesterol, atherogenic index of plasma (AIP), triglyceride-glucose (TyG) index, AST/ALT ratio, and FIB-4 score. Additionally, age, duration of diabetes, and HbA1c levels were recorded.

Results: Among the 209 patients, 95 (57.2%) had no diabetic retinopathy, while 39 (23.5%) had NPDR and 32 (19.3%) had PDR. Group comparisons demonstrated significant differences in LDL/HDL ratio ($P < .001$), non-HDL cholesterol ($P < .001$), AIP ($P = .003$), TyG index ($P = .010$), AST/ALT ratio ($P = .002$), and FIB-4 score ($P = .019$). Significant positive correlations were found between retinopathy presence and severity and age ($r = 0.429$, $P < .001$), diabetes duration ($r = 0.229$, $P < .001$), and HbA1c ($r = 0.219$, $P = .001$). Among metabolic indices, LDL/HDL ratio ($r = 0.346$, $P < .001$), non-HDL cholesterol ($r = 0.271$, $P < .001$), AIP ($r = 0.242$, $P < .001$), and TyG index ($r = 0.239$, $P = .001$) were found to be associated with retinopathy. AST/ALT ratio ($r = 0.238$, $P < .001$) and FIB-4 score ($r = 0.151$, $P = .029$) also showed significant associations with retinopathy.

Conclusions: FIB-4 score, AST/ALT ratio, and atherogenic lipid profile were found to be associated with diabetic retinopathy in patients with type 2 diabetes mellitus. In particular, the association of the LDL/HDL ratio with both the presence and severity of retinopathy suggests that metabolic dyslipidemia may play a role in the development and progression of diabetic retinopathy.

Abstract citation ID: lvag096.609

P501 - LBA_ECE_1260 - Androgen sensitivity and hypogonadotropic hypogonadism correlate differently and independently with cardiovascular risk in severe obesity

Biagio Cangiano[1,2,3], Alessandro Chilà[4], Ilaria Gentile[1], Gabriele Pogliaghi[5], Alice Casiraghi[4], Alessandro Amodeo[1], Nicoletta Del Duca[1], Alessandra Milesi[1], Stefania Mai[1], Ilinka Garavaglia[4], Valeria Vezzoli[1], Luca Persani[1,4], Massimo Scacchi[1] and Marco Bonomi[1,4]
[1]*Division of Endocrine and Metabolic Diseases, Istituto Auxologico Italiano IRCCS, Milan, Italy;* [2]*Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy;* [3]*Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy;* [4]*Seregno, Italy;* [5]*Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Androgen activity has been variably associated with cardiovascular disease (CVD) in the literature. Obesity is known to be linked to both hypogonadism and an increased risk of CVD. However, evidence regarding the relationship between increased androgen sensitivity and CVD remains heterogeneous and inconclusive.

Objective: To evaluate, in a large cohort of patients with severe obesity: (I) the length of CAG repeats in the androgen receptor (AR) gene, as a marker of androgen sensitivity, as compared with the general population; and (II) the potential association between gonadal function and androgen sensitivity with CVD.

Methods: A total of 163 adult male patients (age >18 years) with severe obesity (BMI > 35 kg/m^2) were consecutively enrolled in a cross-sectional observational study. Clinical history was collected for each participant, and gonadal function was assessed by calculating free testosterone (cFT) and measuring gonadotropin levels.

Hypogonadism was defined as persistent cFT <225 pmol/L and classified as hypogonadotropic (HH) or hypergonadotropic based on LH levels (cut-off ≤9.4 IU/L). Androgen receptor sensitivity was evaluated by analyzing the length of CAG repeats in the AR gene, using PCR amplification followed by DNA fragment analysis. Androgen sensitivity was categorized as reduced (>24 CAG repeats), intermediate (21-24 repeats), or increased (<21 repeats).

Funded by the European Union—Next Generation EU—NRRP M6C2—Investment: 1.3.2, Sub-investment 1.3.2.3.3. CUP E43C25005270001

Results: Chi-square analysis assessing androgen sensitivity revealed a significantly higher frequency of AR gene CAG repeats <21 ($P < .0001$) in our cohort, indicating greater androgen sensitivity than the general population. Logistic regression analysis investigating the association between CVD with gonadal function and androgen sensitivity demonstrated an independent association with both a lower number of CAG repeats ($P = .037$) and the presence of HH ($P = .041$), after adjustment for age, BMI, arterial hypertension, type 2 diabetes mellitus, obstructive sleep apnea (OSA), and smoking history (pack-years).

Conclusions: We report, for the first time, a higher prevalence of increased androgen sensitivity in patients with severe obesity compared with the general population. Moreover, both increased androgen sensitivity and, conversely, the presence of HH are independently associated with CVD, suggesting the involvement of distinct pathogenic mechanisms: on the one hand, higher androgens are a known risk factor for CVD; on the other, HH may reflect an underlying systemic inflammatory state capable of exerting deleterious effects on both the cardiovascular system and the central regulation of the hypothalamic-pituitary-gonadal axis.

Abstract citation ID: lvag096.610

P502 - LBA_ECE_1380 - Dual targeting of the HSP70–HSP90 chaperone axis in adrenocortical carcinoma: a novel inhibitor induces G1 arrest and multi-pathway collapse beyond mitotane

Adnan Batman[1], Ezgi Nurdan Yenilmez Tunoğlu[2], Irfan Koca[3], Merve Al[4] and Yusuf Tutar[5]
[1]*Endocrinology and Metabolism, Altunizade Acibadem Hospital, Istanbul, Türkiye;* [2]*Division of Medical Techniques and Services, Demiroglu Science University, Vocational School of Health Services, Şişli, Türkiye;* [3]*Department of Chemistry, Department of Chemistry, Bozok University, Yozgat, Türkiye;* [4]*Istanbul, Türkiye;* [5]*Department of Chemistry, Department of Basic Pharmaceutical Sciences, Recep Tayyip Erdogan University, Istanbul, Türkiye*

Background: Adrenocortical carcinoma (ACC) remains a highly aggressive malignancy with limited therapeutic options, and mitotane provides only modest benefit. Heat shock proteins HSP90 and HSP70 play a significant role in regulating oncogenic protein stability and resistance to apoptosis together. We hypothesised that by targeting the HSP70 and HSP90 chaperone axis simultaneously, the survival networks of tumours could be more fully disrupted compared to a single target strategy.

Materials and Methods: NCI-H295R cells were gradually treated with increasing mitotane and a dual HSP70/HSP90 inhibitor over 48 hours. To assess their viability, cell viability was measured using MTT analysis, and the IC50 value was determined. Apoptosis was measured using Annexin V-PE/7-AAD flow cytometry, and cell cycle distribution was analyzed using Muse™ assays. Gene expression changes were measured using qPCR, and pathway enrichment was analysed for this paper.

Results: The dual HSP70/HSP90 inhibitor showed much better cytotoxic activity than mitotane, resulting in a lower IC50 (3.21 ± 0.03 μM vs 6.96 ± 0.03 μM, $P < .001$). Later apoptosis was much more likely to occur and was of greater magnitude in mitotane treatment compared to that of the HSP70-HSP90 inhibitor. The single chaperone-targeted and inhibitor-targeting mechanism was explained by protein expression profiles at the molecular level, showing that HSP inhibition led to more upregulation of MAPK signaling (MAP2K1 and MAP2K3), cell cycle progression (CDC20, TBX2), GPD2 modulation, angiogenesis (ANGPT1, FOXC2 and SNAI1), and epithelial-mesenchymal transition for cells. The pathways were shown to have been significantly disrupted, specifically the PI3K-Akt and MAPK signalling networks, due to the global destabilization of the client proteins via the HSP70-HSP90 activation axis. This pattern is consistent with a multi-pathway regulatory role of HSP chaperone systems in ACC biology.

Conclusions: Dual inhibition of the HSP70–HSP90 chaperone axis exerts superior antitumor effects than mitotane by inducing multilayered disruption of survival signalling, cell cycle progression, and stress adaptation. This strategy represents a promising next-generation therapeutic approach in ACC and supports further translational development.

Abstract citation ID: lvag096.611

P503 - LBA_ECE_1463 - Anti-Müllerian hormone as a marker of gonadotropic–androgenic interaction during female development

Mariola Krzyścin[1], Anna Paczkowska[2] and Elżbieta Sowińska-Przepiera[1]
[1]*Szczecin, Poland;* [2]*Police, Poland*

Background: The interpretation of anti-Müllerian hormone (AMH) in paediatric and adolescent populations remains uncertain, as its clinical use is largely extrapolated from adult ovarian reserve models. This study aimed to define age-dependent endocrine correlates of AMH across female development, with particular focus on pubertal maturation.

Methods: A retrospective cross-sectional study included 238 females from late infancy to early adulthood undergoing routine

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

endocrine assessment. Participants were stratified by developmental stage. Associations between AMH and gonadotropins (LH, FSH, LH/FSH ratio), androgens, estradiol and selected endocrine parameters were analysed using Spearman correlation. In adolescents, receiver operating characteristic (ROC) analysis was performed using an AMH threshold of 30 pmol/L.

Results: AMH demonstrated stage-dependent associations with hormonal parameters. In early life, AMH was inversely correlated with FSH, most strongly in toddlerhood ($\rho = -0.70$, $P = .0001$) and early childhood ($\rho = -0.30$, $P = .04$), consistent with preserved ovarian–pituitary feedback. During adolescence, the association profile shifted, with positive correlations between AMH and LH ($\rho = 0.30$, $P = .03$) and androstenedione ($\rho = 0.50$, $P = .02$). Adolescents with AMH ≥30 pmol/L showed a higher LH/FSH ratio ($P = .004$) and increased androstenedione levels ($P = .01$), alongside lower total testosterone ($P = .009$). ROC analysis demonstrated the highest discriminatory performance for androstenedione (AUC = 0.78, $P < .01$), followed by LH/FSH ratio and total testosterone (both AUC = 0.70, $P < .05$).

Conclusions: AMH reflects distinct, age-dependent endocrine patterns in females. In adolescence, elevated AMH is associated with LH-dominant gonadotropic activity and increased androgen production, particularly androstenedione, supporting its interpretation as a marker of functional endocrine phenotype rather than ovarian reserve alone.

Abstract citation ID: lvag096.612

P504 - LBA_ECE_1079 - Evaluation of metabolic parameters and glucose dynamics before and after parathyroidectomy in patients with primary hyperparathyroidism

Ece Seçgin Demir[1,2], Müge Yılmaz[1], Büşra Kanbur[1], Mehmet Dönmez[1], Ziya Mithat Bıyıklı[1], Naile Gokkaya[1], Serhat Özçelik[1] and Kadriye Aydin[1]

[1]Department of Endocrinology and Metabolism, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye; [2]Endocrinology and Metabolism, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Türkiye

Objective: Primary hyperparathyroidism (PHPT) is frequently accompanied by metabolic disturbances, including impaired glucose tolerance and dyslipidemia. The prevalence of diabetes mellitus in PHPT is approximately three times higher than in the general population, and nearly 40% of patients exhibit impaired glucose tolerance. Elevated intracellular calcium levels reduce insulin-stimulated glucose transport, thereby increasing insulin requirements. This study aimed to investigate the effects of parathyroidectomy on glucose metabolism, insulin dynamics, and lipid profile in patients with PHPT.

Methods: We retrospectively reviewed 45 PHPT patients who underwent parathyroidectomy between 2014 and 2024. All patients had normal renal and thyroid function and demonstrated normalized parathyroid function postoperatively. Preoperative and one-year postoperative levels of parathyroid hormone (PTH), calcium, phosphorus, 24-hour urinary calcium, 2-hour oral glucose tolerance test (OGTT), total cholesterol, triglycerides, HDL, LDL, HbA1c, and HOMA-IR were analyzed. Paired comparisons and correlation analyses were conducted to assess postoperative changes and their associations with biochemical parameters.

Results: Postoperatively, PTH, serum calcium, 24-hour urinary calcium, total cholesterol, and LDL levels significantly decreased, whereas phosphorus, HbA1c, and OGTT 60-minute glucose levels significantly increased. Other OGTT glucose values and the 90-minute insulin showed non-significant increases. Preoperative PTH were weakly positively correlated with changes in fasting insulin ($r_s = 0.352$, $P = .041$) and moderately positively correlated with fasting glucose changes ($r_s = 0.407$, $P = .017$). Greater reductions in PTH were moderately negatively correlated with increases in fasting glucose ($r_s = -0.424$, $P = .014$). Decreases in serum calcium were weakly negatively correlated with OGTT 30-minute glucose increases ($r_s = -0.352$, $P = .048$), whereas rises in phosphorus were weakly negatively correlated with OGTT 90-minute insulin ($r_s = -0.364$, $P = .041$) and moderately negatively correlated with HbA1c ($r_s = -0.460$, $P = .031$).

Conclusions: Parathyroidectomy may improve glucose tolerance and insulin dynamics in some PHPT patients, although this effect is not universal. Variability may relate to disease severity and diagnostic delay. Postoperative deterioration in postprandial glycemia may reflect these factors. Higher preoperative PTH is associated with more adverse postoperative glucose and insulin outcomes, whereas greater postoperative PTH reduction mitigates fasting glucose deterioration. Modifications in calcium and phosphorus levels may further support metabolic improvement. Early and effective surgical intervention may prevent worsening of glucose and insulin dynamics and improve lipid profiles. Patients with PHPT should undergo regular monitoring for impaired glucose tolerance, diabetes mellitus, and dyslipidemia.

Keywords diabetes mellitus, dyslipidemia, insulin resistance, parathyroidectomy, primary hyperparathyroidism

Abstract citation ID: lvag096.613

P506 - LBA_ECE_1262 - Circulating metabolic profiling in severe obesity represents a new potential biomarker to predict weight loss after bariatric surgery

Chiara Lepri[1], Valentina Balloni[2], Arianna Propato[1], Giorgio Crocetti[3], Giovanni Quartararo[3], Andrea Bernini[2], Michaela Luconi[1] and Giulia Cantini[1,4,5]

[1]Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy; [2]Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Siena, Italy; [3]Department of Surgery, General and Bariatric Surgery Unit, Santa Maria Nuova Hospital, Florence, Italy; [4]University of Florence, Florence, Italy; [5]University of Florence, Florence, Italy

The global prevalence of severe obesity is exponentially increasing worldwide, representing one of the most serious and rapidly growing health problems, alongside with its comorbidities such as type 2 diabetes (T2DM) and cardiovascular disease (CVD).

Bariatric surgery is the elective treatment for patients with body mass index (BMI) greater than 40 kg/m^2 or BMI of 35-40 kg/m^2 in combination with comorbidities, as it leads to a rapid and significant weight loss, resulting in a marked improvement of comorbidities and a reduction of long-term obesity-related mortality.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

However, bariatric surgery does not always result in the expected excess weight loss (EWL) in severely obese patients, making it necessary to identify new prognostic markers in order to predict weight regain and/or improvement in metabolic parameters.

In the present study, we applied untargeted metabolomic based on nuclear magnetic resonance (NMR) spectroscopy to compare the metabolic profiles in serum samples of twenty severely obese patients before and after bariatric surgery (BMI 45.0 ± 6.6 vs 29.6 ± 5.2, $P < .0001$, respectively) as well in paired subcutaneous (SAT) and visceral adipose tissue (VAT) biopsy.

Our analysis revealed that patients affected by severe obesity were characterized by a significant dysregulation of several metabolites associated with lipid metabolism, such as ketone bodies (acetone, 3-hydroxybutyrate, and acetate) and short chain fatty acids (SCFA), and a significant upregulation of metabolites associated with the purine salvage pathway (hypoxanthine and inosine) compared with healthy lean subjects (FC: 13.3 ± 7.4, $P < .0001$; FC: 10.0 ± 6.7, $P < .0001$, respectively).

Parallel RNASeq analysis of patients' SAT and VAT specimens taken before and after bariatric surgery identified the possible cellular pathways that support the NMR results.

Changes in the metabolic profile of circulating and adipose tissue-specific small molecules in patients with severe obesity after bariatric surgery could provide insights into the molecular mechanisms underlying systemic and regional metabolic dysregulations characterizing this pathology and allow prediction of response to bariatric surgery.

Understanding these pathways may offer novel targets to help non-responders patients achieve the EWL in order to prevent the development of comorbidities and their consequences.

Abstract citation ID: lvag096.614

P507 - LBA_ECE_1354 - Association between serum testosterone levels and calcium oxalate stone formation: a propensity score–matched case–control study

Suzy Park[1] and Junho Lee[2]
[1]Cardiff University, Cardiff, United Kingdom; [2]Seoul, South Korea

Introduction: Calcium oxalate (CaOx) stones constitute roughly 70-80% of urinary calculi and are twice as prevalent in men, implying an androgenic influence on lithogenesis. Laboratory data demonstrate that testosterone accelerates CaOx crystallisation, whereas anti-androgenic agents inhibit it, yet clinical confirmation remains limited. The objective of this study was to assess the association between serum testosterone and calcium oxalate stone formation, adjusting for metabolic factors.

Methods: We conducted a retrospective case–control study at a single teaching hospital. Cases were male patients who underwent surgical removal of proven CaOx stones between January 2024 and April 2025 ($n = 44$). Potential controls were 2925 men who, during health screening from 2010 to 2024, showed no renal stones on ultrasonography and had complete metabolic panels, including total testosterone. Propensity scores were calculated from age, body-mass index, systolic and diastolic blood pressure, serum triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and uric acid. A 1:5 nearest-neighbour match without replacement yielded 220 controls. Total testosterone was compared with the Mann-Whitney U test; biochemical hypogonadism (<3.5 nmol/L) was analysed with χ^2 tests and expressed as odds ratios (ORs, 95% CI).

Results: Among 44 men with confirmed CaOx stones and 2925 potential controls without stones, CaOx stone formers were significantly older and had significantly lower HDL-C and LDL-C than controls prior to propensity score matching. Median total testosterone level was significantly lower in stone formers (3.6 vs 4.7 nmol/L, $P < .001$), and biochemical hypogonadism ($T < 3.5$ nmol/L) was more common (47.7% vs 22.4%, $P < .001$). Propensity score matching based on demographic and metabolic factors yielded 220 matched controls (1:5 ratio), eliminating baseline differences, including age (58.5 vs 60.0 years, $P = .981$) and BMI (25.4 vs 24.8 kg/m^2, $P = .492$). After matching, testosterone level remained significantly lower in CaOx stone formers (3.6 vs 4.3 nmol/L, $P = .018$), and hypogonadism ($T < 3.5$ nmol/L) remained more prevalent (47.7% vs 25.0%, $P = .003$). The matched OR for hypogonadism in CaOx stone formers was 2.74 (95% CI 1.41-5.33).

Conclusions: After adjustment for confounders, men with CaOx stones displayed substantially lower serum testosterone and nearly a three-fold higher likelihood of biochemical hypogonadism. These findings link androgen deficiency to CaOx lithogenesis and support that hormonal modulation could become a preventive or adjunctive strategy in recurrent stone disease. Prospective longitudinal studies targeting androgen pathways are warranted to clarify causality and therapeutic potential.

Abstract citation ID: lvag096.615

P508 - LBA_ECE_1052 - Long term neuropsychological evaluation of adults' patients with craniopharyngioma

Julie Guillotin[1], Charlotte Planchon[1], Julien Engelhardt[1], Edouard Gimbert[1], Thomas Cuny[2], Antoine Tabarin[1] and Blandine Gatta-Cherifi[1]
[1]CHU de Bordeaux, Pessac, France; [2]APHM, Marseille, France

Introduction: Neurocognitive function has been studied primarily in children and in patients diagnosed during childhood after treatment of craniopharyngioma. Long-term data in adults are scarce. We report long term neurocognitive outcomes in adult patients treated for craniopharyngioma

Patients and Methods: The sample included adult patients with a history of craniopharyngioma treated at least 5 years earlier that had been invited for a neuropsychological evaluation. Comorbidities impairing cognitive function (eg stroke sequelae, Parkinson's disease), language barrier preventing neuropsychological testing, age >75 years were exclusion criteria.

All assessments were performed by the same neuropsychologist in the neurosurgery department. The battery included standardized tests.

Results: Twenty-two patients (14 women, mean age of 46 ± 12 years mean interval since the last treatment was 15 ± 7 years) went through neuropsychological evaluation. Six patients (27%) were diagnosed during childhood (<18 years) and 16 (73%) in adulthood.

In the whole group, sixteen patients (73%) reported excessive fatigue, including 10 with mild-to-moderate fatigue and 5 with severe fatigue. The Stroop Grefex test (cognitive inhibition) was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

abnormal in 15 patients (68%) and borderline in 4 (18%). The Revised Commission test (organizational abilities) was abnormal in 15 patients (68%) and borderline in 2 (9%).

The Trail Making Test Part B (TMT-B) was impaired in 8 patients (36%), and Part A (TMT-A) in 6 (27%).

The results were very similar when we considered only patients with a craniopharyngioma diagnosed during adulthood.

These findings translated into a high need for supportive care, with half of the patients referred for additional interventions such as speech therapy or psychological counseling.

Discussion and Conclusions: The present study demonstrates that adult survivors face long-term neuropsychological sequelae, many years after treatment, that need specific care. Recent guidelines emphasize the need for systematic neuropsychological follow-up in craniopharyngioma and our findings strongly support this recommendation.

Abstract citation ID: lvag096.616

P509 - LBA_ECE_1035 - Protective effects of the GHRH agonist MR-409 in experimental models of amyotrophic lateral sclerosis

Francesca Pedrolli[1], Carola Torazza[2], Iacopo Gesmundo[1], Tiziana Bonifacino[2], Roberta Schellino[3], Federica La Rocca[3], Federica Bistolfi[1], Chiara Perotti[1], Wei Sha[4], Medhi Wangpaichitr[4], Marina Boido[3], Antonia Ratti[5], Andrew V. Schally[4], Marco Milanese[2] and Riccarda Granata[6]

[1]Department of Medical Sciences, University of Turin, Turin, Italy; [2]Department of Pharmacy (DIFAR), University of Genoa, Genoa, Italy; [3]Department of Neurosciences "Rita Levi Montalcini", University of Turin and Neuroscience Institute Cavalieri Ottolenghi, Turin, Italy; [4]Miami VA Healthcare System, Endocrine and Polypeptide Institute, Miami, FL, United States; [5]Department of Neuroscience, IRCCS Istituto Auxologico Italiano and Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [6]Department of Molecular Biotechnology and Health Sciences, University of Turin, Turin, Italy

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder characterized by progressive upper and lower motor neuron (MNs) loss, skeletal muscle atrophy, neuroinflammation, and mitochondrial dysfunction. Despite extensive research, effective disease-modifying therapies remain limited. Growth hormone-releasing hormone (GHRH), beyond its role in stimulating pituitary growth hormone (GH) secretion, exerts several peripheral actions, including promotion of cell survival and proliferation. Notably, both GHRH and its agonistic analog MR-409 have demonstrated neuroprotective and anti-inflammatory effects in experimental models of ischemic stroke, spinal muscular atrophy, and Alzheimer's disease. However, the role of GHRH in ALS has yet to be elucidated. Therefore, this study investigated the potential protective effects of GHRH and MR-409 in both *in vivo* and *in vitro* ALS models. Male and female wild-type (WT) and $SOD1^{G93A}$ transgenic ALS mice received daily subcutaneous treatment with MR-409 (0.8 mg/kg) or vehicle. For behavioral studies, a longitudinal cohort was treated from postnatal day 70 until sacrifice at the humane endpoint ($n = 8$ females, $n = 11$ males), whereas a separate cohort was treated from day 70 to day 100 for *ex vivo* molecular and histopathological analyses ($n = 5$ females, $n = 5$ males). In female $SOD1^{G93A}$ mice, MR-409 increased body weight, improved motor function, and showed a positive survival trend, with no effects in males. In the spinal cord, MR-409 counteracted MN loss and reduced IL-1β and GFAP mRNA levels in both sexes. In skeletal muscle, we observed attenuated atrophy in females accompanied by reduced expression of the atrophy-related markers MuRF1 and atrogin-1 in both sexes. *In vitro*, GHRH and MR-409 were tested in human SH-SY5Y neuroblastoma cells and iPSC-derived MNs from TARDBP-mutant ALS patients exposed to sodium arsenite to induce mild chronic oxidative stress. In SH-SY5Y cells, GHRH (5 μM) and MR-409 (1 μM) prevented sodium arsenite-induced UNC13A cryptic exon retention and reduced p62 accumulation. Consistently, preliminary results in iPSC-derived MNs showed that GHRH counteracted the sodium arsenite-induced reduction of UNC13A. Overall, these findings suggest a neuroprotective role for GHRH agonists in ALS.

ePoster Presentations

Abstract citation ID: lvag096.617

EP1 - ECE_2238 - Severe orthostatic hypotension due to hyporeninemic hypoaldosteronism in a woman with diabetic autonomic neuropathy: challenges in management

Nehan Shakeel[1,2,3], Hafiz Sohail[3,4], Shakil Qamar[5] and Ma Pyeh Kyithar[5,6,7]

[1]Diabetes & Endocrinology Department, Midland Regional Hospital Portlaoise, Ireland; [2]Diabetes & Endocrinology, Portlaoise, Ireland; [3]College of Physicians and Surgeons Pakistan, Islamabad, Pakistan; [4]Portlaoise, Ireland; [5]Diabetes & Endocrinology Department, Midland Regional Hospital Portlaoise, Ireland Portlaoise, Ireland; [6]School of Medicine, Trinity College Dublin, Ireland; [7]Dublin, Ireland

Orthostatic hypotension is an under-recognized presentation of diabetic neuropathy. Hyporeninemic hypoaldosteronism, classically associated with diabetic nephropathy, may also occur in individuals with autonomic dysfunction and contribute to severe symptomatic orthostatic hypotension.

We report a case of a 39-year-old woman with a 5-year history of poorly controlled type 1 diabetes mellitus due to non-concurrence with insulin therapy (HbA1c 172 mmol/mol). She presented to Emergency Department with significant urinary retention. Further investigations with MRI lumbosacral spine, urology review and urodynamic studies showed neurogenic bladder secondary to diabetic autonomic neuropathy. Additionally, she was found to have severe, painful peripheral neuropathy. Three months following her first admission, the patient re-presented with a six-day history of progressive dizziness, lightheadedness, and near-syncope upon standing. Symptoms were most pronounced in the morning and improved when supine. Physical examination revealed a supine blood pressure of 125/80 mmHg, which decreased to 60/30 mmHg on standing, accompanied by an increase in heart rate from 89 to 119 bpm—findings consistent with severe orthostatic hypotension. Neurological and systemic examinations were otherwise unremarkable. Recent medication changes included initiation of ramipril (1.25 mg daily) and duloxetine (60 mg daily for peripheral neuropathic pain) two weeks before presentation.

Diagnostic work-up excluded adrenal insufficiency, as indicated by a morning cortisol level (344 nmol/L) and short synacthen test (0-minute cortisol: 462 nmol/L; 30-minute cortisol:

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

873 nmol/L). There was no evidence of diabetic nephropathy as urine ACR and renal function were normal and corticomedullary differentiation was intact on renal ultrasound. Further evaluation revealed a low renin level (2.0 pg/mL), undetectable aldosterone (<26 pg/mL) and a non-calculable aldosterone-to-renin ratio due to the absence of measurable aldosterone. In the context of suboptimal glycemic ranges with autonomic and peripheral neuropathies, hyporeninemic hypoaldosteronism was determined to be a key factor contributing to severe orthostatic hypotension.

Management included intravenous fluid administration and discontinuation of potentially exacerbating medications (ramipril and duloxetine). Midodrine was initiated and titrated up to 10 mg three times daily, with the addition of fludrocortisone. Peripheral neuropathic pain was managed with low-dose gabapentin and topical therapies. The patient demonstrated substantial clinical improvement with resolution of postural symptoms within three days.

This case highlights hyporeninemic hypoaldosteronism as a significant contributor to severe orthostatic hypotension in individuals with diabetic autonomic neuropathy. Pharmacological agents such as ACE inhibitors and SNRIs may exacerbate orthostatic hypotension in susceptible patients. Early recognition and tailored management of orthostatic symptoms with midodrine and fludrocortisone can lead to marked symptomatic improvement and enhanced quality of life.

Abstract citation ID: lvag096.618

EP2 - ECE_3553 - Hypokalemia metabolic alkalosis—could this be Cushing's syndrome?

Khurram Qayyum, Muhammad Masroor Amjad, Muhammad Haroon Riasat, Sega Pathmanathan, Rehmat Karim and Najeeb Shah
Hull University Teaching Hospitals NHS Trust, Hull, United Kingdom

Cushing's syndrome is a rare but serious endocrine disorder with a diverse clinical presentation, often posing diagnostic challenges, particularly in ACTH-dependent cases. Severe metabolic abnormalities such as hypokalaemia may provide important clues to an ectopic source, even when classical clinical features are absent or imaging findings are equivocal.

We present a case of a 64-year-old female with a background of hypothyroidism who presented with weakness, lethargy, difficulty climbing stairs, and intermittent blurred vision for 2 weeks. Clinically, she was hypertensive with proximal myopathy and easy bruising, without classical cushingoid features. Biochemistry revealed severe metabolic alkalosis (Ph 7.72 and bicarbonate 38.5 mmol/L) and persistent hypokalaemia (lowest, 2.1 mmol/L). Two 24-hour urinary free cortisol measurements were markedly elevated at 11 710 and 17 014 nmol (normal 0–165), and cortisol failed to suppress following 1 mg overnight dexamethasone suppression testing (>1650 nmol/L). ACTH was elevated at 64 ng/L, confirming ACTH-dependent Cushing's syndrome.

Although the ACTH levels were mildly elevated which would usually suggest a central source, the onset, severity of hypokalaemia and absence of cushingoid features suggested ectopic ACTH secretion. Pituitary MRI demonstrated a 4 mm are with slight enhancement, but this was considered equivocal. CT imaging of the thorax, abdomen, and pelvis revealed a small hyperattenuating right pericardial lesion and a non-specific pancreatic finding, with no definite tumour identified. Whole-body FDG-PET showed mild uptake in the para-mediastinal pleural lesion abutting the right heart border; however, octreotide scanning was negative. Neuroendocrine markers, including chromogranin A and urinary 5-HIAA, were normal.

Medical management with antihypertensives including spironolactone, and metyrapone was initiated to control hypercortisolaemia. Following multidisciplinary discussion (MDT) within endocrinology and the respiratory team, the para-mediastinal lesion was deemed to be the most likely ectopic source. The patient underwent bronchoscopy and right video-assisted thoracoscopic surgery. A lesion was identified in the right middle lobe which was excised. Histology confirmed a completely excised atypical carcinoid tumour (pT2 Nx) with Ki-67 of 10%. Pre-operatively, metyrapone was discontinued and hydrocortisone replacement commenced peri-operatively to prevent adrenal insufficiency on removal of the lesion.

Following surgery, the patient experienced significant symptomatic improvement with normalisation of her biochemistry. Hydrocortisone is being weaned off. She will be followed up closely to pick up recurrence in view of a high Ki-67 index. This case underscores the importance of integrating biochemical findings, clinical features, and MDT input in the evaluation of ACTH-dependent Cushing's syndrome, particularly when imaging results are inconclusive.

Abstract citation ID: lvag096.619

EP3 - ECE_3361 - Accuracy and clinical utility of founder mutation testing for familial hypercholesterolemia in Finnish population

Antti Jokiniitty and Saara Metso
Endocrinology, Tampere University Hospital, Tampere, Finland

Background: In Finland, due to a founder effect, seven pathogenic variants are estimated to account for approximately 80% of the genetic spectrum of Familial Hypercholesterolemia (FH). National current care guidelines recommend these founder variants be tested in patients with probable or definite FH according to the Dutch Lipid Clinic Network Criteria (DLCNC). If testing is negative but clinical suspicion remains high, broader genetic testing is advised. However, the clinical characteristics of patients referred for founder mutation testing and its diagnostic yield are not well defined. With the increasing availability of next-generation sequencing (NGS), the optimal testing strategy should be reassessed to improve variant detection and guide best practice.

Aims: To evaluate clinical characteristics, family history, and FH probability (based on DLCNC) of patients referred for FH founder mutation testing in the Pirkanmaa Health Services region, Finland (2000–2024); to assess the proportion of positive founder-mutation results; and to determine the proportion of patients with negative founder testing underwent broader genetic evaluation and were diagnosed with a pathogenic FH variant.

Methods and Results: We performed a retrospective analysis of 1126 patients referred for FH founder variant testing between 2000 and 2024. Clinical and genetic data were collected from electronic health records.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Testing was conducted as cascade screening in 37 patients with a known familial FH founder mutation and in 1089 unrelated patients. A positive FH variant was detected in 67.6% of those with a known familial mutation and 1.5% of those without.

Out of founder mutation–negative patients, 121 underwent extended genetic testing, revealing an FH variant in 9.9%.

Based on DLCNC clinical classification, FH variant prevalence was 64.3% in patients with definite FH, 10.7% in probable FH, 2.7% in possible FH, and 1.2% in unlikely FH categories.

Overall, 137 patients had premature atherosclerotic cardiovascular disease (ASCVD) and 989 did not; FH prevalence was similar in both groups (5.1% vs 4.8%).

Conclusions: Founder mutation testing remains an effective first-line genetic screening approach for patients with definite FH or family history of FH in Finland. However, its diagnostic yield is low among unrelated individuals without known familial variants. Broader genetic testing after a negative founder result identified additional FH cases in 10% of patients, highlighting the need to combine targeted founder screening with comprehensive sequencing for optimal FH detection.

Abstract citation ID: lvag096.620

EP4 - ECE_2923 - Primary bilateral macronodular adrenal hyperplasia associated with an ARMC5 variant: early detection in a presymptomatic carrier

Lina Panceraitė[1], Radvilė Matukaitienė[1,2], Lina Kievišienė[3] and Birutė Žilaitienė[1,2]

[1]*Department of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [2]*Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [3]*Department of Genetics and Molecular Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania*

Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a rare disease, accounting for <2% of cases of Cushing's syndrome (CS). Patients with PBMAH have varying levels of cortisol secretion and are often diagnosed with PBMAH due to incidental radiological findings of the adrenal glands, as in our case. During evaluation for angioedema, a CT scan in a 53-year-old woman revealed an incidental finding of nodular thickening up to ~11 mm in the left adrenal gland (most likely hyperplasia). Further abdominal MRI showed that the left adrenal gland is nodular, with a suspicious solid lesion measuring 1.2 × 0.9 cm with small fatty-density inclusions, based on MRI, a small pheochromocytoma was suspected; the right adrenal gland is structurally normal with no additional lesions. Further evaluation of this finding by an endocrinologist was carried out. An overnight dexamethasone suppression test was performed, and cortisol suppression was not achieved (56.24 nmol/L, $n < 50$). DXA showed normal BMD, and spinal X-ray revealed degenerative changes. Other laboratory findings included free metanephrines (metanephrine 0.08 nmol/L, *n* 0-0.507; normetanephrine 0.41 nmol/L, *n* 0-1.18), ACTH (2.1 pmol/L, *n* 1.63-14.15), TSH (2.03 mU/L, *n* 0.4-3.6), and a normal aldosterone-renin ratio (43). Whole-exome sequencing identified a heterozygous pathogenic variant in the ARMC5 gene NM_001105247.2:c.517C>T (p.Arg173Ter). This gene is associated with autosomal dominant PBMAH and has incomplete penetrance, as a second hit in the gene is required for PBMAH to develop. A repeat overnight dexamethasone suppression test again showed inadequate suppression (58 nmol/L, $n < 50$). A low-dose dexamethasone test was then performed, and suppression was achieved (40.6 nmol/L, $n < 50$); overall, the tests revealed mild autonomous cortisol hypersecretion. The patient case was discussed at a MDT on rare endocrine and adrenal diseases. Although the patient carries this variant, because adrenal hyperplasia is unilateral and she currently does not have typical clinical features of CS, she does not at present meet the criteria for PBMAH and can be considered a presymptomatic carrier of a genetic variant. In patients with pathogenic ARMC5 variants, PBMAH and CS most often present in the fifth or sixth decade of life, ie, with later onset compared with unilateral cortisol-producing adrenal adenomas. Therefore, the patient requires regular endocrinological follow-up, as there is a high likelihood of developing PBMAH and CS in the future. Monitoring facilitates early treatment initiation and helps prevent progression of CS-related complications such as cardiovascular, metabolic, and musculoskeletal disorders.

Abstract citation ID: lvag096.621

EP5 - ECE_3437 - Adrenocortical adenoma with ischemic necrosis

Athanasios Kasotas[1], Grigoris Effraimidis[2], Dionysios Vrachnis[1], Nektarios Adamopoulos[1], Maria Galani[1], Eleni Georgiou[1], Ioannis Gkountios[1], Anastasia-Konstantina Sakali[1], Maria Apostolopoulou[2] and Alexandra Bargiota[2]

[1]*Department of Endocrinology and Metabolic Diseases, University General Hospital of Larissa, Larissa, Greece;* [2]*Department of Endocrinology and Metabolic Diseases, Faculty of Medicine, School of Health Sciences, University of Thessaly, University General Hospital of Larissa, Larissa, Greece*

Introduction: Adrenocortical adenomas are by definition benign neoplasms and in most cases are discovered incidentally during imaging evaluation. Large adenomas (>4–5 cm) may very rarely develop ischemic necrosis with imaging features that mimic malignancy, making the differential diagnosis a significant challenge.

Case Presentation: A 74-year-old woman was referred for evaluation of a large right adrenal mass (7.4 × 7.5 cm), which was incidentally detected on magnetic resonance imaging (MRI) of the spine for spondyloarthritis.

The patient reported mild right-sided low back pain and had no clinical symptoms or signs of adrenal dysfunction or other pathological findings. Past medical history included type 2 diabetes mellitus, arterial hypertension, and dyslipidemia. Biochemical evaluation revealed mild autonomous cortisol secretion (MACS), with cortisol of 3.9 μg/dL after a 1-mg overnight dexamethasone suppression test (ODST), normal 24-hour urinary free cortisol, preserved circadian rhythm of salivary cortisol, and normal urine metanephrine and normetanephrine.

Computed tomography (CT) of the retroperitoneum demonstrated a 7.5 × 8.9 × 7.5 cm mass of mixed density, with well-defined margins, heterogeneous contrast enhancement, dystrophic calcifications, lipid components, extending to the upper pole of the right kidney and to the right hepatic lobe. Adrenal MRI confirmed the atypical imaging features (heterogeneity, calcifications, progressive heterogeneous enhancement, and extending to the kidney and liver).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

The patient underwent laparoscopic surgical excision of the lesion. Histological and immunohistochemical examination was consistent with extensive ischemic necrosis of a benign adrenocortical adenoma, with rare mitoses, absence of cellular atypia, and preservation of architecture.

The patient remains free of recurrence 7 months post-surgery.

Conclusions: Large adrenal masses with extensive necrosis, despite of radiological findings that could not exclude malignancy, could be benign, underscoring the decisive role of histopathological evaluation and immunohistochemical confirmation.

Abstract citation ID: lvag096.622

EP6 - ECE_2007 - Genetic pleiotropy between primary aldosteronism and hypertension maps to adrenal cell states

Zhuolun Sun, Changying Jing and Tracy Ann Williams
Medizinische Klinik und Poliklinik IV, Ludwig-Maximilians-Universität (LMU) München, Klinikum der Universität München, München, Germany

Background: Primary aldosteronism (PA) is a major yet underdiagnosed cause of secondary hypertension. While genome-wide association studies (GWAS) have identified genetic variants associated with PA and blood pressure (BP) separately, their shared genetic basis across multiple biological levels remains undefined. We aimed to systematically characterise the shared genetic architecture between PA and BP regulation, from pleiotropic loci and genes to pathways, and to integrate these findings with single-cell and spatial transcriptomic profiling of adrenal tissue.

Methods: We analysed genetic overlap between PA and BP using two independent PA datasets (French COMETE Network and Million Veteran Program) and three BP phenotypes (systolic, diastolic, and pulse pressure). Our stepwise analytic strategy included measuring genome-wide and regional genetic correlations, identifying shared risk loci through cross-trait meta-analysis, and prioritising candidate genes influencing both conditions. Biological relevance was evaluated using functional annotation, tissue-specific expression, and integrated single-cell and spatial transcriptomic analyses.

Results: PA demonstrated significant positive genetic correlations with all BP traits, with six specific genomic regions showing strong shared signals. We identified 143 independent loci associated with both PA and BP, predominantly in regulatory regions influencing gene expression across adrenal, vascular, cardiac, adipose, and neuroendocrine tissues. Gene-based analyses prioritised 43 shared genes, implicating pathways related to vascular remodelling and extracellular matrix turnover. Single-cell and spatial analyses revealed that *SLC24A3* is highly expressed in aldosterone-producing adenoma cells and exhibits marked intratumoural heterogeneity. *SLC24A3*-positive regions corresponding to a functionally specialised, high secretory endocrine state, whereas *SLC24A3*-negative regions were characterised by a stress-adaptive, low-secretory state.

Conclusions: This study defines a shared genetic architecture linking PA and BP regulation. It demonstrates that their frequent clinical association arises not only from the direct haemodynamic effects of aldosterone but also from a substantial, pre-existing genetic predisposition that dysregulates common endocrine-vascular pathways.

Abstract citation ID: lvag096.623

EP7 - ECE_3227 - Diagnostic performance of an inflammation-based score for mild autonomous cortisol secretion in adrenal incidentalomas—data from a tertiary Romanian center

Beatrice Cristea[1], Vlad Radulescu[1], Roxana Fota[1], Ioana Maria Posea[1], Cristina Stancu[1,2], Anda Dumitrașcu[1], Monica Livia Gheorghiu[1,3] and Corin Badiu[1,3]
[1]Research Department, Endocrinology IV, C.I. Parhon National Institute of Endocrinology, București, Romania; [2]Laboratory of Molecular, Cellular and Structural Endocrinology Research, Endocrinology IV, C.I. Parhon National Institute of Endocrinology, București, Romania; [3]Endocrinology, Endocrinology IV, "C Davila" University of Medicine and Pharmacy, Bucharest, Romania

Background: Risk stratification and confirmation of autonomous cortisol secretion for adrenal incidentalomas remains challenging when relying on isolated hormonal or imaging markers. Low-grade systemic inflammation may contribute to metabolic risk in mild autonomous cortisol secretion (MACS). We aimed to develop and compare simple point-based scores integrating hormonal, imaging, and inflammatory markers for improved identification of MACS.

Methods: We retrospectively analyzed **321 patients** with adrenal incidentalomas (135 MACS, 186 non-functioning adenomas [NFA]). Inclusion criteria were age ≥18 years, available blood count and imaging results at the time of the diagnosis, before any intervention. Baseline ACTH, DHEAS, neutrophil-to-lymphocyte ratio (NLR), and maximal tumor diameter were assessed. Patients with known infections, haematological/autoimmune disease, other functional adrenal masses were excluded. ROC analysis determined optimal cut-offs. The score was constructed by assigning one point to each abnormal parameter. Therefore, we propose the **NLR-based score with four items**: a) ACTH ≤ 10.08 pg/mL, b) DHEAS ≤ 42.1 µg/dL, c) imaging by CT or MRI scan-largest diameter ≥24.5 mm, d) NLR ≥ 2.21 (0–4 points). Diagnostic performance was evaluated using ROC analysis of both the raw score and predicted probabilities from the logistic model.

Results: Individual parameters showed moderate discrimination: a) ACTH:AUC = 0.79, b) DHEAS: AUC = 0.72, c) tumor diameter AUC 0.70, d) NLR:AUC = 0.60 (all with $P < .001$). The **NLR-based score** demonstrated good diagnostic accuracy (AUC **0.817**, 95% CI 0.763–0.870), with each one-point increase associated with a **3.47-fold increase** in MACS odds (95% CI 2.49-4.81, $P < .001$). A threshold of ≥2 points yielded sensitivity **82.6%** and specificity **61.4%**, while ≥3 points achieved high specificity (**92.1%**).

Discussion: The NLR-based score provides valuable clinical support when standard 1 mg overnight dexamethasone suppression testing is inconclusive or unreliable. Its high specificity (92.1% at ≥3 points) is particularly useful for borderline cortisol results near diagnostic threshold, offering additional diagnostic confidence without further testing. The score also serves as a practical alternative when dexamethasone testing is compromised by drug interactions or unavailable in resource-limited settings.

However, the clinical applicability of this score is limited in patients with active inflammation, infections, or hematological

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

disorders, where elevated NLR values unrelated to autonomous cortisol secretion may generate false-positive results.

Conclusions: A multimodal clinical score incorporating systemic immune-inflammation improves the identification of MACS in adrenal incidentalomas. The score demonstrates robust diagnostic performance and offers flexible thresholds for both screening and confirmatory clinical use.

Abstract citation ID: lvag096.624

EP8 - ECE_3239 - Real-world application of the 2025 Endocrine Society Guideline on primary aldosteronism: a 10-year retrospective study in Hong Kong

Kelly Hiu Ching Wong, David Lui, Carol Ho Yi Fong, Alan Chun Hong Lee, Kathryn Choon-Beng Tan and Paul Chi-Ho Lee
The University of Hong Kong, Hong Kong, Hong Kong

Background: In the 2025 Endocrine Society guideline on primary aldosteronism (PA), aldosterone suppression testing is only recommended to individuals with a positive PA screen and intermediate probability of lateralizing PA. Mineralocorticoid receptor antagonists (MRA) should be tried among individuals who have low probability of lateralizing PA without confirmatory testing, and prescribed also among those who have intermediate probability of lateralizing PA even if their aldosterone suppression test was negative. Here, we evaluated the real-world application of this probabilistic framework using a 10-year retrospective cohort of patients who underwent aldosterone suppression testing in our institution.

Methods: All patients with a positive PA screen, defined as plasma aldosterone ≥200 pmol/L, plasma renin activity (PRA) <1 mg/mL/h and aldosterone-to-renin ratio (ARR) ≥400 in our institution, who underwent saline infusion test (SIT) between January 2015 and September 2025 at Queen Mary Hospital, were included.

Results: Among the 304 patients with positive PA screen and underwent SIT between 2015 and Sep 2025, 12 (3.9%), 259 (85.2%) and 33 (10.9%) patients were classified into the low, intermediate and high probability of lateralization PA, respectively. Positive SIT was found in 33%, 54.8% and 97% in the low, intermediate and high probability groups, respectively ($P < .001$). Consistently, 8.3%, 13.5% and 51.5% eventually underwent adrenalectomy in the three groups, respectively ($P < .001$). Among the 142 patients with positive SIT in the intermediate probability group, 35 (24.6%) underwent adrenalectomy. The probability of lateralizing PA was not influenced by most indications of ARR testing including young hypertension, hypokalaemic hypertension and obstructive sleep apnoea, except in the setting of adrenal incidentaloma (AI) ($P = .002$), where the majority of patients were in the intermediate probability group. Compared with patients without AI, those with AI were significantly older ($P = .033$), requiring less anti-hypertensive medications (1.48 vs 2.2, $P < .001$), and none of them had hypokalaemia. Patients with AI were also significantly less likely to be tested positive at SIT compared to those without (22.7% vs 64.6%, $P < .001$), and only 1 patient eventually underwent adrenalectomy in the AI group.

Conclusions: Our findings confirmed the limited clinical utility of aldosterone suppression testing among patients categorized as high probability for lateralizing PA. However, whether the recommendations of trial of MRA without confirmatory testing in low-probability groups, and prescribing MRA in intermediate-probability groups even with negative SIT, should be applied among individuals with AI, given their high prevalence and low-risk of true PA, require further larger studies for confirmation.

Abstract citation ID: lvag096.625

EP9 - ECE_3658 - Diagnostic performance of late-night plasma ACTH in Cushing's syndrome

Georgios Kostopoulos[1], Evangelia Makri[2] and Zoe Efstathiadou[2]
[1]Thessaloniki, Greece; [2]Endocrinology, Hippokration General Hospital, Thessaloniki, Greece

Background: Endogenous Cushing's syndrome (CS) is associated with substantial morbidity and mortality and remains a significant diagnostic challenge. Following biochemical confirmation of endogenous hypercortisolism, determination of adrenocorticotropic hormone (ACTH) dependency represents a critical step in the diagnostic algorithm. Current guidelines recommend measurement of morning plasma ACTH levels for disease classification; however, ACTH secretion follows a circadian rhythm with physiological late-night suppression that is frequently lost in ACTH-dependent CS.

Objective: To evaluate the diagnostic performance of late-night plasma ACTH for determining ACTH dependency in endogenous CS.

Methods: We conducted a retrospective cohort study including patients evaluated for CS at a tertiary endocrine center between January 1, 2010 and December 31,2025. Patients with biochemical evidence of endogenous CS and available morning and late-night plasma ACTH measurements were included. ACTH dependency was established based on final clinical diagnosis incorporating biochemical testing, imaging, dynamic testing, and pathology where applicable. Diagnostic performance was assessed using receiver operating characteristic (ROC) analysis. Area under the curve (AUC) with 95% confidence intervals (CI) was calculated using the DeLong method. The optimal cutoff was determined using Youden's index, and clinically relevant rule-out and rule-in thresholds were explored.

Results: Twenty-eight patients with CS were included (71.4% female, median age of diagnosis 53.5 years). Etiologies included adrenal adenoma ($n = 16$), corticotroph adenoma ($n = 10$), thymic carcinoid ($n = 1$), and adrenocortical carcinoma ($n = 1$). Median late-night ACTH was 46.8 pg/mL in ACTH-dependent disease and 8.6 pg/mL in ACTH-independent disease. Late-night ACTH demonstrated excellent discrimination between ACTH-dependent and independent CS (AUC 0.995, 95% CI 0.98–1.00). Lower thresholds (7.5 and 10 pg/mL) achieved maximal sensitivity, supporting a rule-out strategy, whereas higher thresholds (>20 pg/mL) provided near-complete specificity, consistent with a rule-in approach. Morning ACTH showed slightly lower diagnostic accuracy (AUC 0.984), with no statistically significant difference compared with late-night ACTH ($P = .48$).

Conclusions: Late-night plasma ACTH shows high diagnostic accuracy for determining CS etiology and may enhance decision-making, but external validation is warranted.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.626

EP10 - ECE_2752 - Impaired glucocorticoid metabolism, rather than mineralocorticoid excess, is an independent predictor of cardiovascular risk in chronic kidney disease

Maria Tomkins[1,2], Darran Mc Donald[1,2], Fozia Shaheen[3], Angela Taylor[3], Olive McEnroe[4], Declan de Freitas[4], Carol Traynor[4], Amy Hudson[4], Ciara N. Magee[4], Peter Conlon[4], Colm Magee[4], Mark Denton[4], Conall O'seaghdha[4], Diarmuid Smith[2], Wiebke Arlt[3,5,6], Michael W. O'reilly[1,2] and Mark Sherlock[1,2]

[1]Department of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland; [2]Department of Endocrinology, Beaumont Hospital, Dublin, Ireland; [3]Institute of Metabolism and Systems Research, Birmingham, United Kingdom; [4]Department of Nephrology, Beaumont Hospital, Dublin, Ireland; [5]Medical Research Council Laboratory of Medical Sciences, London, United Kingdom; [6]Institute of Clinical Sciences, Imperial College London, London, United Kingdom

Introduction: Chronic kidney disease (CKD) is a prevalent chronic disease with associated increased mortality. Cardiovascular disease (CVD) is the predominant cause of death in CKD and risk of CVD is potentiated by mineralocorticoid receptor (MR) activation. Historically, aldosterone has been the primary corticosteroid of concern for driving excess CVD risk in CKD. Importantly, however, MR activation can occur from both mineralocorticoid and glucocorticoid binding. The enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) converts active cortisol (F) to inactive cortisone (E) thereby protecting the MR from illicit glucocorticoid activation. 11β-HSD2 activity is impaired in CKD.

Methods: To investigate the contribution of disrupted adrenal steroid metabolism to renal disease and CVD risk in CKD we performed multi-steroid profiling via liquid chromatography–tandem mass spectrometry on paired serum and 24-hour urine samples from non-diabetic patients across the stages of CKD ($n = 103$) and age-, sex-, and BMI-matched healthy controls ($n = 39$) alongside detailed cardiometabolic phenotyping, including pulse wave velocity (PWV) and bioimpedance body composition analysis. Patients with recent or current use of MR antagonist, glucocorticoids or other interfering medications were excluded. Statistical analysis included Spearman correlation tests with multivariable regression analysis. Values were log-transformed, where appropriate.

Results: Despite elevated plasma aldosterone concentrations [357 pmol/L (157-564) vs 235 pmol/L (138-309), $P = .01$], patients with CKD had significantly lower urinary excretion of total mineralocorticoid metabolites [398 nmol/L (256-611) vs 882 nmol/L (613-1197), $P < .0001$] compared to controls, suggesting impaired renal clearance. 11β-HSD2 activity declined with worsening renal function evidenced by an elevated F/E ratio [11.1 (8.2-13.9) in CKD vs 5.7 (4.6-7.1) in controls, $P < .0001$]. Multivariable regression identified elevated serum aldosterone, lower total urinary mineralocorticoid metabolites and increased F/E ratio to be independently associated with lower eGFR when accounting for age, sex, antihypertensives, urine volume and urine creatinine concentration.

We also found an independent association of both the F/E ratio ($\beta = 0.1$, $P = .04$) and total urinary glucocorticoid metabolites ($\beta = 0.09$, $P = .007$) with arterial stiffness (PWV), controlling for age, sex, renal function, blood pressure, and antihypertensive use. Mineralocorticoid markers showed no independent associations with cardiometabolic outcomes.

Conclusions: This is the first study to interrogate the complete steroid metabolome in CKD providing an insight into renal determinants of steroid metabolism. Our findings highlight the important role of impaired 11β-HSD2 activity, reflected by an elevated F/E ratio, in driving glucocorticoid-mediated MR activation and arterial stiffness. Additionally, impaired glucocorticoid metabolism is a greater contributor to CVD risk than aldosterone and should be considered as a potential therapeutic target in CKD.

Abstract citation ID: lvag096.627

EP11 - ECE_1092 - Work loss and income before and after diagnosis of Addison's disease: a population-based longitudinal study

Stavros Stergianos[1,2], Åsa Hallqvist Everhov[3,4], Jonas Söderling[3], Jakob Skov[5,6] and Sophie Bensing[1,2]

[1]Department of Medicine, Solna, Experimental Endocrinology Division, Karolinska Institutet, Stockholm, Sweden; [2]Department of Endocrinology, Karolinska University Hospital, Stockholm, Sweden; [3]Department of Medicine, Solna, Clinical Epidemiology Division, Karolinska Institutet, Stockholm, Sweden; [4]Department of Clinical Science and Education, Karolinska Institutet, Södersjukhuset, Stockholm, Sweden; [5]Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden; [6]Region Värmland, Center for Clinical Research, Karlstad, Sweden

Background: The effects of autoimmune Addison's disease (AAD) on employment and income over time remain inadequately characterized.

Objective: To assess how a diagnosis of AAD influences work-loss days, taxable earnings and disposable income in the working-age population compared with matched controls from the general population.

Methods: We conducted a nationwide register-based cohort study in Sweden. By linking the Swedish Addison Register with national health and labour-market registers, we identified 716 individuals aged 20–62 years with incident AAD diagnosed between 2003-2019, and 3271 comparators from the general population matched on sex, age, county, calendar year and education level. We examined outcomes over a 10-year window around diagnosis: annual lost work-days (via linear regression) and median taxable earnings and disposable income (via quantile regression).

Results: Compared with matched comparators, patients with AAD had significantly greater work-loss from one year before to three years after diagnosis. The maximal difference occurred in the first year post-diagnosis (mean excess of 30.5 days; 95% CI 22.9–38.0; $P < .001$). At the median level, patients with AAD had lower taxable earnings by USD 1,107 (95% CI −2042 to −173; $P = .02$) one year before diagnosis, and by USD 1105 (95% CI −2166 to −43; $P = .04$) one year after diagnosis. Their disposable income was also reduced by USD 1084 (95% CI −1813 to −354; $P = .004$) one year post-diagnosis. Importantly, both work loss and income differences attenuated over time, returning close to comparator levels by approximately four years after diagnosis.

Conclusions: In this large national cohort, AAD was associated with a transient increase in work absence and reductions in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

earnings and income, particularly concentrated around the time of diagnosis and peaking in the subsequent year. Encouragingly, both employment participation and income recovered to near-normal levels within about four years. These findings highlight the importance of supportive interventions around diagnosis to mitigate socioeconomic impact in individuals with AAD.

Abstract citation ID: lvag096.628

EP12 - ECE_1663 - Abiraterone acetate as a treatment option for canine Cushing's syndrome

Sara Galac[1,2,3], Nynke Deckers[4], Els Wouters[4], Patricia Peeters[4] and Hans S. Kooistra[5]
[1]*Faculty of Veterinary Medicine, Clincial Sciences, Utrecht, The Netherlands;* [2]*Faculty of Veterinary Medicine, Clinical Sciences, Utrecht, The Netherlands;* [3]*Faculty if Veterinary medicine, Clinical Sciencesnet, Utrecht, The Netherlands;* [4]*Regivet, Oirschot, The Netherlands;* [5]*Utrecht University, Utrecht, The Netherlands*

Introduction: Abiraterone acetate (ABA) is a selective and irreversible inhibitor of cytochrome P450 17A1 that profoundly suppresses cortisol synthesis, making it a promising candidate for the medical treatment of Cushing's syndrome (CS). Naturally occurring CS in dogs is approximately 1000 times more prevalent than in humans and closely resembles the human disease in terms of anatomy, pathophysiology, clinical presentation, and diagnostic and therapeutic approaches. This positions canine patients as a valuable translational model for the evaluation of novel therapeutic strategies for CS.

Objectives: To evaluate the clinical and hormonal effects of ABA in dogs with naturally occurring CS.

Methods: This prospective clinical study included ten dogs with CS, in which the diagnosis was confirmed by endocrine testing and diagnostic imaging. The starting dose of ABA was 1 mg/kg administered twice daily, with subsequent dose adjustments guided by clinical response and ACTH stimulation test results. Dogs were monitored at two- to three-week intervals until a stable dose—defined by well-controlled clinical signs and sufficient adrenocortical reserve—was achieved, followed by three-monthly evaluations for up to one year.

Results: Clinical improvement was observed in 8/10 dogs; however, polyuria resolved only after the addition of desmopressin acetate. In 3/8 clinically improved dogs, ABA therapy was discontinued after 1, 3, and 10 months, respectively, due to deterioration of the patient's condition. The remaining 5/8 dogs were followed for 16, 14, 10, 6, and 4 months.

Two dogs were excluded before reaching an optimal dose because of minimal clinical improvement and concurrent gastrointestinal signs, which were considered possible side effects of ABA treatment.

Hormonal evaluation demonstrated a decrease in urinary cortisol excretion to within the reference range, as assessed by the urinary cortisol-to-creatinine ratio, in all clinically improved dogs. Endogenous ACTH concentrations did not differ from baseline values at any follow-up time point, suggesting that ABA-treatment was not associated with hypocortisolism. Median serum aldosterone concentrations increased significantly ($P < .001$) during treatment, and hypokalemia was detected in 4/10 dogs. In one patient, mineralocorticoid excess syndrome was suspected, and concurrent treatment with spironolactone was initiated. ABA-treatment induced a significant increase in progesterone concentrations ($P < .001$), consistent with its mechanism of action.

Conclusions: ABA may represent an effective medical treatment option for dogs with CS; however, mineralocorticoid excess should be closely monitored. The canine model provides important translational insights into the efficacy, endocrine adaptations, and adverse effects associated with CYP17A1 inhibition.

Abstract citation ID: lvag096.629

EP14 - ECE_2531 - Predictive factors of hypertension remission in patients with medically and surgically treated primary aldosteronism: a single center study

Bogdan Baluta[1], Stéphanie Le Scouiller[2], Fabio Bioletto[3], Thierry Frouget[4], Caroline Dourmap[5], Juliette Hascoet[6], Benoit Peyronnet[6] and Patricia Vaduva[1]
[1]*Endocrinology, Diabetes, and Nutrition Department, Rennes University Hospital, Rennes, France;* [2]*Clinical Pharmacology Department–CIC Inserm 1414, Rennes University Hospital, Rennes, France;* [3]*Endocrinology Department, Torino University Hospital, Torino, Italy;* [4]*Nephrology Department, Rennes University Hospital, Rennes, France;* [5]*Cardiology Department, Rennes University Hospital, Rennes, France;* [6]*Urology Department, Rennes University Hospital, Rennes, France*

Introduction: Primary aldosteronism (PA) is the most frequent endocrine cause of secondary hypertension, characterized by aldosterone production independent of the renin-angiotensin-aldosterone system. Compared to essential hypertension, PA is associated with significantly higher cardiovascular (CV) morbidity and renal damage. This study aimed to identify predictors of hypertension remission and factors associated with the occurrence of cardiovascular and renal events in PA patients.

Methods: We conducted a retrospective single-center study at Rennes University Hospital, including 202 patients (aged ≥18 years) diagnosed with PA who underwent adrenal vein sampling (AVS) for lateralization assessment. Data were extracted from electronic medical records. Logistic regression models were used to identify independent factors associated with hypertension remission and the onset of CV or renal complications.

Results: The cohort had a mean age of 48.9 ± 11 years (63% male). At diagnosis, mean systolic blood pressure (SBP) was 152.4 ± 24.3 mmHg, mean diastolic blood pressure (SBP) was 92.38 ± 13.42 and the mean duration of hypertension was 7.6 ± 7.3 years. Comorbidities included type 2 diabetes in 19.8%, and hypercholesterolemia in 20.3% of the patients.

AVS identified lateralized PA in 44.5% (85/191) of patients, with a 37.7% (66/175) discordance rate between CT scans and AVS results. Medical therapy was the primary treatment for 61.5% (118/192) of the cohort.

Overall, hypertension remission was achieved in 45% (91/202) of patients. Multivariable analysis identified three significant predictors of remission: preoperative hypokalemia <3.4 mmol/L (OR 2.24; 95% CI 1.21–4.17; $P = .01$), lateralized PA on AVS (OR 3.69; 95% CI 2.02–6.73; $P < .001$) and surgical treatment (OR 4.08; 95% CI 2.19–7.61; $P < .001$).

At the end of follow-up, the absence of hypertension remission was significantly associated with an increased prevalence of left

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

ventricular hypertrophy, microalbuminuria, and coronary artery disease ($P < .05$).

Conclusions: In patients with PA, hypokalemia, lateralization on AVS, and adrenalectomy are strong predictors of hypertension remission. Notably, failure to achieve remission is linked to a higher burden of cardiovascular and renal complications, emphasizing the need for early diagnosis and optimized targeted therapy.

Abstract citation ID: lvag096.630

EP15 - ECE_2175 - Glucocorticoid actions in the liver at single-cell resolution

Ronja Mueller[1], Ronny Scheundel[1], Aliana Harris[1], Gizem Oeztuerk[2], Anke Kunstmann[1], Sabine Vettorazzi[2] and Franziska Greulich[1]

[1]*Metabolic Programming, Technical University of Munich/School of Life Sciences Weihenstephan, Freising, Germany;* [2]*Institute of Comparative Molecular Endocrinology and Physiology, University of Ulm, Ulm, Germany*

Glucocorticoids (GCs) are adrenal steroid hormones that play a central role in the regulation of energy homeostasis and immune function and are widely prescribed as anti-inflammatory agents. Their clinical use, however, is limited by significant adverse effects, including hepatic steatosis, osteoporosis, and hyperglycaemia. Sustained exposure to elevated endogenous or exogenous GCs, as observed in Cushing's syndrome or during long-term GC therapy, leads to profound metabolic dysregulation, yet the underlying tissue- and cell-type–specific mechanisms remain incompletely understood.

GCs exert their effects through the glucocorticoid receptor (GR), a ubiquitously expressed nuclear hormone receptor that translocates to the nucleus upon ligand binding. GC exposure induces rapid and highly tissue-specific transcriptional responses, driven in part by context-dependent GR binding to chromatin regions with distinct DNA accessibility landscapes. How these tissue-level responses are further resolved into cell-type–specific actions and integrated to generate metabolic phenotypes such as diabetes is largely unknown.

To address this, we performed single-cell multiome sequencing of liver tissue from wild-type and GR-deficient mice subjected to chronic synthetic GC treatment for two weeks. Cell-type resolved analyses revealed pronounced and distinct GC-responsive transcriptional programs across hepatic cell populations. Prolonged GC exposure reprogrammed hepatocyte metabolic pathways and was associated with a marked reduction in F4/80-positive hepatic macrophages, indicating coordinated molecular and cellular adaptation to sustained GR signalling. By integrating single-cell transcriptomic profiles with chromatin accessibility and GR binding data, we delineate the cell-type–specific contributions of GC action in the liver and construct a comprehensive cellular response network underlying hepatic adaptation to chronic glucocorticoid exposure.

Abstract citation ID: lvag096.631

EP16 - ECE_2735 - Corticomedullary mixed tumor of the adrenal gland

Mariam Chkholaria[1,2]

[1]*Tbilisi, Georgia;* [2]*Endocrinology, Caucasus Medical Centre, Tbilisi, Georgia*

Background: Pheochromocytoma is a rare neuroendocrine tumor, occurring in less than 0.2 percent of patients with hypertension and primary aldosteronism alone occurring in 5-10% of all hypertension patients, mixed pheochromocytoma and primary aldosteronism is very rare in those patients.

Case Presentation: In 2024 60 years old female patient presented with high blood pressure (T/A max 200/100 mmHg). She was taking combined medication—ace inhibitor/ calcium channel blocker for her high blood pressure. Past medical history: rheumatoid arthritis, she was taking corticosteroid, but she stopped taking them 4 months prior. Before endocrinologist she was consulted by a cardiologist and urologist. She had made Computed Tomography (CT) scan of the abdomen, where in the right adrenal gland area was seen a fluid filled dense mass with clear contours measuring 6.7 × 7.7 cm in cross-sectional and 7 cm in craniocaudal dimensions. Antihypertensive medications were changed to alpha-adrenergic blocker and calcium channel blocker, with all rules followed, the lab tests were performed: ACTH and urine cortisol were in normal ranges, Aldosterone 79.0 ng/L (reference range—11.7–236), Renin <1.0 ng/L (reference range 1.7–23.9), Aldosterone renin ratio >79 (reference range <20), Urine Metanephrine i.u (24 h) 6615 ug/24 h (reference range 43.4-260), Normetanephrines i.u. (24 h) 11515 ug/24 h (reference range—128-484), Dopamine i.u. (24 h)—2138 ug/24 h (reference range—59.7-403), electrolytes and blood glucose levels were in normal ranges. Primary aldoseronism and/or pheochromocytoma was suspected. Patient underwent laparoscopic unilateral (right) adrenalectomy. Postoperative histopathomorphology report: adrenal cortical adenoma and pheochromocytoma. After surgery mild hypertension persisted, she is taking calcium channel blocker. Although mild hypertension persisted in lab tests on follow up after surgery: aldosterone, renin, aldosterone renin ratio in blood were in normal ranges, also urine 24 h metanephrine, normetanephrine and dopamine were in normal ranges.

Conclusions: Most primary neoplasms of the adrenal gland arise either from adrenal cortical cells or adrenal medulla chromaffin cells. Mixed adrenal tumors composed of more than one cell type of adrenal gland is very rare. This case describes a single adrenal neoplasm composed of the cells of adrenal cortex and medulla.

Abstract citation ID: lvag096.632

EP17 - ECE_3324 - When the adrenal breaks the rules: ACTH-expressing adrenocortical carcinoma: a case report

Andreea-Alexandra Grosu[1], Ioana Claudia Dan[1], Cristina Stancu[1,2], Dumitru Ioachim[1] and Corin Badiu[1,3]

[1]*Adult Endocrinology, Endocrinology IV, National Institute of Endocrinology "C.I Parhon", Bucharest, Romania;* [2]*National Institute of Endocrinology, Bucharest, Romania;* [3]*Endocrinology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*

Adrenocortical carcinoma (ACC) is a rare and aggressive endocrine malignancy, most often causing adrenocorticotropic hormone (ACTH)—independent hypercortisolism. ACTH expression by ACC is extremely rare and represents a major diagnostic challenge.

This report presents the case of a 41-year-old female patient who was incidentally diagnosed in June 2025 with a large mass

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

involving the right adrenal gland (1.21/1.15/0.79 cm) by an abdominal magnetic resonance imaging (MRI). This lesion showed diffusion restriction with necrotic and hemorrhagic areas, extending into inferior vena cava (IVC), nearly occluding the lumen. Physical examination revealed only an elevated arterial blood pressure (153/100 mmHg) without clinical signs of hypercortisolism. Biochemical evaluation showed borderline hypokalemia (3.5 mmol/L) with normal electrocardiography. Hormonal assessment demonstrated low-normal ACTH levels (4.99 pg/mL), normal levels of morning serum cortisol (11.76 µg/dL), adrenal androgens, aldosterone and renin. Serum cortisol ailed to suppress after both low and high-dose dexamethasone suppression tests (suppressed cortisol = 9.4 ug/dL; respectively 11.99 ug/dL) and 24-hour urinary free cortisol was three times the upper limit of normal (4316 ug/dL), indicating autonomous cortisol secretion. Neoadjuvant mitotane therapy (up to 4 g/day) was initiated. In July 2025, the patient underwent right adrenalectomy with IVC tumor thrombus excision. However, postoperative evolution was unfavorable, with rapid thrombus recurrence causing 75% IVC obstruction. Histopathological examination revealed diffuse architecture, focal necrosis, vascular and capsular invasion, significant nuclear atypia and a mitotic rate >5/50 high-power fields with a Ki-67 index of 20% (Weiss score 9). The cells exhibited positive immunohistochemical staining for inhibin, calretinin, Melan-A and most important, focal ACTH, proving the ability to synthesize ACTH. Microsatellite instability was absent. This case was reviewed by a Multidisciplinary Tumor Board, which decided for chemotherapy in combination with mitotane and oral anticoagulant therapy. Unfortunately, the tumor exhibited aggressive behavior, in November 2025 on 4 g mitotane/day, with a plasma level of 11.46 mg/L, ACTH levels were markedly elevated (257.6 pg/mL), with high serum cortisol (38.22 ug/dL) and persistent lack of suppression after dexamethasone. Functional imaging test revealed marked enlargement of the IVC tumor thrombus and newly developed left macronodular adrenal hyperplasia. In January 2026, systemic chemotherapy was initiated.

This case highlights a rare ACC with aberrant ACTH production causing ACTH-dependent hypercortisolism. ACTH expression in adrenocortical tumors is an unusual finding and is thought to reflect tumor dedifferentiation and aggressive biological behavior. Up until now, only two other cases of ACC with ectopic ACTH secretion have been reported.

Abstract citation ID: lvag096.633

EP19 - ECE_3636 - Primary aldosteronism beyond potassium: a multi-electrolyte disorder

Kalliopi Pantelia, Vasiliki Antonopoulou, Andromachi Panagiotopoulou, Marinella Tzanela and Theodora Stratigou

Department of Endocrinology "D. Ikkos", Diabetes Center, EndoERN-Evangelismos General Hospital, Athens, Greece

Background: Primary aldosteronism (PA) is a common cause of secondary hypertension, typically presenting with hypokalemia and metabolic alkalosis. Less recognized are disturbances in calcium homeostasis.

Case Presentation: We describe the case of a 39-year-old woman with a four-year history of hypertension, initially diagnosed during pregnancy, who presented with severe hypokalemia (K^+ 1.9 mmol/L), metabolic alkalosis (pH 7.508, HCO_3^- 33.1 mmol/L), and electrocardiographic abnormalities (U waves, ST-segment depression). Notably, during blood pressure measurement on admission, a positive Trousseau sign was elicited; the patient reported that it had been present for approximately four years during prior blood pressure measurements. Biochemical evaluation revealed suppressed renin (<0.5 µU/mL) and markedly elevated plasma aldosterone (33.9–35.9 ng/dL), with an aldosterone-to-renin ratio (ARR) >67.8, supporting a diagnosis of PA. Imaging identified a 3-cm right adrenal lesion; adrenal venous sampling confirmed right-sided aldosterone excess.

During hospitalization, the patient exhibited symptomatic hypocalcemia (albumin-corrected Ca 7.44 mg/dL) with mild vitamin D insufficiency (25[OH]D 18.9 ng/mL), high-normal PTH (62 pg/mL), and hypercalciuria (479 mg/24 h). Serum magnesium and phosphorus levels were within reference ranges. Bone mineral density, trabecular bone score, and bone turnover markers were within normal limits. Hypocalcemia required high-dose oral calcium (4 g/day) for stabilization; after correction the Trousseau sign resolved. Potassium supplementation was administered, and spironolactone was initiated and titrated to150 mg/day.

The patient underwent right adrenalectomy; histology confirmed a 3-cm adrenal cortical adenoma with strong, diffuse CYP11B2 positivity. Ten days postoperatively, serum potassium and calcium, as well as blood pressure normalized without supplementation or antihypertensive therapy. According to PASO criteria, the patient achieved complete clinical and biochemical success.

Conclusions: This case illustrates that PA can present with chronic, multisystem electrolyte disturbances including hypokalemia, hypocalcemia and hypercalciuria, associated with long-standing neuromuscular irritability. Expansion of effective circulating volume in PA patients decreases proximal tubule reabsorption of calcium as well as sodium because calcium reabsorption is coupled to transtubular sodium uptake. Although the distal nephron can reabsorb calcium, excessive delivery can overwhelm its absorptive capacity. This could lead to hypercalciuria and hypocalcemia. Curative adrenalectomy can fully reverse these disturbances, highlighting that PA is not solely a disorder of potassium homeostasis.

Abstract citation ID: lvag096.634

EP20 - ECE_2858 - Down syndrome and autoimmune polyglandular syndrome

Rugile Braukyliene[1], Laura Dudonytė[1], Agne Rimkute[1], Agne Kadusauskiene[2], Birutė Žilaitienė[2], Rasa Verkauskiene[3] and Aiste Kondrotiene[2]

[1]*Medical Academy, Lithuanian University of Health Sciences, Kaunas 44307, Lithuania;* [2]*Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas 44307, Lithuania;* [3]*Kaunas, Lithuania*

Introduction: Autoimmune polyglandular syndrome (APS) is a rare group of immune-mediated disorders. APS type 2 is the most common subtype with a characteristic clinical triad, which includes adrenal insufficiency, autoimmune thyroiditis and diabetes mellitus (DM) type 1.[1]

Case Presentation: A 37-year-old woman with Down syndrome (DS) and autoimmune thyroiditis treated with levothyroxine, was admitted to the emergency department with an 8-day

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

history of progressive weakness, nausea, and dizziness. The patient's height 142 cm, weight 47 kg, BMI 23 kg/m^2.'Initial laboratory evaluation revealed hyperkalemia 8.02 mmol/L (3.5-5.1) and hyponatremia 130 nmol/L (136-144). Patient was hospitalized to the intensive care unit. Patient developed persistent hypotension (79/50 mmHg) and ongoing hyperkalemia (6.1 mmol/L), hyponatremia (130 nmol/L) raising suspicion for adrenal crisis. Diagnostic evaluation confirmed adrenal insufficiency with markedly elevated ACTH level of 210.8 pmol/L (1.63-14.5) and low cortisol level of 101.18 nmol/L. Immediate treatment consisted of intravenous hydrocortisone 100 mg IV bolus. Hydrocortisone 200 mg /24 h was administered further using automatic syringe pump. After correcting the electrolyte imbalance, maintaining stable blood pressure, oral hydrocortisone was administered, gradually decreasing to a maintenance dose (30 mg/day). In the presence of a tendency to slight hypotension, with signs of aldosterone deficiency, elevated renin concentration of 134.9 ng/L (3.78-32.61), fludrocortisone was added resulting in systolic blood pressure increase toto 90-100 mmHg. Anti-GAD65, anti-IA2 antibodies were negative and glucose tolerance test was within normal range. At discharge, the patient's treatment consisted of hydrocortisone (15/10/5 mg), fludrocortisone 50 μg per day and levothyroxine 75 μg per day. A month later, laboratory tests revealed elevated renin level of 401 ng/L (3.78-32.61) and elevated TSH level of 14.78 mU/L (0.4-3.6), sodium 133 mmo/L (135-144), potassium 4.7 nmol/L (3.5-5.1), a tendency to a lower blood pressure was found. Fludrocortisone dose was increased to 75 μg per day and levothyroxine—to 100 μg per day, hydrocortisone dose was unchanged and follow up visit was planned in 2 months.

In conclusion, DS is associated with an increased risk of autoimmune diseases due to disruption of immune tolerance.[2] This case highlights the challenges and risks of APS type 2 in patients with DS, indicating the need for screening and timely treatment of these serious endocrine conditions.[3]

References

1. Kounatidis D, Kontos G, Kotsi E, et al. Autoimmune polyglandular syndrome with shock and high anion gap metabolic acidosis. *Am J Med Sci* 2024;368(2):162-166. https://doi.org/10.1016/j.amjms.2024.05.019
2. Khor B, Buckner JH. Down syndrome: insights into autoimmune mechanisms. *Nat Rev Rheumatol*. 2023;19(7):401-402. https://doi.org/10.1038/s41584-023-00970-0
3. Rivelli A, Fitzpatrick V, Wales D, et al. Prevalence of Endocrine Disorders Among 6078 Individuals With Down Syndrome in the United States. *J Patient Cent Res Rev*. 2022;9(1):70-74. https://doi.org/10.17294/2330-0698.1877

Abstract citation ID: lvag096.635

EP21 - ECE_1753 - GDF15 in patients with autoimmune primary adrenal insufficiency

Aleksandra Zdrojowy-Welna, Jowita Halupczok-Żyła, Katarzyna Kolačkov, Justyna Kuliczkowska-Płaksej, Aleksandra Jawiarczyk-Przybyłowska, Barbara Stachowska, Anna Brona, Iga Zendran-Zahorska and Marek Bolanowski
Wroclaw Medical University, Department of Endocrinology and Internal Diseases, Wrocław, Poland

Background: GDF15 is a stress response protein that acts as a hormone signaling distress from cells to the brain. Increased GDF15 is associated with reduced appetite and weight loss, symptoms that resemble the clinical picture of primary adrenal insufficiency (PAI). It has been shown that GDF15 levels are elevated in glucocorticoid deficiency. However, there are no studies analyzing clinical factors related to GDF15 in patients with PAI.

Objectives: The aim of our study was to evaluate circulating GDF15 in patients with autoimmune PAI in comparison to controls and to assess correlations between GDF15 and anthropometric, metabolic, and hormonal parameters in both groups.

Materials and Methods: We included 37 patients (59.5% females, mean age 48.9 ± 13.1 years) with autoimmune PAI, and 47 age-, sex- and BMI-matched controls. The mean duration of PAI was 11.3 ± 12.7 years. Laboratory examinations, including serum GDF15 levels, hormonal and biochemical parameters were performed. The percentage of body fat was evaluated using dual-energy X-ray absorptiometry.

Results: Patients with PAI had significantly higher GDF15 levels than controls (1276.8 ± 952.1 vs 682.8 ± 270.2 pg/mL, $P < .001$). In both groups of patients with PAI and controls, GDF-15 levels correlated positively with age ($P < .001$). In the PAI group, there were positive correlations between GDF15 and the duration of PAI and autoimmune thyroid disease, gonadotropin levels, waist-to-hip ratio, and the percentage of body fat, while negative correlations with DHEAS and sex hormones levels. In controls, GDF15 correlated positively with fasting glucose, while negatively with IGF-1.

Conclusions: Circulating GDF15 levels are significantly higher in patients with PAI than in controls and correlate with older age and the duration of autoimmune diseases. There are also correlations between GDF15 and metabolic parameters related to unfavorable body composition.

Abstract citation ID: lvag096.636

EP23 - ECE_2270 - Routine inflammation-based blood indices reflect cortisol excess severity and might identify mild autonomous cortisol secretion in adrenal incidentalomas

Vlad Radulescu[1,2], Beatrice Cristea[2], Roxana Fota[2], Ioana Maria Posea[2], Anda Dumitrașcu[2], Madalina Musat[1,2], Monica Livia Gheorghiu[1,2] and Corin Badiu[1,2]
[1]Endocrinology, Endocrinology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [2]Adult Endocrinology, Endocrinology IV, National Institute of Endocrinology "C.I Parhon", Bucharest, Romania

Objective: Mild autonomous cortisol secretion (MACS) is associated with increased cardiometabolic risk but remains difficult to recognize using simple clinical parameters. While overt Cushing's syndrome (CS) is known to induce immune and hematological changes, the diagnostic value of inflammation-based indices in detecting low-grade cortisol excess has not been clearly established. We aimed to evaluate whether routinely available inflammation-based blood indices reflect cortisol excess severity and can discriminate between non-functioning adrenal tumors (NFAT), MACS and overt CS.

Design and Methods: We retrospectively analyzed 350 patients with benign adrenal adenomas evaluated at a tertiary endocrine center: 186 NFAT, 136 MACS and 28 CS in a cross-sectional

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

approach before any adrenal-directed treatment. Patients aged between 18-75 years old were analyzed. Patients with other secreting adrenal tumors, active infections, malignancy, hematologic disorders, chronic kidney disease ≥G3b, or current glucocorticoid/immunosuppressive/psychiatric therapy as well as other acute conditions that could modify full blood count values at time of testing were excluded. Neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), systemic immune-inflammation index (SII) and eosinophil-to-basophil ratio (EBR) were calculated from complete blood counts. Group differences were assessed using non-parametric tests. Receiver operating characteristic analyses were performed to assess discrimination between groups, and optimal cutoffs were derived using Youden's index.

Results: Inflammation-based indices showed a graded response to cortisol excess. NLR and SII increased progressively from NFAT to MACS and were highest in CS, while LMR and EBR decreased across the same spectrum (all adjusted $P < .01$). For identification of MACS versus NFAT, NLR showed an AUC of 0.604 (95% CI 0.542–0.667) with an optimal cutoff of 2.21 (sensitivity 64.7%, specificity 55.4%), while SII showed an AUC of 0.597 (95% CI 0.533–0.660) with a cutoff of 635 (sensitivity 50.7%, specificity 69.4%). LMR and EBR demonstrated statistically significant but lower discriminatory accuracy. Similar progressive changes were observed in total leukocyte, neutrophil and monocyte counts.

Conclusions: Inflammation-based indices derived from routine blood tests demonstrate a clear gradient of increased cardiometabolic risk across increasing degrees of cortisol excess and can distinguish patients with MACS from those with non-functioning adrenal tumors. Although individual diagnostic accuracy is moderate, these markers reflect early immune dysregulation in low-grade hypercortisolism and may support clinical risk stratification and follow-up decisions in patients with adrenal incidentalomas.

Abstract citation ID: lvag096.637

EP24 - ECE_2306 - Lipotoxic versus glucotoxic phenotypes: differential visceral adiposity profiles in Cushing's disease and mild autonomous cortisol secretion

Aslihan Pekmezci[1], Mehmet Arikan[2], Merve Korkmaz[1], Aytul Yardımcı[2], Mutlu Niyazoğlu[1,3] and Esra Hatipoglu[1,3]
[1]*Department of Endocrinology and Metabolism, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye;* [2]*Department of Radiology, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye;* [3]*Pituitary Disorders Research Center, University of Health Sciences, Istanbul, Türkiye*

Background and Objective: Cortisol excess is associated with adverse cardiometabolic outcomes, yet its metabolic expression is heterogeneous and inadequately captured by conventional anthropometric measures. Using magnetic resonance imaging (MRI)–derived proton density fat fraction (PDFF), we aimed to characterize differential adiposity profiles across the spectrum of cortisol excess, distinguishing adipose tissue expansion from organ-specific fat accumulation.

Methods: Herein, preliminary results from an ongoing study included patients with overt Cushing's disease (CD) ($n = 19$, 7 active,12 in remission), mild autonomous cortisol secretion (MACS) ($n = 12$), and age- and sex-matched metabolically healthy controls (HC) ($n = 10$). Regional adipose tissue distribution and organ-specific fat accumulation were assessed using quantitative MRI–derived PDFF. Bonferroni correction was applied for multiple group comparisons, with a corrected significance threshold of $P < .0167$.

Results: Quantitative MRI demonstrated increased subcutaneous adipose tissue (SAT) in both CD (310.4[IQR:207.3–513] cm^2) and MACS (253.2[209.8–409.5] cm^2) compared with HC (182.9[136.2–198.3] cm^2; both $P < .0167$), with no difference between the two cortisol excess groups ($P > .0167$). Visceral adipose tissue (VAT) was higher in MACS than in HC (251[203.7–293.7] vs 107.5[83.7–176.5] cm^2; $P = .003$), whereas the increase in CD (195.8[158.5–267.2] cm^2) did not remain statistically significant ($P > .0167$). Within-group analyses demonstrated that SAT exceeded VAT in all groups; reaching statistical significance only in CD($P = .016$). Among patients with CD, a significant predominance of subcutaneous over visceral adipose tissue was observed in the active disease state ($P = .02$), whereas this difference was no longer evident in patients in remission ($P = .398$). Body mass index (BMI) was higher in both cortisol excess groups compared with HC (32.5 and 32.2 vs 25.4 kg/m^2; $P < .0167$). SAT showed a positive correlation with BMI in both CD and MACS (all $P < .01$), whereas VAT was associated with triglyceride (TG) levels in CD and with HbA1c in MACS(all $P < .01$). MRI-derived PDFF of the liver and pancreas did not differ between groups or between active and remission states in CD(all $P > .05$).

Conclusions: Our findings suggest differential visceral adiposity–related metabolic profiles across the spectrum of hypercortisolism, with CD showing a predominantly lipotoxic pattern (VAT–TG association) and MACS a more glucotoxic pattern (VAT–HbA1c association). SAT correlated with BMI irrespective of disease severity, indicating a marker of general adiposity rather than cortisol-specific effects. Notably, hepatic and pancreatic MRI-derived PDFF values did not differ between groups or disease states, suggesting limited discriminatory value for metabolic phenotyping. These associations support a phenotype-oriented approach to cardiometabolic risk stratification in cortisol autonomy.

Abstract citation ID: lvag096.638

EP25 - ECE_2685 - Steroidomics in adrenal tumors

Alexandros Lafioniatis[1], Christos Velesiotis[2], Chrysoula Mytareli[1], Vasiliki Siampanopoulou[1], Petros Papalexis[1], Georgia Tsirou[1], Varvava Chalmantzi[1], Despoina Tsopouzidou[1], Paschalia Bekiaridou[1], Eleni Memi[1], Nikolaos Tentolouris[3], Gregory Kaltsas[4], Paraskevi Moutsatsou[2] and Anna Angelousi[1]
[1]*First Department of Internal Medicine, European Reference Network on Rare Endocrine Conditions (ENDO-ERN), Laikon General Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece;* [2]*Department of Clinical Biochemistry, National and Kapodistrian University of Athens, School of Medicine, "ATTIKON" University Hospital, Athens, Greece;* [3]*Diabetes Center, First Department of Propaedeutic Internal Medicine, Medical School, National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece;* [4]*Department of Propaedeutic and Internal Medicine, European Reference Network on Rare Endocrine Conditions (ENDO-ERN), Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Mild autonomous cortisol secretion (MACS) as well as non-functional adrenal incidentalomas (NFAI) are associated with increased metabolic and cardiovascular risk suggesting a subtle secretion of cortisol or of other precursors of steroidogenesis.

Aim: To investigate steroid metabolites levels in patients with MACS and NFAI benign adrenal tumours as well as in adrenocortical carcinomas (ACC). Controls were defined as patients with normal adrenals on imaging.

Methods: Liquid chromatography-tandem mass spectrometry (LC-MS/MS) was used for the steroidomics analysis of several steroid precursors [cortisol (F), corticosterone (B,CORT),11-deoxycorticosterone (DOC), 11-deoxycortisol (11-DOC, compoundS), 21-deoxycortisol (21-DOF), aldosterone (ALDO), testosterone (T), dihydrotestosterone (DHT), androstenedione (A4), androsterone (AN), dehydroepiandrosterone (DHEA), dehydroepiandrosterone Sulfate (DHEAS), progesterone (P4), 17-hydroxyprogesterone (17-OHP4), pregnenolone (P5), 17-hydroxypregnenolone (17-OHP5), estradiol (E2), estrone (E1)] in the blood of 53 patients. The categorisation of patients in functional or NFAI was based on functional hormonal blood tests [1 mg overnight dexamethasone suppression test (ODST)] based on current guidelines. All ACC cases were confirmed histopathologically.

Results: A total of 46 patients (12 males) with adrenal tumors [($n = 20$ with NFAI, $n = 15$ with MACS and $n = 11$ with ACC] and 7 controls were included. Tumor size was significantly higher in ACC compared to NFAI and MACS patients.

LC-MS/MS analysis showed that the median blood steroid levels of cortisol, 11-deoxycorticosterone, 21-deoxycortisol were significantly higher ($P < .05$) in ACC patients compared with NFAI, MACS.

Regarding patients with benign tumors, median levels of baseline morning cortisol, 11-deoxycorticosterone and 21-deoxycortisol were significantly higher in MACS compared with NFAI ($P = .04$, $P = .01$, $P = .01$ respectively). Baseline median levels of 11-deoxycorticosterone were significantly higher in NFAI compared with controls ($P = .03$) whereas progesterone was significantly lower in NFAI and MACS compared with controls ($P = .001$, $P = <0.001$ respectively).

Among comorbidities hypertension, hyperlipidemia and diabetes mellitus prevalence was higher in patients with adrenal tumors compared to controls as well as between NFAI and controls.

Conclusions: Cortisol, 11-deoxycorticosterone, and 21-deoxycortisol levels were significantly higher in ACC compared with MACS and NFAI. In benign adrenal tumors, cortisol, 11-deoxycorticosterone, 21-deoxycortisol, and progesterone differed significantly between MACS and NFAI and may represent supplementary biochemical markers of adrenal functional status**.**

Abstract citation ID: lvag096.639

EP27 - ECE_2912 - Non-functioning adrenal incidentalomas: a diagnosis we can still trust?

Vittoria Favero[1,2], Cristina Eller Vainicher[3], Valentina Morelli[4], Serena Palmieri[3], Alfredo Scillitani[5], Irina Bancos[6] and Iacopo Chiodini[1,2]

[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [2]ASST Grande Ospedale Metropolitano Niguarda, Unit of Endocrinology, Milan, Italy; [3]Unit of Endocrinology, Fondazione IRCCS Cà Granda-Ospedale Maggiore Policlinico, Milan, Italy; [4]Department & Lab of Endocrine and Metabolic Research, IRCCS Istituto Auxologico Italiano, Milan, Italy; [5]IRCCS Ospedale "Casa Sollievo della Sofferenza", San Giovanni Rotondo, Foggia, Italy; [6]Mayo Clinic; [7]Division of Endocrinology, Metabolism, and Nutrition, Department of Laboratory Medicine and Pathology, Rochester, Italy

Introduction: Non-functioning adrenal incidentalomas (NFAI) are defined by post–1 mg dexamethasone suppression test (F-1mgDST) cortisol levels <1.8 µg/dL. However, emerging evidence suggests that many individuals classified as having NFAI may exhibit subtle cortisol excess associated with increased cardiometabolic and skeletal risk.

Objective: To compare F-1mgDST levels between patients with NFAI and control subjects and to identify the F-1mgDST threshold most accurately associated with the presence of NFAI.

Materials and Methods: Pooled individual participant data analysis of 7 retrospective and prospective studies evaluating cortisol secretion in patients with type 2 diabetes, osteoporosis and/or fragility fractures, hypertension, or adrenal incidentalomas. The study included 1681 participants (915 with NFAI and 766 controls), all with F-1mgDST <1.8 µg/dL. Data collected included age, sex, body mass index (BMI), F-1mgDST, and adrenocorticotroph hormone (ACTH, available for all NFAI patients and for 176 controls).

Main outcomes included between-group differences in F-1mgDST and ACTH levels; diagnostic accuracy of F-1mgDST for identifying NFAI via receiver operating characteristic (ROC) analysis; and sensitivity, specificity, and odds ratios (ORs) for predicting NFAI across various F-1mgDST thresholds.

Results: Compared to controls, patients with NFAI were younger and had lower BMI and ACTH levels but significantly higher F-1mgDST values. ROC analysis demonstrated that an F-1mgDST threshold of 1.1 µg/dL (30 nmol/L) provided the best balance of sensitivity (54.8%) and specificity (57.2%), while an F-1mgDST threshold of 0.6 µg/dL (17 nmol/L) and of 1.7 µg/dL (47 nmol/L) the best sensitivity (93%) and specificity (93.5%), respectively, for distinguishing between control subjects and patients with NFAI. An F-1mgDST >1.1 µg/dL was independently associated with NFAI (OR, 1.58; 95% CI, 1.30–1.92) after adjusting for age, BMI, sex and presence of hypertension, type 2 diabetes and osteoporosis. The combination of obesity and male sex amplified the association, with obese men and F-1mgDST >1.1 µg/dL showing a nearly 3-fold higher likelihood of NFAI (OR, 2.87; 95% CI, 2.02–4.09).

Conclusions and Relevance: Among individuals with cortisol concentrations within the currently accepted normal range after dexamethasone suppression, those with NFAI display significantly higher F-1mgDST levels than control subjects. These findings indicate that the widely used threshold of 1.8 µg/dL may not reliably exclude mild autonomous cortisol secretion. A lower threshold of 1.1 µg/dL is the may improve identification of individuals with NFAI.

Abstract citation ID: lvag096.640

EP29 - ECE_3608 - Metabolic determinants of hepatic steatosis in primary aldosteronism, mild autonomous cortisol secretion, and Cushing's syndrome

Tugce Apaydin[1,2], Isabel Stüfchen[2], Júnia Ribeiro De Oliveira Longo Schweizer[2], Elisabeth Nowak[2], Christine Schmid-Tannwald[3], Felix Herr[3], Martin Reincke[2], Friederike Völter[2] and Nabeel Mansour[3]

[1]Acıbadem Ataşehir Hospital, Istanbul, Türkiye; [2]Department of Medicine IV, LMU University Hospital, Munich, Germany;

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[3]Department of Radiology, LMU University Hospital, Munich, Germany

Background: Metabolic dysfunction–associated steatotic liver disease (MASLD) is closely linked to obesity, diabetes mellitus, and dyslipidemia. Patients with primary aldosteronism (PA), mild autonomous cortisol secretion (MACS), and Cushing's syndrome (CS) frequently exhibit metabolic abnormalities; however, the prevalence of MASLD and the relative contribution of hormonal excess versus metabolic factors remain unclear. We aimed to evaluate the prevalence of MASLD and its metabolic and hormonal determinants in patients with PA, CS, and MACS.

Methods: This cross-sectional study included 229 treatment-naive patients who underwent unenhanced abdominal computed tomography (CT). Eigthy-eigth with PA, 81 with MACS (including 34 with concomitant PA and cortisol cosecretion), and 60 with CS. Hepatic steatosis was assessed using the liver-to-spleen (L/S) attenuation ratio. Noninvasive steatosis and fibrosis indices, including the hepatic steatosis index (HSI), triglyceride–glucose (TyG) index were calculated.

Results: The prevalence of MASLD was 28.4% in PA, 26.6% in CS, and 29.6% in MACS ($P > .05$). Liver attenuation and L/S ratio did not differ significantly among groups but were strongly correlated with visceral adiposity, fasting glucose, insulin, HbA1c, triglyceride levels, HSI, and TyG index (all $P < .05$). In the multivariable linear regression diabetes mellitus was independently associated with lower liver attenuation after adjustment for age, sex, and body mass index ($\beta = -11.10$ HU, 95% CI: −16.40 to −5.79). In contrast, no significant associations were observed between hepatic steatosis and measures of cortisol excess (serum cortisol, 24-hour urine free cortisol, or midnight salivary cortisol) or aldosterone levels.

Conclusions: Hepatic steatosis is prevalent and shows a comparable distribution among patients with PA, CS, and MACS. Its presence is primarily driven by metabolic factors, particularly diabetes mellitus, BMI, visceral adiposity, and hypertriglyceridemia, rather than by the direct effects of hormonal excess.

Abstract citation ID: lvag096.641

EP30 - ECE_2006 - Sex differences in clinical phenotype and therapeutic response of renin-independent aldosterone production in adrenal incidentalomas: a prospective Latin American cohort study

Thomas Uslar[1,2], Benjamín Sanfuentes[1], Roberto Olmos[3], Alberth Burnier[4], Pauline Böhm[5], Cristian Carvajal[1], Carlos Fardella[1], Fidel Allende[1], Sandra Solari[1], Anand Vaidya[6], Felix Beuschlein[2] and René Baudrand[1]

[1]CETREN-UC, Red de Salud UC-CHRISTUS, Endocrinology, Pontificia Universidad Católica de Chile, Santiago, Chile; [2]Department of Endocrinology, Diabetology and Clinical Nutrition, University of Zurich, Universitätsspital Zürich, Zürich, Switzerland; [3]Fund Arturo López Pérez, Endocrinology, Santiago, Chile; [4]Hospital Las Higueras, Talcahuano, Chile; [5]Pontificia Universidad Católica de Chile, Santiago, Chile; [6]Endocrinology, Brigham and Women's Hospital, Harvard Medical School, Boston, United States

Background: Biological sex influences clinical presentation and treatment response in primary aldosteronism (PA). However, sex-related differences across the spectrum of renin-independent aldosterone production, including mild phenotypes, remain insufficiently characterized. This knowledge gap is particularly relevant in Latin America, where data on adrenal incidentalomas and PA are scarce.

Objective: To evaluate sex differences in clinical presentation and therapeutic response across the spectrum of renin-independent aldosterone production in patients with incidental adrenal adenomas from a Latin American population.

Design: Prospective cohort study.

Methods: We included 383 consecutive patients with incidental adrenal adenomas (298 women, 85 men). Baseline clinical and biochemical characteristics were compared by sex. Low-renin was defined by direct renin <10 μU/mL and the severity of aldosterone production was classified according to plasma aldosterone concentrations (PAC), measured by immunoassay, as mild (PAC > 5 ng/dL), moderate (PAC 5-15 ng/dL), or severe (PAC > 15 ng/dL). Hypertensive patients ($n = 253$) were followed for a median of 20 (10-33) months and managed according to the level of adrenal hormone excess: conventional treatment for non-functioning lesions, or mineralocorticoid receptor antagonists (MRA) or adrenalectomy for low-renin hypertension. Treatment response was assessed using PAMO criteria for MRA therapy and PASO criteria for surgical treatment.

Results: At baseline, men showed a higher prevalence of hypertension (66% vs 52%, $P = .021$) and required more antihypertensive medications (defined daily dose 2.00 [1.00–3.00] vs 1.25 [0.60–2.50], $P = .018$). A low-renin phenotype was identified in 153 patients (40%). Women more frequently presented with mild aldosterone production (61.8% vs 33.3%, $P = .005$), whereas men had higher prevalence of severe phenotype (43.3% vs 13.8%, $P < .001$). Men exhibited higher PAC, aldosterone-to-renin ratio, and 24-hour urinary aldosterone and potassium excretion, along with lower plasma potassium, while natriuresis was similar between sexes. With individualized aldosterone-targeted therapy, blood pressure and renin improved across all magnitudes of renin-independent aldosterone production. There were no sex differences in treatment modality (MRA vs surgery) or MRA dose. Complete clinical response was comparable between sexes, whereas complete biochemical response was more frequent in men (100% vs 79%, $P = .016$).

Conclusions: In this prospective Latin American cohort, renin-independent aldosterone production was highly prevalent among patients with adrenal incidentalomas and was associated with a more severe clinical and biochemical phenotype in men. Aldosterone-directed therapy improved outcomes even in the mild phenotype, with superior biochemical response in men. These findings highlight the relevance of biological sex in the evaluation and personalized management of renin-independent aldosterone production, particularly in underrepresented populations.

Abstract citation ID: lvag096.642

EP31 - ECE_2675 - Impact of preprocedural supine time on adrenal venous sampling outcomes in primary aldosteronism: a retrospective single-center study

Xiaoxiao Song[1,2], Minzhi He[3], Minyue Jia[4], Yongli Ji[5], Yuhao Zhang[1], Xin Pan[1,6] and Zhenjie Liu[3]

[1]Endocrinology, The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China; [2]Endocrinology, The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China; [3]Vascualr Surgery, The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China; [4]The Second

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China; [5]Hangzhou, China; [6]Endocrinology, The First People's Hospital of Xiaoshan District, Hangzhou, China

Background: Primary aldosteronism (PA) is a common cause of refractory hypertension, and adrenal venous sampling (AVS) is the gold standard for lateralizing PA. Although preprocedural supine rest is recommended to reduce posture-related hormonal fluctuations, its optimal duration remains unclear.

Objective: To evaluate whether a preprocedural supine time of overnight versus 2 hours before AVS affects PA subtype classification.

Methods: This single-center retrospective study included patients with confirmed PA who underwent AVS between 2016 and 2025. AVS was performed without adrenocorticotropic hormone stimulation. Patients were retrospectively grouped according to preprocedural supine duration (overnight vs 2 hours). Successful catheterization was defined by a selectivity index (SI) ≥ 2.0, and lateralization by a lateralization index (LI) ≥ 2.0. Between-group comparisons were performed using appropriate parametric or nonparametric tests. A two-sided $P < .05$ was considered statistically significant.

Results: A total of 251 patients with successful AVS were included (overnight group, $n = 116$; 2-hour group, $n = 135$). AVS results revealed no significant differences in aldosterone concentrations between the overnight and 2-hour groups (right adrenal vein: 2472.50 [821.75–12,262.50] pg/mL vs 3130.00 [1100.00–18600.00] pg/mL, $P = .3266$; left adrenal vein: 2285.00 [716.75–8220.00] pg/mL vs 2220.00 [654.50–9390.00] pg/mL, $P = .7802$). Cortisol concentrations were also comparable between groups (right adrenal vein: 2902.00 [1121.50–6626.00] nmol/L vs 2407.00 [1216.00–7692.00] nmol/L, $P = .9381$; left adrenal vein: 2040.00 [912.89–4620.50] nmol/L vs 2056.00 [899.00–3763.50] nmol/L, $P = .7417$), resulting in similar SI values (right adrenal vein: 13.14 [6.32–22.65] vs 14.03 [5.24–28.05], $P = .7058$; left adrenal vein: 10.07 [4.81–21.61] vs 8.65 [4.29–19.80], $P = .6027$).

LI and contralateral suppression index (CI) values showed no significant differences between the overnight and 2-hour groups in patients with left-sided dominance ($n = 94$; LI 7.55 [3.26–28.60] vs 23.41 [3.60–87.80], $P = .0895$; CI 0.35 [0.15–0.72] vs 0.32 [0.12–0.80], $P = .7883$), right-sided dominance ($n = 100$; LI 12.03 [4.50–30.75] vs 14.15 [4.09–38.65], $P = .9132$; CI 0.30 [0.13–0.53] vs 0.35 [0.13–0.67], $P = .4751$), or bilateral aldosterone secretion ($n = 57$; LI 0.97 [0.77–1.36] vs 1.09 [0.73–1.30], $P = .8795$).

Conclusions: In this retrospective cohort, overnight versus 2-hour preprocedural supine rest was not associated with differences in AVS selectivity index, lateralization, or PA subtype classification. These findings suggest that a shorter supine duration may be feasible without compromising AVS interpretation.

Abstract citation ID: lvag096.643

EP32 - ECE_2312 - Long-term effectiveness and safety of finerenone versus spironolactone in patients with primary aldosteronism in China: a real-world multicenter prospective cohort study

Fan Yang[1], Yuxing Lou[2], Ziwei Zhang[1], Yunfeng Du[3], Jie Zhang[3], Yan Ren[4], Anli Tong[5], Zuoling Xie[6], Bimin Shi[7], Jianping Liu[8], Libin Liu[9], Dalong Zhu[1] and Ping Li[1]

[1]Department of Endocrinology, Endocrine and Metabolic Disease Medical Center, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, China; [2]Department of Endocrinology, Endocrine and Metabolic Disease Medical Center, Nanjing Drum Tower Hospital Clinical College of Nanjing University of Chinese Medicine, Nanjing, China; [3]The Second People's Hospital of Changzhou, the Third Affiliated Hospital of Nanjing Medical University, Changzhou, China; [4]Department of Endocrinology, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China Chengdu, China; [5]Department of Endocrinology, Key Laboratory of Endocrinology, National Health Commission of the People's Republic of China, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, No.1 Shuaifuyuan, Beijing 100730, People's Republic of China; [6]Nanjing, China; [7]Department of Endocrinology, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu 215006, China Suzhou, China; [8]Department of Endocrinology and Metabolism of the Second Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang, Jiangxi, 330031, People's Republic of China Nanchang, China; [9]Department of Endocrinology, Fujian Medical University Union Hospital, Fuzhou, China

Background: Finerenone, a novel nonsteroidal mineralocorticoid receptor antagonist (MRA), has demonstrated short-term efficacy and safety in patients with primary aldosteronism (PA). However, evidence for its long-term effectiveness and safety versus spironolactone in real-world settings remains scarce.

Aim: To compare the long-term effectiveness and safety of treatment strategies centered on finerenone versus spironolactone in PA patients in a real-world setting.

Methods: The multicenter prospective cohort included PA patients from eight hospitals in China who had completed a prior single-arm trial of finerenone. According to the actual treatment during follow-up (>6 months), the patients were categorized into finerenone continuation (FIN) or spironolactone switch (SPI) groups. Concomitant antihypertensive therapy followed routine practice. The primary endpoint was the integrated control rate (office BP <140/90 mmHg and normokalemia without potassium supplementation). Secondary endpoints included changes in ambulatory and office BP parameters, plasma renin activity (PRA), Primary Aldosteronism Medical Treatment Outcome (PAMO) response rates, and adverse events. Multivariable models were adjusted for baseline and defined daily dose (DDD) changes.

Results: A total of 37 PA patients were included (FIN: 26; SPI: 11) and received mean daily doses of 21.9 mg of finerenone or 40 mg of spironolactone, respectively. Baseline characteristics were comparable between the groups. Primary endpoint: After adjustment for the DDD, no significant difference in integrated control rate was observed (FIN: 53.8% vs. SPI: 63.6%; adjusted OR = 0.289; 95% CI 0.039–2.127; $P = .223$). Secondary endpoints: Office BP decreased significantly in both groups (FIN: −15.4/−10.0 mmHg; SPI: −19.9/−10.9 mmHg; adjusted $P > .05$ between groups). Daytime systolic BP decreased similarly (FIN: 11.0 mmHg; SPI: 13.7 mmHg; adjusted $P = .677$). No significant differences were observed in posttreatment serum potassium concentrations (FIN: 4.06 mmol/L vs. SPI: 4.10 mmol/L; $P = .611$) or PRA (FIN: 0.41 [0.14–1.01] ng/mL/h vs. SPI: 0.53 [0.09–1.11] ng/mL/h; $P = .088$). The PAMO complete biochemical (23.1% vs. 27.3%; adjusted $P = .179$) and clinical (11.5% vs. 9.1%; adjusted $P = .772$) response rates were comparable. No gonadal adverse events occurred in the FIN group; 3 cases of breast

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

pain (27.3%) were reported in the SPI group ($P = .021$). No hyperkalemia occurred, and eGFR remained stable in both groups.

Conclusions: This real-world study indicates that finerenone- and spironolactone-based strategies demonstrate similar efficacy against PA in terms of long-term blood pressure control, biochemical improvement, and PAMO response. Furthermore, finerenone is not associated with gonad-related adverse effects. This study extends the evidence and supports the use of finerenone in the management of PA.

Abstract citation ID: lvag096.644

EP33 - ECE_2563 - Revisiting the 10-HU threshold: unenhanced CT attenuation in functional adrenal adenomas

Tugce Apaydin[1,2], Isabel Stüfchen[2], Júnia Ribeiro De Oliveira Longo Schweizer[2], Elisabeth Nowak[2], Christine Schmid-Tannwald[3], Felix Herr[4], Martin Reincke[2], Nabeel Mansour[3] and Friederike Völter[2]

[1]Acıbadem Ataşehir Hospital, Istanbul, Türkiye; [2]Department of Medicine IV, LMU University Hospital, Munich, Germany; [3]Department of Radiology, LMU University Hospital, Munich, Germany; [4]Radiology, Department of Radiology, LMU University Hospital, Munich, Germany

Background: Although adrenocortical adenomas typically show low unenhanced attenuation (≤10 HU) on CT, this benignity criterion has limited sensitivity, particularly in lipid-poor and hormonally active tumors. We aimed to evaluate unenhanced CT attenuation across different functional and non-functioning adrenal adenoma subtypes.

Methods: In this retrospective study, 167 surgically proven patients with non-enhanced CT of the adrenals as well as complete clinical and biochemical records were included: unilateral primary aldosteronism (PA) defined by complete or partial biochemical success after adrenalectomy ($n = 64$), mild autonomous cortisol secretion (MACS) ($n = 48$), Cushing's syndrome (CS) ($n = 31$), and compared to non-functioning adrenal adenomas (NFA) ($n = 24$, no surgical proof). After testing for normality, attenuation values were compared using the Kruskal-Wallis test. Frequencies were compared using Fisher's exact test.

Results: Adrenal adenomas in CS showed higher attenuation (19.3 ± 14.0 HU) than PA (10.5 ± 12.7 HU), MACS (6.8 ± 16.0 HU), and NFA (5.4 ± 19.9 HU, $P = .003$). Notably, lesions with >10 HU were common not only in CS (67.7%) but also in PA (48.4%) and MACS (43.7%). Values >20 HU were significantly more common in CS than in the other groups (51.6%, $P = .029$). In CS, attenuation correlated positively with baseline cortisol ($r = 0.508$, $P = .035$), midnight salivary cortisol ($r = 0.454$, $P = .013$), and 1 mg DST ($r = 0.611$, $P < .001$). In multivariable analysis, cortisol ($P = .014$) and 1 mg DST ($P = .015$) independently predicted attenuation ($R^2 = 26.2\%$).

Conclusions: Unenhanced CT attenuation >10 HU is common in cortisol-producing adenomas, observed in approximately two-thirds of patients, and is also frequently seen in PA and MACS. This finding should be carefully considered in routine clinical decision-making.

Abstract citation ID: lvag096.645

EP34 - ECE_2717 - Evaluation of 18-oxocortisol (18-OXOF) as a marker of disease control in Congenital Adrenal Hyperplasia (CAH): uncertain origins and potential diagnostic implications

Joseph Tonge[1], Irina A Bacila[1,2], Sabah Alvi[3], Tim Cheetham[4], Liz Crowne[5], Urmi Das[6], Mehul Dattani[7], Justin Davies[8,9], Evelien Gevers[10], David Marshall[11], Ruth Krone[12], Leena Patel[13], Tabitha Randell[14], Fiona Ryan[15], Ajay Thankamony[16], Faisal Ahmed[17], Nils Krone[1,2] and Brian Keevil[11]

[1]Division of Clinical Medicine, School of Medicine and Population Health, University of Sheffield, Sheffield, United Kingdom; [2]Department of Paediatric Endocrinology, Sheffield Children's Hospital, Sheffield, United Kingdom; [3]Leeds General Infirmary, Leeds, United Kingdom; [4]Great North Children's Hospital, Newcastle upon Tyne, United Kingdom; [5]Bristol Royal Hospital for Children, Bristol, United Kingdom; [6]Alder Hey Children's Hospital, Liverpool, United Kingdom; [7]Great Ormond Street Hospital, London, United Kingdom; [8]University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom; [9]University of Southampton, Southampton, United Kingdom; [10]Centre For Endocrinology, William Harvey Research Institute, Queen Mary University, London, United Kingdom; [11]Biochemistry, Manchester University NHS Foundation Trust, Manchester, United Kingdom; [12]Birmingham Women's & Children's Hospital, Birmingham, United Kingdom; [13]Stockport, United Kingdom; [14]Nottingham Children's Hospital, Nottingham, United Kingdom; [15]Oxford Children's Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom; [16]Department of Paediatrics, University of Cambridge, Cambridge, United Kingdom; [17]Developmental Endocrinology Research Group, University of Glasgow, Glasgow, United Kingdom

Introduction: 18-OXOF is a hybrid adrenal steroid extensively studied in primary aldosteronism (PA), where its production reflects dysregulated aldosterone synthesis under combined renin–angiotensin and adrenocorticotropic hormone (ACTH) influence. Although typically considered a marker of mineralocorticoid pathway activation, we identified measurable 18-OXOF concentrations in patients with CAH, raising the possibility that it reflects altered adrenal steroidogenic activity beyond mineralocorticoid regulation.

Methods: Clinical, biochemical, and treatment data were analysed in patients with CAH to evaluate 18-OXOF as a candidate marker of disease control. Established biochemical markers included 17-hydroxyprogesterone (17-OHP), androstenedione, testosterone, 11-ketotestosterone, hydrocortisone dose normalised to body surface area (HCBSA), and 21-deoxycortisol. Mineralocorticoid control was assessed using plasma renin concentrations adjusted for fludrocortisone dose per body surface area. Serum steroids were measured by LC-MS/MS. Multivariable linear regression models were used to examine associations between 18-OXOF and biochemical indicators of CAH control, conceptualised as a marker of ACTH and renin modulated adrenal steroidogenesis.

Results: Eighty-four patients from 13 UK sites were included (age 8–18 years; mean HCBSA 14.03 mg/m^2, SD 3.8). 18-OXOF, detectable in sixty patients, showed strong independent associations with 18-OHF, 21-deoxycortisol, and 17-OHP, explaining a significant proportion of variance after adjustment for age and sex (R^2

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

= 0.66, $P < .001$). There is a significant positive correlation between 18-OXOF with both actual hydrocortisone dose and when controlled for using HCBSA ($P = .01$, $P = .047$ respectively). 18-OXOF was not associated with plasma renin concentrations after adjustment for fludrocortisone dose normalised to body surface area and age ($R^2 = 0.23$, $P = .20$), nor was it strongly associated with blood pressure, indicating that 18-OXOF does not reflect mineralocorticoid control in CAH. Although 18-OXOF is traditionally considered a marker of aldosterone pathway activation in PA, the physiological basis for its measurable concentrations in CAH is unclear. This finding suggests that 18-OXOF may reflect alternative steroidogenic pathways in CAH and highlights its potential as a confounding factor in the biochemical evaluation of PA.

Conclusions: 18-OXOF is produced via hybrid adrenal steroidogenic pathways that involve both cortisol and aldosterone biosynthesis, rendering it sensitive to altered steroid flux characteristic of CAH. Its strong association with proximal pathway intermediates and lack of association with mineralocorticoid control suggest that 18-OXOF may reflect glucocorticoid dependent adrenal activity rather than treatment dosing or haemodynamic status. These findings support 18-OXOF as a pathway specific biomarker of biochemical CAH disease control, with potential utility for monitoring disease, warranting further investigation.

Abstract citation ID: lvag096.646

EP36 - ECE_3906 - Study design of a phase 3, randomized, double-blind, placebo-controlled trial (CALM-CAH) to evaluate atumelnant in adult patients with congenital adrenal hyperplasia

Nicole Reisch[1], Deborah Merke[2], Tania Bachega[3], Richard Auchus[4], Alejandro Ayala[5], Yang Wu[5], Eduardo De La Torre[5] and Umasuthan Srirangalingam[6]

[1]Medizinische Klinik and Poliklinik IV, Klinikum der Universität München, LMU München, Munich, Germany; [2]National Institutes of Health Clinical Center and Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD, United States; [3]Laboratorio de Hormonios e Genetica Molecular-LIM 42, da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; [4]Division of Metabolism, Endocrinology, and Diabetes and the Departments of Internal Medicine and Pharmacology, University of Michigan, Ann Arbor, MI, United States; [5]Crinetics Pharmaceuticals, Inc., San Diego, CA, United States; [6]Endocrinology & Diabetes, University College London Hospitals NHS Foundation Trust, London, United Kingdom

In classic (21-hydroxylase deficiency) congenital adrenal hyperplasia (CAH), normal steroidogenesis pathways are disrupted, leading to hypocortisolism and hyperandrogenism. CAH management traditionally relied on glucocorticoid (GC) dosing to suppress excess adrenocorticotropic hormone. This approach often fails to normalize adrenal androgens without supraphysiologic GC exposure, which results in considerable health impairment in patients with CAH. There is substantial unmet need for therapies that reduce GC dosing to physiologic levels while maintaining normalized androgen levels. Atumelnant (CRN04894) is a first-in-class, once-daily, oral, selective melanocortin type 2 receptor antagonist in development for CAH treatment. In a 12-week, Phase 2, open-label study in patients with CAH (NCT05907291), atumelnant induced rapid, substantial, and sustained reductions in serum androstenedione (A4) and 17-hydroxyprogesterone (17-OHP) levels and reduced total adrenal volume in most participants. CALM-CAH (NCT07144163) is a Phase 3, randomized, double-blind, placebo-controlled trial to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of atumelnant in adults (≥18-75) with classic CAH. Patients on a stable GC dose for ≥3 months and A4≥the upper limit of normal (ULN) or those with A4<ULN receiving ≥14 mg/m^2/d GC doses are eligible. Patients will be randomized 2:1 to atumelnant 80 mg or placebo once daily for 32 weeks with optional dose escalation to 120 mg once daily at Week 20. GC dose reduction occurs from Weeks 2-12 and Weeks 16-28, to reach the target physiologic dose of <11 mg/m^2/d hydrocortisone equivalent. Patients who complete treatment may enroll in an open-label extension. The primary endpoint is proportion of patients with morning post-GC (2-3 hours after GC dosing) A4≤ULN who are on physiologic GC replacement at Week 32. Key secondary endpoints include Week 2 morning A4 percent change from baseline (CFB) and, at Week 32, proportion of patients with morning pre-GC A4≤ULN who are on physiologic GC replacement, percent CFB in morning 17-OHP, and CFB in GC daily dose when post-GC A4≤ULN. In an optional male reproductive health substudy, endpoints include changes in semen quality, reproductive biomarkers, and testicular adrenal rest tumor volume. Safety endpoints include incidence of treatment-emergent adverse events. This global Phase 3 trial, currently enrolling participants, will evaluate efficacy and safety of atumelnant in patients with CAH. These results will determine if atumelnant's novel mechanism of action at the adrenal gland allows for clinically meaningful GC reductions without compromising androgen control, providing critical insight into patient benefits and risks.

Abstract citation ID: lvag096.647

EP37 - ECE_2711 - Two cases of renovascular hypertension diagnosed after stillbirth and successfully treated with percutaneous transluminal renal angioplasty

Saya Takebe[1], Yasufumi Seki[1], Saori Kitayama[1], Kiyotaka Hirata[1], Noriyoshi Takano[1], Daisuke Watanabe[1], Tomohiro Kawaji[2], Satoru Morita[2] and Atsuhiro Ichihara[1]

[1]Department of Endocrinology and Hypertension, Tokyo Women's Medical University, Tokyo, Japan; [2]Department of Diagnostic Imaging & Nuclear Medicine, Tokyo Women's Medical University, Tokyo, Japan

Background: Renovascular hypertension (RVHT) is a potentially reversible etiology of secondary hypertension if treated with vascular intervention. Recently, RVHT has been reported as a risk of stillbirth in pregnancy. However, the association between vascular intervention and subsequent fetal outcomes in patients with RVHT has been unclear. Herein, we report two cases of RVHT diagnosed after stillbirth and treated with percutaneous transluminal renal angioplasty (PTRA), resulting in successful subsequent pregnancies.

Case 1: A 40-year-old woman (gravida 2, para 1) presented with elevated blood pressure (BP) of 150/100 mmHg and proteinuria at 10 weeks' gestation. She had a history of preeclampsia during her first pregnancy at 36 years of age, and the BP normalized

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

after the delivery. Although α-methyldopa 500 mg daily was initiated and reduced her BP to 140/90 mmHg, intrauterine fetal death occurred at 17 weeks' gestation. Antihypertensive therapy was switched to nifedipine 40 mg daily. Contrast-enhanced computed tomography angiography three months postpartum demonstrated right renal artery stenosis. PTRA successfully normalized her BP and diminished the proteinuria, which allowed discontinuation of the antihypertensive drug. Three months after the PTRA, she conceived again and remained normotensive without proteinuria during her third pregnancy, resulting in a successful delivery.

Case 2: A 41-year-old woman (gravida 1, para 0) with no prior history of hypertension developed hypertension during her first pregnancy and experienced intrauterine fetal death at 15 weeks' gestation. Hypertension persisted postpartum with BP of 145/90 mmHg, and treatment with amlodipine 5 mg daily was initiated. One month postpartum, contrast-enhanced computed tomography angiography revealed left renal artery stenosis. PTRA improved her BP and allowed discontinuation of antihypertensive medication, but residual stenosis was revealed six months after the PTRA. One year after the PTRA, she conceived again. From 25 weeks' gestation, her BP gradually increased, and she underwent a cesarean delivery at 35 weeks' gestation, resulting in the birth of a healthy baby. Antihypertensive therapy with amlodipine 2.5 mg daily was resumed after delivery.

Discussion: We present two cases of RVHT suspected to be caused by fibromuscular dysplasia (FMD), which were diagnosed after stillbirth and treated with PTRA, resulting in successful subsequent fetal outcomes. Our cases suggest that PTRA may be associated with improved pregnancy outcomes in pregnant women with RVHT and a history of stillbirth.

Abstract citation ID: lvag096.648

EP38 - ECE_2770 - Peritoneal dialysis is superior to haemodialysis in removal of adrenal corticosteroid metabolites

Maria Tomkins[1,2], Darran Mc Donald[1,2], Merah Al Busaidy[2], Fozia Shaheen[3], Angela Taylor[3], Abigail Armstrong[4], Christina Martyn[4], Olive McEnroe[4], Amy Hudson[4], Ciara N. Magee[4], Declan de Freitas[4], Mark Denton[4], Peter Conlon[4], Carol Traynor[4], Colm Magee[4], Conall O'seaghdha[4], Wiebke Arlt[5,6], Michael W. O'reilly[1,2] and Mark Sherlock[1,2]
[1]Department of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland; [2]Department of Endocrinology, Beaumont Hospital, Dublin, Ireland; [3]Institute of Metabolism and Systems Research, Birmingham, United Kingdom; [4]Department of Nephrology, Beaumont Hospital, Dublin, Ireland; [5]Medical Research Council Laboratory of Medical Sciences, London, United Kingdom; [6]Institute of Clinical Sciences, Imperial College London, London, United Kingdom

Background: Disruption of adrenal steroid metabolism is increasingly recognised as a feature of advanced chronic kidney disease (CKD), yet the influence of dialysis modalities and the extent of dialytic steroid clearance remain unclear. We have previously shown the contributing role of impaired 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) activity to cardiovascular risk in CKD. We sought to further review the impact of renal replacement therapy on adrenal steroid metabolism and biosynthesis providing the first comprehensive evaluation of adrenal steroidogenesis in end-stage renal disease (ESRD).

Methods: Thirty patients [intermittent haemodialysis (HD) $n = 15$; nocturnal automated peritoneal dialysis (PD) $n = 15$] underwent serial serum and dialysate sampling over approximately four hours during a morning HD session or peritoneal equilibrium test (PET). Two matched control cohorts: non-dialysis dependent CKD stage 5 ($n = 15$) and healthy controls ($n = 15$), were included in the analysis of baseline samples. Samples were analysed using liquid chromatography–tandem mass spectrometry.

Results: ESRD was associated with profound adrenal steroid perturbations, driven primarily by reduced 11β-HSD2 activity and impaired urinary clearance of steroids which did not resolve with either dialysis modality. HD caused a marked fall in serum aldosterone [542.5 pmol/L (196.5-1550) at baseline vs 65.3 pmol/L (29.2-376.4) at end, $P < .01$] in parallel with potassium reduction, whereas PD showed no significant aldosterone change.

Neither modality effectively cleared mineralocorticoids in dialysate fluid. PD produced a significant decline in serum cortisol falling from 362.0 nmol/L (261.0–445.9) at baseline to 267.0 nmol/L (202.0–287.0) at 240 minutes ($P = .02$) with reciprocal glucocorticoid accumulation in dialysate. HD showed minimal steroid recovery in effluent and no change in circulating serum glucocorticoids. To further demonstrate removal of glucocorticoids in dialysate we calculated delta fluid concentrations which were significantly higher in PD compared to HD [δPD fluid cortisol 9.3 nmol/l (7.7-12.4) vs δHD fluid cortisol 1.3 nmol/L (−7.1 to 5.8), $P = .0004$; δPD fluid cortisone 8.8 nmol/L (6.7-10.0) vs δHD fluid cortisone 1.0 nmol/L (−0.8 to 2.5), $P < .0001$].

PD also demonstrated superior clearance of adrenal androgens (androstenedione, 11β-hydroxyandrostenedione and 11-ketoandrostenedione), which were largely unquantifiable in HD fluid. These differences likely reflect the greater permeability of the peritoneal membrane to protein-bound solutes.

Conclusions: PD achieved meaningful glucocorticoid and androgen clearance and preserved expected cortisol decline, whereas HD showed negligible corticosteroid dialysate concentration. These differences likely reflect superior clearance of protein-bound solutes, higher membrane permeability and haemodynamic stability associated with PD. PD may therefore better support physiological adrenal corticosteroid exposure in patients with ESRD.

Abstract citation ID: lvag096.649

EP39 - ECE_1123 - Hyporeninemic hypoaldosteronism as a manifestation of long-COVID: a case report

Maria Chrysoula Tatarida Palla, Marika Kokkorou, Galateia Stathori, Andreas Bampilis, Michalis Magklis, Myrsini Chamakioti, Olga Tsantarlioti, Eleni Papanikolaou and George Chrousos
Endocrine Unit, National and Kapodistrian University of Athens, Athens, Greece

COVID-19 is increasingly recognized to cause persistent multisystem dysregulation, including autonomic and/or renin–angiotensin–aldosterone system (RAAS) disturbances. Hyporeninemic hypoaldosteronism (HH) is a rare finding after COVID-19 and may reflect autonomic or systemic dysfunction.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

We report a case of a previously healthy 56-year-old man who presented with persistent mild hyperkalemia during follow-up at a post-COVID (Long COVID) clinic. The patient had a history of SARS-CoV-2 infection several months earlier, followed by chronic fatigue, scapular pain, and reduced exercise tolerance. He had no prior renal, rheumatologic, or endocrine disorders.

Nephrological evaluation excluded kidney disease, and rheumatologic screening for fibromyalgia and autoimmune pathology was negative. Endocrine assessment revealed low plasma renin activity and aldosterone levels, consistent with hyporeninemic hypoaldosteronism. Cortisol and other hormonal parameters were within normal limits. The patient did not report symptoms of hypotension or volume depletion.

In the absence of structural renal or adrenal pathology, the findings suggest post-COVID dysregulation of RAAS, likely secondary to autonomic dysfunction or persistent ACE2/angiotensin II imbalance. This case highlights a potential mechanism of post-viral RAAS impairment manifesting as subclinical hyporeninemic hypoaldosteronism without overt electrolyte derangement.

Hyporeninemic hypoaldosteronism may represent an underrecognized endocrine manifestation of long COVID, reflecting persistent autonomic or systemic dysregulation. Awareness of this entity is important for the evaluation of unexplained hyperkalemia in post-COVID patients.

Abstract citation ID: lvag096.650

EP40 - ECE_1628 - Case of differential diagnosis in a male patient with adrenal incidentaloma

Irina A. Vaychulis

Internal Medicine Department, South-Ural State Medical University, Chelyabinsk, Russia

Adrenal incidentalomas represent a heterogeneous condition, requiring a large differential diagnosis. Clinical, biochemical and radiological assessment is mandated to stratify patients into those requiring radiological surveillance, medical management or surgical intervention.

A 48-year-old male was referred to a surgeon with complaints of the left thigh muscle pain, weakness and heaviness in the legs, ossalgias, arthralgias, frequent feeling of heat and cold, subfebrile temperature, weight loss for about 6-8 months. US, MRI and CT showed a left thigh soft tissue mass with muscle rupture, edema, periostitis and contact destruction of the left femoral bone anterior surface. Diffuse connective tissue diseases were ruled out.

CT of the abdomen revealed right adrenal incidentaloma 39 × 23 mm, suspicious for malignancy (precontrast phase +50 HU, venous phase +65 HU, delayed phase +58 HU, absolute washout 47%, relative washout 11%). Laboratory examination showed elevated total and free normetanephrine in 24 h urine—721 (ULN 451) and 79,5 (ULN 43,2) mcg/24 h, respectively, and patient was referred for the preoperative preparation with preliminary diagnosis of (malignant?) pheochromocytoma (PCC).

On admission to our endocrine department, the diagnosis of PCC seemed doubtful, considering the presence of two separate lesions, accompanied by the signs of paraneoplastic syndrome, in the absence of arterial hypertension (AH) and any clear paroxismal manifestations. No alfa-adrenoblockers were administered. Further examination demonstrated normal serum electrolytes, TSH and PTH, adequate suppression of cortisol after overnight DST, normal blood pressure on 24 h monitoring, anemia, elevated ESR and CRP, hypoproteinemia.

Chest CT revealed the signs of central right cancer, the right lung and intrathoracic lymphatic nodules metastases. Biopsy results confirmed non-small cell lung cancer (adenocarcinoma). The same cells were found in the lymphatic nodules and femoral soft tissue mass. Repeated CT of the abdomen showed the rapid growth of adrenal mass up to 53 mm. Bone metastases were detected on SPECT. Preliminary diagnosis was reconsidered, and adrenal neoplasm was interpreted as a metastatic lesion, secondary to the lung adenocarcinoma with multiple metastases. Systemic anti-cancer therapy has been initiated.

Conclusions: We present the case of metastatic adrenal mass that had been revealed prior to the previously unknown primary lung cancer. Clinically silent adrenal incidentaloma was accompanied by moderate hormonal hyperscretion, and initially was regarded as PCC. Discordance between the laboratory and clinical data (elevated metanepfrines in the absence of AH and paroxysmal manifestations) requires rigorous systematic examination to avoid misdiagnosis and incorrect treatment.

Abstract citation ID: lvag096.651

EP41 - ECE_1093 - Changes in carotid arterial stiffness and strain parameters after treatment in primary aldosteronism: A prospective follow-up study using speckle tracking ultrasonography

Tugba Barlas[1], Mahinur Cerit[2], Halit Sendur[2], Sabri Engin Altıntop[1], Mehmet Muhittin Yalcin[1], Altinova Alev[1], Mujde Akturk[1], Fusun Toruner[1], Ayhan Karakoc[1] and Ethem Turgay Cerit[1]

[1]*Gulhane Training and Research Hospital, Endocrinology and Metabolism, Ankara, Türkiye;* [2]*Faculty of Medicine, Radiology, Gazi University, Ankara, Türkiye*

Aim: Although cardiovascular morbidity in primary aldosteronism (PA) can be partly prevented with appropriate treatment, the reversibility of vascular alterations remains uncertain. This study investigated vascular alterations in patients with PA using speckle tracking carotid strain (STCS) ultrasonography, which allows simultaneous assessment of arterial structure and function. It also aimed to evaluate changes in arterial stiffness and strain parameters during follow-up, comparing outcomes between unilateral adrenalectomy and mineralocorticoid receptor antagonist (MRA) treatment.

Methods: This study was conducted with a prospective follow-up design. All participants underwent a standardized diagnostic work-up for PA according to the current clinical guidelines, and the sample size was determined based on a priori power analysis. STCS ultrasonography was performed at baseline and six months post-treatment (surgical/medical). A 5-mm segment of the common carotid artery below the bulb was analyzed to quantify arterial compliance and distensibility (reflecting elasticity); elastic modulus, β-stiffness index, and pulse wave velocity (reflecting stiffness); as well as strain-related parameters, including displacement, strain, and strain rate.

Results: Thirty patients were included, of whom 22 received MRA therapy and 8 underwent unilateral adrenalectomy. Arterial

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

compliance increased in the overall cohort in both transverse and longitudinal planes and this improvement was significant in the surgical group in subgroup analyses ($P < .05$). Between-group comparisons revealed greater improvements in arterial compliance in the surgical than medical groups ($P = .033$). Arterial distensibility also increased in the transverse plane ($P < .05$), whereas no significant changes were observed in β-stiffness index, elastic modulus, PWV, or strain parameters in the overall group ($P > .05$). CIMT significantly decreased after treatment in the overall and medical groups ($P < .05$). Negative correlation was observed between the duration of hypertension and the post-treatment changes in PWV ($r = -0.429$, $P = .041$), β-stiffness index ($r = -0.389$, $P = .034$), and elastic modulus ($r = -0.537$, $P = .002$). Multivariate linear regression analysis identified younger age, shorter hypertension duration, male sex, and surgical treatment as independent predictors of greater post-treatment improvement in arterial compliance ($P < .05$).

Conclusions: This study is the first to longitudinally assess vascular changes in PA using STCS technique. Arterial compliance improved after treatment, particularly after adrenalectomy, whereas other stiffness parameters remained unchanged. Surgical treatment, younger age, male sex, and shorter hypertension duration independently predicted greater compliance improvement.

Abstract citation ID: lvag096.652

EP42 - ECE_2361 - Diagnostic value of positive saline infusion test for predicting lateralisation in intermediate-probability primary aldosteronism

Prethivan Pillai Gopalakrishnan, Ian Dorrington, Mohammed Shamsaldeen, Hamza Khan, Sarah Davies, Pallavi Hegde and Andrew Davison
Royal Liverpool University Hospital, Liverpool, United Kingdom

Background: Endocrine Society guidelines recommend aldosterone suppression testing to predict the likelihood of unilateral primary aldosteronism (PA) in patients with intermediate probability of lateralisation before adrenal vein sampling (AVS). This is based on limited evidence that incomplete suppression may suggest unilateral disease in intermediate subgroup. We aimed to evaluate whether saline infusion test (SIT) predicts unilateral disease among SIT-positive patients.

Method: We retrospectively reviewed 102 patients with biochemical evidence of PA from 2016-2025. Thirty-three patients with a positive SIT (post-SIT aldosterone >160 pmol/L) underwent AVS and or 18F-CETO PET-CT. AVS lateralisation was defined as a lateralisation index >4 without ACTH stimulation. Diagnostic performance of pre- and post-SIT aldosterone (iSyS immunoassay, IDS), renin (iSyS immunoassay, IDS), aldosterone-renin ratio, nadir potassium during screening, age, and sex were assessed using multivariable logistic regression and ROC analysis with 1000-bootstrap validation. Lateralisation probability was defined as: high; hypokalaemia (K < 3.5 mmol/L), aldosterone >554 pmol/L, and suppressed renin <5 mIU/L (assay detection limit), low; normokalaemia (3.5-5.3 mmol/L) and aldosterone <305 pmol/L and intermediate; aldosterone 305-554 pmol/L, aldosterone >554 pmol/L with normokalaemia and/or unsuppressed renin, or aldosterone <305 pmol/L with hypokalaemia.

Results: Of 33 SIT-positive patients, 39% had unilateral disease. Most were intermediate-probability ($n = 30$, 40% unilateral). Median age was 47 years in unilateral disease and 44 years in bilateral disease. Unilateral disease was more frequent in males (53%) than females (25%). In the intermediate subgroup, unilateral disease was associated with lower nadir potassium (median 3.0 mmol/L [IQR 2.8-3.6] vs 3.8 [3.6-3.9], $P = .002$) and higher post-SIT aldosterone (518 pmol/L [IQR 400-704] vs 248 [205-428], $P = .002$). Other variables were not significant. In multivariable analysis, only nadir potassium was independently associated with unilateral disease (adjusted OR 1.3 per 0.1 mmol/L decrease, 95% CI 1.1-1.9). Hypokalaemia had 89% specificity which increased to 100% when the cut off of K is ≤2.8 mmol/L. Among normokalaemic intermediate patients, post-SIT aldosterone is significantly higher in unilateral cases (466 pmol/L [IQR 450-524] vs 235 [197-421], $P = .02$) with AUC 0.89 (95% CI 0.68-1.00).

Conclusions: Post-SIT aldosterone does not independently predict PA subtype in SIT-positive patients with intermediate probability of lateralisation and most patients had bilateral disease. However, it shows good discrimination in normokalaemic intermediate patients. Hypokalaemia is a strong predictor of unilateral disease. SIT may aid surgical decision-making selectively in normokalaemic intermediate-probability patients. Threshold interpretation should consider local assay context when applying guideline-recommended cut-offs. Further research should include SIT-negative patients to assess overall diagnostic performance.

Abstract citation ID: lvag096.653

EP43 - ECE_3524 - Visceral adiposity index predicts metabolic syndrome and cardiometabolic risk in patients with adrenal incidentalomas

Sanja Ognjanovic, Bojana Popovic, Valentina Elezovic Kovacevic, Dusan Ilic, Milica Opalic Palibrk, Lena Radic, Katarina Krstic, Natalija Dragicevic and Djuro MacUt
Department for Endocrine Tumors and Hereditary Cancer Syndromes, Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Belgrade, Serbia

Introduction: Patients with non-functioning adrenal incidentalomas (AIs) and autonomous cortisol secretion (ACS) are at increased risk of cardiometabolic disorders and mortality. Visceral adipose tissue accumulation contributes to insulin resistance and metabolic syndrome (MetS), and the Visceral Adiposity Index (VAI), a mathematical model that indirectly reflects cardiometabolic risk, has been proposed as a marker of visceral adipose tissue dysfunction. This study aimed to determine whether the VAI can serve as a predictor of MetS in patients with AIs.

Subjects and Methods: This retrospective cross-sectional study (2019–2024) included 167 patients with adrenal incidentalomas (AIs) (men, $n = 41$, 24.6%; women, $n = 126$, 75.4%). Anthropometric (BMI, waist circumference), biochemical (LDL, HDL, triglycerides), and hormonal (cortisol at 08:00 and 24:00, ACTH at 08:00, post-1 mg dexamethasone cortisol) assessments were performed. Insulin sensitivity was evaluated using HOMA-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

IR, and MetS was assessed according to IDF, AHA/NHLBI, and NCEP-ATP III criteria.

Results: Mean age, BMI, and waist circumference, as well as prevalence of diabetes, hypertension, and dyslipidemia, were similar between sexes. The prevalence of MetS according to IDF, AHA/NHLBI, and NCEP-ATP III criteria was 48.4%, 46.3%, and 41.5% in men, and 55.6%, 50.0%, and 44.4% in women, respectively. Unilateral AIs were present in 27 men (65.9%) and 69 women (54.8%), while bilateral AIs occurred in 14 men (34.1%) and 57 women (45.2%), with men exhibiting larger tumors (42.9 ± 21.5 mm vs 32.5 ± 17.7 mm, $P = .002$) and higher frequency of ACS (64.1% vs 45.7%, $P = .047$). Men had a higher prevalence of coronary artery disease, with no significant sex differences in cerebrovascular events. No significant differences were observed in ACTH, morning, midnight, or post-DST-1 mg cortisol levels. The VAI was significantly associated with blood pressure, fasting glucose, HbA1c, diabetes, HOMA-IR, and MetS, and emerged as the strongest predictor of MetS development (OR = 12.7, 95% CI 2.390–20.057, $P = .001$), alongside age and post-DST-1 mg cortisol.

Conclusions: In patients with AIs, VAI strongly predicts MetS and is associated with hypertension, impaired glucose metabolism, and insulin resistance, emphasizing the need for regular assessment to reduce long-term cardiometabolic risk.

Abstract citation ID: lvag096.654

EP44 - ECE_3714 - Adrenal incidentaloma and risk of metabolic dysfunction–associated fatty liver disease (MAFLD) and liver fibrosis assessed by non-invasive scores

Theodora Michalopoulou[1,2], Cristina Franco[1], Laia Martinez Guasch[1], Silvia Näf Cortes[1], Ariadna Prats Custal[1], Maria Castell[1], Luis Herrador[1], Nerea Tomas[1] and Ana Megia[1]
[1]*Hospital Universitario de Tarragona Joan XXIII, Tarragona, Spain;* [2]*Universitat Rovira I Virgili, Tarragona, Spain*

Background: Adrenal incidentalomas (AI) are frequently associated with adverse metabolic profiles, even in the absence of overt hormonal hypersecretion. Mild autonomous cortisol secretion (SAC) may contribute to insulin resistance, dyslipidemia, and chronic low-grade inflammation, key drivers of MAFLD and liver fibrosis (LF). However, the prevalence of MAFLD and its relationship with AI characteristics remain poorly defined.

Objective: To assess the prevalence of MAFLD and LF using non-invasive scores (FIB-4 and APRI) in patients with AI and to evaluate their association with tumor characteristics after adjustment for metabolic risk factors.

Methods: Retrospective observational study including 76 patients with radiologically diagnosed AI followed at a specialized adrenal pathology clinic. Epidemiological and metabolic data were collected. AI were classified according to hormonal functionality (non-functioning vs SAC), maximal tumor diameter, and laterality (unilateral vs bilateral). MAFLD was defined according to standard criteria using liver imaging and metabolic factors. LF risk was estimated using FIB-4 and APRI scores and categorized as low vs intermediate/high. Group comparisons were performed using t-tests, chi-square tests, and Pearson correlations. Multivariable binary logistic regression was used to identify independent predictors of intermediate/high fibrosis risk.

Results: Mean age was 63 ± 10.5 years, 54% were women, and 49% had obesity. Non-functioning adenomas were present in 44.7% and SAC in 55.3%. Low fibrosis risk was observed in 92.1% by APRI and 56.6% by FIB-4, while 43.4% had intermediate/high risk by FIB-4. MAFLD prevalence was 27.6%. In multivariable analysis, age was inversely associated with low fibrosis risk (OR 0.85, 95% CI 0.77–0.93; $P < .001$). Metabolic factors (BMI, type 2 diabetes, dyslipidemia, and hypertension) were independently associated with intermediate/high fibrosis risk (adjusted OR 1.3–2.5, all $P < .05$). Tumor functionality, size, and laterality were not independently associated with fibrosis scores.

Conclusions: More than one-quarter of patients with AI have MAFLD, and a substantial proportion show intermediate/high risk of liver fibrosis. Fibrosis risk is mainly driven by metabolic comorbidities rather than adrenal tumor characteristics, highlighting the need for systematic metabolic and hepatic assessment in all patients with AI.

Abstract citation ID: lvag096.655

EP45 - ECE_3825 - Urinary bladder paraganglioma: experience from a mini case series

Amina Al-Qaysi[1], Anoud Ramadan[1], Aisha Naseer[2] and Christine May[1]
[1]*Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM), Oxford, United Kingdom;* [2]*Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom*

Background: Urinary bladder paraganglioma is a rare neuroendocrine tumour and an uncommon cause of urinary bladder neoplasia. Because of its low incidence and variable clinical presentation, diagnosis may be delayed, particularly in non-functional cases. Functional tumours carry a risk of catecholamine-mediated perioperative complications.

Methods: A retrospective review was undertaken of patients with histologically confirmed urinary bladder paraganglioma managed at the Oxford University Hospitals NHS Foundation Trust. Data on clinical presentation, biochemical assessment, imaging, perioperative management, surgical treatment, and follow up outcomes were analysed.

Results: Four patients were included: three females and one male, with ages at presentation ranging from 16 to 41 years. None had a prior history of pheochromocytoma or paraganglioma. Clinical presentation was variable. One patient experienced functional symptoms characterised by post-micturition headache; one presented with haematuria; two also reported abdominal pain; and one tumour was detected incidentally during SDHB surveillance. Preoperative biochemical evaluation varied. One patient did not undergo testing because the diagnosis was not suspected preoperatively and was only made on histopathological examination. Two patients had urinary metanephrines measured, and one underwent both plasma and urinary assessment. Elevated normetadrenaline levels were identified in three patients. MIBG scintigraphy was performed in three patients, demonstrating uptake in two cases, while one lesion was non-avid; this lesion was smaller than those in the other cases. Preoperative blockade was administered in three patients, as one tumour was not suspected preoperatively. Surgical management consisted of transurethral resection of bladder tumour in three cases and laparoscopic partial cystectomy in one.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

No intraoperative haemodynamic instability or other complications were observed. Ongoing follow-up revealed no metastatic disease, recurrence, or additional pheochromocytoma or paraganglioma, with follow-up periods ranging from 50 to 118 months.

Conclusions: This mini case series highlights the heterogeneous clinical and biochemical presentations of urinary bladder paraganglioma, as well as the diagnostic challenges associated with this rare tumour. With appropriate perioperative preparation, surgical management can be undertaken safely and yield favourable outcomes. Increased awareness is essential to facilitate timely diagnosis, optimise perioperative care, and guide long term surveillance.

Abstract citation ID: lvag096.656

EP46 - ECE_2305 - CYP11B2 immunohistochemistry should be incorporated into the routine clinical diagnostic workup of primary aldosteronism: a case report

Iciar Martín Timón, Marta Leon del Campo, Olalla Meizoso-Pita, Isabel Huguet, Maria Llavero Valero, Mikaela Zubillaga, Alberto García Piorno, Inmaculada Moreno-Ruiz and Cristina Sevillano-Collantes
Endocrinology, Infanta Leonor University Hospital, Madrid, Spain

Primary aldosteronism (PA) is associated with an increased risk of cardiovascular complications compared with primary hypertension. Despite effective methods for diagnosing and treating PA, it remains markedly underdiagnosed and undertreated. This may in part be due to misconceptions that PA is only present in the setting of hypokalemia, adrenal macro-nodules, frankly elevated aldosterone levels, or severe hypertension

Case Report: A 48-year-old male was referred to our outpatient clinic of endocrinology for poorly controlled arterial hypertension despite treatment with Olmesartan 40 mg, Amlodipine 5 mg, Hydrochlorothiazide 25 mg, and Nebivolol 5 mg, also presenting with active smoking, type 1 obesity, obstructive sleep apnea, and dilated cardiomyopathy. Given the suspicion of secondary arterial hypertension, a PA screening test was performed with results of direct renin concentration: 2.95 mUI/mL, aldosterone: 25.50 ng/dL, and aldosterone/renin ratio: 8.24

A confirmation test is performed using the Captopril test, which shows an aldosterone increase of 28% (aldosterone before and after of 11.9 ng/dL and 15.3 ng/dL, respectively), with renin levels before and after of 0.51 mUI/mL and 1.3 mUI/mL, and cortisol remaining stable at 11.2 µg/dL. After the biochemical confirmation of primary aldosteronism (PA), a computed tomography (CT) scan is requested, which shows no adrenal lesions, leading to an adrenal vein sampling that ultimately demonstrates right adrenal lateralization. After the right adrenalectomy, pathological anatomy confirms the presence of multiple micronodules producing aldosterone (Immunohistochemistry positive for CYP11B2).

Currently, 3 months after surgery, the patient presents a complete response according to PASO criteria, maintaining normal blood pressure without antihypertensive treatment

Conclusions: PA is a form of curable arterial hypertension; therefore, it is important to make an accurate diagnosis. Adrenal venous sampling is the gold standard for diagnosing PA, being particularly important when imaging tests are inconclusive, either due to the high prevalence of non-functioning adrenal incidentalomas or due to the presence of millimetric lesions producing aldosterone. In our case the relevance of histopathology with morphologic and IHC evaluation in the clinical management of unilateral PA is confirmed. Histopathologic examination of adrenalectomy specimens with CYP11B2 IHC is therefore recommended for all patients operated for unilateral PA

Abstract citation ID: lvag096.657

EP48 - ECE_1265 - Psychosocial wellbeing index short form and cardiovascular disease risk: updated associations beyond Life's Essential 8 in a Korean Prospective Cohort

Seung Jin Han, Ja Young Jeon, Hae Jin Kim, Dae Jung Kim and Kwan-Woo Lee
Ajou University School of Medicine, Suwon, South Korea

Background: Psychological health is increasingly recognized as a relevant determinant of cardiovascular disease (CVD), yet psychosocial stress remains unaccounted for in the recently updated cardiovascular health metrics, known as Life's Essential 8 (LE8). Whether psychosocial stress independently contributes to CVD risk beyond LE8 components remains unclear. This study aimed to evaluate the association between psychosocial stress and incident CVD using updated analyses from a large Korean community-based cohort.

Methods: A total of 6410 adults from the Ansung–Ansan cohort of the Korean Genome and Epidemiology Study were included after excluding individuals with baseline CVD and those without complete data on psychosocial stress or LE8 metrics. Psychosocial stress was assessed using the Psychosocial Wellbeing Index Short Form (PWI-SF). LE8 cardiovascular health metrics were calculated according to modified American Heart Association recommendations. Incident CVD events—including myocardial infarction, coronary artery disease, cerebrovascular disease, and congestive heart failure—were identified via physician-diagnosed self-report. Cox proportional hazards models were used to evaluate associations, adjusting for age, sex, socioeconomic factors, and all LE8 metrics.

Results: Over a median follow-up of 13.8 years, 500 new CVD cases occurred. Higher PWI-SF scores were significantly associated with a greater risk of incident CVD even after full adjustment, including all LE8 components (HR: 1.321; 95% CI: 1.067–1.636; $P = .011$). This association remained robust in sensitivity analyses stratified by sex and baseline cardiovascular health status.

Conclusions: Elevated psychosocial stress is independently associated with increased CVD risk beyond Life's Essential 8 metrics in a large Korean adult cohort. These findings highlight a meaningful gap in current cardiovascular health assessment frameworks and support the integration of psychosocial factors into future risk stratification and prevention strategies.

Abstract citation ID: lvag096.658

EP49 - ECE_3754 - Aldosterone, renin and their ratio (ARR) in patients with newly diagnosed and untreated hypertension

Harpa Gunnarsdottir[1], Gudmundur Sigthorsson[1], Isleifur Olafsson[1], Thor Aspelund[2,3], Vilmundur Gudnason[2,4] and Helga Sigurjónsdóttir[1,2]
[1]*Landspitali University Hospital, Reykjavik, Iceland;* [2]*University of Iceland, Reykjavik, Iceland;* [3]*Borgarbyggd, Iceland;* [4]*Icelandic Heart Associations, Reykjavik, Iceland*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Primary aldosteronism (PA) is a common and potentially curable cause of hypertension, yet it remains substantially underdiagnosed. In Iceland, little is known about the prevalence and biochemical characteristics of PA among patients with newly diagnosed, untreated hypertension.

Objectives: To evaluate baseline serum aldosterone, plasma renin, and the aldosterone-to-renin ratio (ARR) in newly diagnosed, untreated hypertensive individuals, and to compare these measures with normotensive counterparts.

Methods: This cross-sectional study was conducted within the REFINE-Reykjavik Study, a population-based cohort established in Iceland between 2005 and 2006. From the original cohort, 420 participants with newly diagnosed untreated hypertension at inclusion and 220 normotensive controls were selected. Stored baseline plasma samples were analyzed for aldosterone, direct renin, potassium, and ARR. Possible PA was defined according to the newly presented Endocrine Society screening criteria (2025): plasma aldosterone $\geq$ 277 pmol/L, plasma renin $\leq$ 8.2 mIU/L, and ARR > 70. Clinical and biochemical characteristics were compared between participants who met and did not meet these criteria.

Results: Complete aldosterone and renin measurements were available for 609 participants. Of these, 32 individuals (5.2%) fulfilled the biochemical criteria for possible PA. Participants meeting PA criteria were significantly older (57.3 ± 7.4 vs 50.4 ± 12.0 years, $P = .001$) and had higher systolic (151.0 ± 19.1 vs 138.6 ± 21.1 mmHg, $P = .009$), diastolic (84.6 ± 11.3 vs 77.1 ± 12.9 mmHg, $P < .001$), and mean arterial blood pressure (106.7 ± 12.0 vs 97.6 ± 13.9 mmHg, $P < .001$) compared with those who did not meet criteria. Serum potassium concentrations were slightly but significantly lower in the PA group (4.1 ± 0.3 vs 4.2 ± 0.3 mmol/L, $P = .014$). No significant differences were observed between groups with respect to sex distribution, body mass index, smoking status, or diabetes prevalence.

Conclusions: In this population-based Icelandic cross-sectional study of newly diagnosed, untreated hypertensive individuals, approximately 5% met biochemical screening criteria for possible primary aldosteronism. These findings indicate that PA may be present in a substantial proportion of patients at the time of hypertension diagnosis and support broader implementation of systematic PA screening in accordance with recent international guidelines.

Abstract citation ID: lvag096.659

EP50 - ECE_1994 - Cortisol regulation, cardiometabolic risk factors and genetic variants in the glucocorticoid receptor in patients without Cushing's syndrome

Franziska Schnait, Konstantin Fuhrberg, Helena Niziolek, Nicole Kober, Greisa Vila, Sabina Baumgartner-Parzer and Marie Helene Schernthaner-Reiter
Wien, Austria

Background: Genetic variants in the glucocorticoid receptor gene have been shown to modulate hypothalamus-pituitary-adrenal axis activity. Moreover, there is increasing evidence that cortisol levels exert a continuous effect on cardiometabolic risk factors even in patients with physiological cortisol suppression during dexamethasone suppression testing (DST). As existing data are largely based on patient collectives with non-functioning adrenal adenomas, this study aims to investigate associations in a more heterogeneous cohort.

Method: Cardiometabolic risk factors were collected retrospectively in 470 patients with physiological suppression in the 1 mg overnight DST (cortisol < 1.8 µg/dL). Exons and flanking intronic regions in the glucocorticoid receptor gene (*NR3C1*) were analysed in 23 patients using Sanger sequencing.

Results: In comparison to patients with lower post-DST cortisol values (<1,2 µg/dL), the prevalence of diabetes (11.2% vs 23.7%; $P = .002$), hypertension (57.7% vs 74.2%; $P = .004$) and hyperlipidaemia (45.2% vs 57.0%; $P = 0{,}042$) was higher in patients with higher post-DST cortisol values of 1.2-1.79 µg/dL. They had older age (median: 37.8 vs. 56.2; $P < 0{,}001$), but BMI and sex distribution were comparable. The most frequent indications for performing DST were hypertension (32.6%), obesity (32.1%), and adrenal incidentalomas (26.8%).

Post-DST cortisol values were significantly associated with glucose and glycated hemoglobin (HbA1c) in patients without current antidiabetic medication. This association remained significant even when controlling for age, BMI and sex in a partial Spearman´s rank correlation analysis (glucose: $r_s = 0.184$, $P = .001$; HbA1c: $r_s = 0.157$, $P = .013$). No significant associations were detected for blood pressure, BMI or lipid parameters.

Sequence analysis identified the following *NR3C1*-variants: ER22/23EK (rs6189, rs6190), GR-9β (rs6198), rs4986593, rs6188 and rs6196. The respective allele frequencies were 4.5%, 21.7%, 28.3%, 32.6% and 15.2% and they were comparable to prevalences reported for the general population (gnomAD). Furthermore, in one sample a novel duplication was detected adjacent to the exon-intron 5 boundary (c.1747 + 13dup).

Conclusions: Patients without endogenous hypercortisolism showed a significant association between post-DST cortisol values and parameters of glucose metabolism. Moreover, a higher prevalence of cardiovascular risk factors, including diabetes, hypertension and hyperlipidaemia, was found in patients with post-DST cortisol values of 1.2-1.79 µg/dL.

Abstract citation ID: lvag096.660

EP51 - ECE_3020 - Role of glucocorticoid receptor polymorphisms on blood pressure control and lipid profile in a group of patients with apparent essential hypertension

Antonio Musolino[1], Chiara Parazzoli[1,2], Elisa Delle Donne[1,3], Vittoria Favero[1,2], Carmen Aresta[1,2], Grzegorz Bilo[4,5], Alessandro Croce[4], Martino Pengo[4,5], Gianfranco Parati[4], Luca Persani[1,3], Alfredo Scillitani[6], Biagio Cangiano[1,3], Gabriele Pogliaghi[1,3], Ilaria Gentile[1,3], Iacopo Chiodini[1,2] and Valentina Morelli[3]
[1]Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [2]ASST Grande Ospedale Metropolitano Niguarda, Unit of Endocrinology, Milano, Italy; [3]Endocrinology Department & Lab of Endocrine and Metabolic Research, Istituto Auxologico Italiano IRCCS, Milan, Italy; [4]Department of Cardiology, Istituto Auxologico Italiano IRCCS, Milan, Italy; [5]Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy; [6]Casa Sollievo della Sofferenza, Unit of Endocrinology, San Giovanni Rotondo, Italy

Objective: four glucocorticoid receptor polymorphisms (GRp) have been linked with increased resistance (ER22/23EK, GR-9β)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

or sensitivity (N363S, BclI) to glucocorticoids (GC) conferring a better, or worse, metabolic and cardiovascular risk. The aim of the present study was to evaluate the biochemical and clinical impact of GRp in a group of patients with apparent essential hypertension.

Methods: in this cross-sectional study, we evaluated in 99 hypertensive patients (aged 37-70 years, 51 females): anthropometric variables; hypotalamus-pituitary-adrenal (HPA) axis parameters [(basal cortisol levels, cortisol after 1 mg-Dexamethasone suppression test, ACTH levels, urinary free cortisol (UFC)]; glycemic and lipidic profile; carotid intima-media thickness (cIMT) and presence of carotid stenosis; presence of uncontrolled blood pressure (UBP) defined as 24 h-mean BP at ambulatory blood pressure monitoring or mean office BP > 140/90 mmHg despite antihypertensive treatment; gene variants of ER22/23EK, GR-9β, N363S and BclI. Exclusion criteria were signs suggestive for secondary hypertension and presence of obesity or diabetes mellitus. Patients were defined as carriers of a resistant (RS) or sensitive (SN) phenotype based on the presence of at least one associated GRp. Thirteen patients who presented both types of GRp were excluded from statistical analysis to avoid phenotype overlapping.

Results: we found 32 RS (32.3%), 54 SN (54.5%) and 26 wild-type patients (26.3%). GR-9β was the most prevalent GRp in RS (32/32 cases) while BclI was the most prevalent among SN patients (52/54 cases).

Comparing RS patients with non-RS patients, no differences were found in anthropometric variables, glycemic and lipidic profile, HPA axis parameters, number of antihypertensive drugs. We did not observe any difference in the prevalence of impaired fasting glucose/impaired glucose tolerance (IFG/IGT) and altered cIMT. RS patients showed a higher prevalence of carotid stenosis (36% vs 61%, $P = .056$) and UBP (34.3% vs 63.2%, $P = .024$) than non-RS patients. RS phenotype was associated with UBP (OR:5.6, $P = .007$) independently of age, sex, BMI, number of antihypertensive drugs, smoking status, prevalence of IFG/IGT, UFC.

SN patients showed lower ACTH (30.4 vs 24.0 ng/L, $P = .042$) and higher HDL cholesterol ($P = .043$) than non-SN patients. We did not find any statistically significant difference in any other variables. After stratification for sex, we found that HDL cholesterol levels remained statistically significant in female SN patients (57.3 vs 66.3 mg/dL, $P = .046$) but not in male ones (50 vs 51.1 mg/dL, $P = .77$).

Conclusions: GR-9β polymorphism, associated with RS, could be linked with UBP independently from common cardiovascular risk factors. In female SN patients higher HDL cholesterol was observed, suggesting a sex-dependent effect of GC on cholesterol.

Abstract citation ID: lvag096.661

EP52 - ECE_1187 - When weight loss hides Cushing's: a tirzepatide pitfall

Aparajita Roy[1], David Llewellyn[1], Amina Khanam[1], Ben Whitelaw[2] and Mohamed Bakhit[1]
[1]*Lewisham University Hospital, London, United Kingdom;* [2]*King's College Hospital NHS Foundation Trust, London, United Kingdom*

Background: The increasing use of glucagon-like peptide-1/glucose-dependent insulinotropic polypeptide receptor agonists may modify the clinical presentation of endocrine disorders. We describe a case of autonomous cortisol excess in which treatment with Tirzepatide (Mounjaro) potentially masked classical clinical features.

Case Presentation: A 37-year-old woman was referred following the incidental discovery of a right adrenal lesion on cardiac MRI performed for hypertension and exercise intolerance. Dedicated adrenal CT demonstrated a 3.3 cm right adrenal lesion.

At initial endocrine review, she reported significant weight gain of 50 kg from 2018 to 2021, accompanied by anxiety, palpitations and sweating, initially attributed to long COVID. She had commenced Tirzepatide privately, titrated to 15 mg weekly, achieving a 50 kg weight loss in 4 years. On examination her weight was 92 kg (BMI 33.8 kg/m^2) with no overt Cushingoid features. Her past medical history included essential hypertension, ovarian cysts and liver haemangioma. Medications included ramipril, amitriptyline and sertraline.

Overnight dexamethasone suppression tested twice showed non-suppressed cortisol levels of 113 nmol/L and 130 nmol/L with a corresponding dexamethasone level of 7.5 nmol/L. ACTH was 5 ng/L, DHEAS was 1.8 µmol/L(0.9-11.6),24-hour urinary free cortisol was 43 nmol/L, plasma metanephrines, normetanephrines, 3-methoxytyramine, renin and aldosterone were normal. HbA1c was 28 mmol/mol. A repeat CT adrenal imaging showed a 3 cm right adrenal lesion, pre-contrast attenuation of 22 HU and absolute contrast washout of 44% stable over three years.

Follow-Up: Continued Tirzepatide therapy led to further reduction in BMI to 19 kg/m^2, prompting dose reduction. Blood pressure improved significantly, allowing cessation of antihypertensive therapy.

Further review revealed symptoms suggestive of cortisol excess, including easy bruising, recurrent urinary tract infections, poor wound healing and proximal muscle weakness. Following discussion at a regional adrenal multidisciplinary team meeting, right adrenalectomy was recommended. Metyrapone 250 mg once daily was initiated as bridging therapy, later stopped due to side effects.

Conclusions: This case demonstrates that Tirzepatide may mask clinical features of cortisol excess by improving weight, blood pressure, and glycaemic control. Combined catabolic effects of hypercortisolism and rapid weight loss may worsen sarcopenia. Clinicians should retain suspicion for cortisol excess in patients using incretin mimetics, even without a Cushingoid appearance. Measuring serum dexamethasone levels during ONDST is essential, as GLP-1 agonists can affect gastric emptying and drug absorption. Such therapies must be prescribed and monitored by clinicians with endocrinology and/or obesity management expertise to ensure that endocrine causes of obesity are not missed.

Abstract citation ID: lvag096.662

EP53 - ECE_1701 - Prognostic nutritional index and inflammatory indices as predictors of perioperative infection in patients with Cushing syndrome: a retrospective single-center study

Onour Chasan[1], Mehves Besisik Terzioglu[2], Ümmü Mutlu[1], Duygu Dolen Burak[3], Hulya Hacisahinogullari[1], Nurdan Gul[1], Ozlem Soyluk Selcukbiricik[1], Ayse Kubat Uzum[1] and Gulsah Yenidunya Yalin[1]
[1]*Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, Istanbul University, Istanbul, Türkiye;* [2]*Istanbul Faculty of Medicine, Department of Internal Medicine, Istanbul University, Istanbul, Türkiye;* [3]*Istanbul Faculty of Medicine, Department of Neurosurgery, Istanbul University, Istanbul, Türkiye*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Objective: Endogenous Cushing syndrome (CS) is associated with increased risk of morbidity and mortality, and infections are among its major complications. This study aimed to evaluate the predictive value of cortisol-related indices, blood cell-derived inflammatory indices, and the prognostic nutritional index (PNI) for perioperative infection and to identify risk factors.

Methods: A total of 113 patients with confirmed CS were included: 71 pituitary CS, 37 adrenal CS, and 5 ectopic CS. Perioperative systemic infection statuses were determined. Cortisol-related indices, blood cell-derived inflammatory indices, PNI, and clinical features were evaluated. Receiver Operating Characteristic (ROC) analysis identified optimal cut-off values for predicting infection. Variables associated with perioperative infection in univariate analysis were entered into multivariable regression models, and the model with the best discrimination was chosen as the final model.

Results: Thirty-five CS patients (31%) developed infection. The most common infections were urinary tract infections, followed by pneumonia. PNI demonstrated significant negative correlations with all cortisol-related indices, particularly for 1-mg overnight dexamethasone suppression test (1-mg DST) ($\rho = -0.605$, $P < .001$) and 24-hour urinary free cortisol (UFC) × upper limit of normal (xULN) ($n = 38$, $\rho = -0.605$, $P < .001$). Among the blood cell-derived indices, neutrophil-to-lymphocyte ratio demonstrated significant positive correlations with all cortisol-related indices, particularly UFC (xULN) ($n = 38$, $\rho = 0.735$, $P < .001$), low dose dexamethasone suppression test ($n = 104$, $\rho = 0.621$, $P < .001$), and 1-mg DST ($\rho = 0.589$, $P < .001$).ROC analysis demonstrated that 1-mg DST (AUC = 0.852; cut-off ≥ 17.2 µg/dL; $P < .001$) and PNI (AUC = 0.845; cut-off ≤51.4; $P < .001$) were the strongest predictors of infection. In the final multivariable model, 1-mg DST values ≥17.2 µg/dL (OR: 9.741; 95% CI: 2.801–33.883; $P < .001$), PNI values ≤51.4 (OR: 9.569; 95% CI: 2.683–34.122; $P < .001$), the presence of diabetes mellitus (OR: 3.963; 95% CI: 1.128–13.925; $P = .032$), and presence of bone fracture(s) or a T-score ≤–3 (OR: 3.574; 95% CI: 1.003–12.730; $P = .049$) were identified as independent risk factors for infection.

Conclusions: Perioperative infection was associated with elevated cortisol and lower PNI levels in patients with CS. Infection risk is modulated by hormonal, nutritional, and clinical parameters. Assessment of 1-mg DST and PNI, in conjunction with diabetes mellitus status and bone health, may enhance the identification of high-risk patients and guide targeted preventive strategies.

Abstract citation ID: lvag096.663

EP54 - ECE_1741 - Metyrapone treatment improves blood pressure and lowers epicardial fat in patients with mild autonomous cortisol secretion

Helena Niziolek[1], Ivica Just[1], Clemens Baumgartner[1], Anna Tosin[1], Konrad Körmöczi[1], Hansjörg Habisch[2], Paul Fellinger[1], Hannes Beiglboeck[1], Oliver Domenig[3], Luise Bellach[1], Anton Luger[1], Marie Helene Schernthaner-Reiter[1], Siegfried Trattnig[4], Maximilian Zeyda[5], Thomas Scherer[1], Alexandra Kautzky-Willer[1], Florian Kiefer[1], Greisa Vila[1], Andreas Kammerlander[6], Tobias Madl[2,7,8], Michael Leutner[1], Michael Krebs[1], Martin Krssak[1] and Peter Wolf[1]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria; [2]Medical University of Graz, Graz, Austria; [3]Vienna, Austria; [4]Department of Biomedical Imaging and Image Guided Therapy, Medical University of Vienna, Vienna, Austria; [5]Division of Pediatric Pulmonology, Allergology and Endocrinology, Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria; [6]Division of Cardiology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria; [7]BioTechMed-Graz, Graz, Austria;

Background: Mild autonomous cortisol secretion (MACS) is associated with increased mortality, mainly because of cardiovascular disease. Here we investigated the effects of cortisol-lowering medical treatment on blood pressure regulation, cardiac fat depots, heart function and morphology, the lipid profile and branched-chain amino acid (BCAA) concentrations.

Methods: In this secondary analysis of our prospective, open-label, exploratory study, we investigated 15 patients with MACS (12 females; age 59 [53–64] years) before and after 12 weeks of treatment with evening doses of metyrapone (500 mg at 6 p.m. and 250 mg at 10 p.m.). Cardiac fat stores, morphology and myocardial function were evaluated using cardiac magnetic resonance imaging and spectroscopy. Orthostatic blood pressure regulation was measured by standardized protocols. Lipidomics, renin-angiotensin-aldosterone-system activity and BCAA concentrations were assessed.

Results: Mean supine systolic (137[121-139] vs 122[115-129] mmHg; $P = .041$) and diastolic (89[80-93] vs 75[71-86] mmHg; $P = .045$) blood pressure decreased after treatment. Epicardial fat was lower at follow up compared to baseline (1032.70[894.23-1482.90] vs 929.37[736.12-1317.15]mm^2; $P = .022$). No changes in paracardial- and intramyocardial fat, as well as in cardiac function and morphology were observed. The aldosterone-to-angiotensin II ratio(AA2-ratio) was lower at follow up (1.56[0.87–2.82] vs 1.21[0.98–1.92]; $P = .042$) and alterations in lipid profiles, but not in BCAA levels were identified.

Conclusions: Treatment with evening doses of metyrapone improved blood pressure and reduced epicardial adipose tissue, highlighting the causal role of hypercortisolism for the development of cardio-vascular comorbidities in MACS.

Abstract citation ID: lvag096.664

EP55 - ECE_3941 - Identification of false-positive dexamethasone suppression tests using LC-MS/MS

Georgiana Constantinescu[1,2], Christina Pamporaki[1], Sybille Fuld[1], Manuel Schulze[3], Nicole Bechmann[4], Mirko Peitzsch[4], Jens Passauer[1], Hanna Remde[5,6], Lydia Kuerzinger[5,6], Sven Gruber[7], Jimmy Masjkur[8], Martin Fassnacht[5,6], Felix Beuschlein[7], Jun Yang[9,10,11], Jacques Lenders[12,13] and Graeme Eisenhofer[1]

[1]Universitätsklinikum Carl Gustav Carus Dresden, Dresden, Germany; [2]Iaşi, Romania; [3]Center for Information Services and High Performance Computing (ZIH), Department of Distributed and Data Intensive Computing, Technische Universität Dresden, Dresden, Germany; [4]Institute of Clinical Chemistry and Laboratory Medicine, University Hospital "Carl Gustav Carus", Dresden, Germany; [5]Würzburg University Hospital, Würzburg, Germany; [6]Department of Medicine I, Würzburg, Germany; [7]Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, University Hospital, Zurich, Switzerland; [8]eSwiss Medical and Surgical Center, Klinik Stephanshorn, St Gallen, Switzerland; [9]Center of Endocrinology and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Metabolism, Hudson Institute of Medical Research, Clayton, Victoria, Australia; [10]Department of Medicine, Monash University, Clayton, Victoria, Australia; [11]Melbourne, Australia; [12]Radboud University Medical Center, Nijmegen, The Netherlands; [13]Department of Internal Medicine, Nijmegen, The Netherlands

Introduction: The 1-mg overnight dexamethasone suppression test (DST) is widely used to assess autonomous cortisol secretion (ACS) in patients harboring adrenal adenomas or in whom there is suspicion of cortisol excess. Interpretation of DST results assumes adequate dexamethasone concentrations. However, insufficient or no dexamethasone intake may result in apparent failure of cortisol suppression and false-positive test results. Measurement of plasma dexamethasone (DXM) concentrations is therefore critical to ensure valid interpretation of DST outcomes.

Results: Among 347 patients undergoing DST with concomitant plasma dexamethasone measurement, 22 individuals were identified with insufficient dexamethasone exposure, defined as plasma concentrations below 3.3 nmol/L. These patients included twelve females and ten males. Mean age was 53.6 years in female patients and 52 years in male patients. Underlying diagnoses were heterogeneous and included adrenal adenoma ($n = 10$), primary aldosteronism ($n = 3$), and primary hypertension ($n = 9$). Median DXM concentrations were below the limit of detection (0.510 nmol/L) in 7 cases (32%), suggesting non-compliant DXM intake. In these patients, DST cortisol concentrations were frequently elevated, ranging from 11.65 to 396.05 nmol/L, with a median cortisol concentration of 54.6 nmol/L. Concentrations exceeded the diagnostic threshold for cortisol suppression in eleven cases, 3.2% of the total.

Conclusions: Absent or insufficient dexamethasone concentration represents a clinically relevant cause of false-positive dexamethasone suppression tests, accounting for 3.2% of all tested patients in our cohort. Elevated post-DST cortisol concentrations in the context of low or undetectable dexamethasone highlights the necessity of measuring dexamethasone to ensure valid interpretation of DST results. Routine incorporation of plasma dexamethasone measurement improves diagnostic accuracy and prevents misclassification of patients evaluated for cortisol autonomous secretion.

Abstract citation ID: lvag096.665

EP56 - ECE_3989 - Potential impact of multiple paired adrenal vein samples on lateralisation interpretation in adrenal vein sampling for primary aldosteronism: a retrospective case series

August Palma[1], James MacFarlane[1], Nicholas Hilliard[2] and Mark Gurnell[1,3]

[1]Endocrinology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [2]Radiology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [3]University of Cambridge, Cambridge, United Kingdom

Background: Adrenal vein sampling (AVS) is widely used to differentiate unilateral from bilateral disease in primary aldosteronism (PA). However, rates of successful bilateral adrenal vein cannulation vary considerably between centres, commonly reflecting differences in interventional radiologist expertise. Furthermore, reliance on a single paired adrenal vein samples may reduce the likelihood of identifying unilateral disease, even when present, due to fluctuations in hormonal secretion and catheter instability. We hypothesised that obtaining multiple paired adrenal vein samples during AVS would improve confirmation of selectivity and increase detection of aldosterone lateralisation.

Objectives: To examine within-patient variability in adrenal vein sampling (AVS) findings using a tertiary referral centre database in which multiple paired adrenal vein samples were systematically collected, and to assess whether additional paired samples improved confirmation of successful bilateral cannulation and enhanced detection of aldosterone lateralisation, thereby influencing AVS interpretation and clinical decision-making.

Methods: A retrospective review of AVS procedures performed by a single operator at Cambridge University Hospitals between January 2020 and January 2025 was conducted. The practice of the operator is to take multiple samples from the site of each adrenal vein (minimum 3). We identified five patients with confirmed PA who had undergone adrenocorticotropic hormone (ACTH)-stimulated AVS and demonstrated variability in selectivity indices (SI) and lateralisation indices (LI). Sequential paired samples were obtained from both adrenal veins during each procedure. SI was calculated using standard adrenal-to-peripheral cortisol ratios for ACTH-stimulated AVS ($SI \geq 3.0$), and LI was calculated for each paired sample using a standard cut-off of ≥ 4.0. Diagnostic interpretations based on the initial paired sample were compared with interpretations incorporating all paired samples.

Results: Multiple paired adrenal vein samples were successfully obtained in all cases. Sequential sampling demonstrated that, in some patients, the initial paired sample did not meet selectivity criteria for successful bilateral cannulation, whereas subsequent paired samples confirmed adequate cannulation. All 5 cases had pairs of samples yielding LI both above and below 4.0 resulting in differing diagnostic interpretations, with some samples indicating unilateral disease and others suggesting bilateral disease. Significant intrasampling variability was captured, including a case with LI varying between 2.3 and 8.51.

Conclusions: In this small case series, systematic collection of multiple paired adrenal vein samples was feasible and improved confirmation of bilateral cannulation and diagnostic confidence. This approach may enhance the diagnostic yield of AVS, support more accurate clinical decision-making, and reduce the need for repeat procedures in patients with PA.

Abstract citation ID: lvag096.666

EP57 - ECE_1147 - Optimisation of performance of Seated Saline Infusion Test (SSIT) for diagnosis of primary hyperaldosteronism—comparison of two protocols

Krzysztof Lewandowski[1], Katarzyna Wojciechowska-Durczyńska[2], Kinga Krawczyk-Rusiecka[2], Marta Mikulak[1], Ewa Bieniek[1], Wojciech Horzelski[3] and Małgorzata Karbownik-Lewińska[4]

[1]Faculty of Medicine—Collegium Medicum, Chair of Internal Medicine, Endocrinology & Diabetes, Mazovian University in Plock, Plock, Poland; [2]Department of Paediatric and Adult Endocrinology,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Medical University of Lodz, Lodz, Poland; [3]Faculty of Mathematics and Computer Science, University of Lodz, Lodz, Poland; [4]Department of Endocrinology & Metabolic Diseases, Medical University of Lodz, Lodz, Poland

Background: Seated Saline Infusion Test (SSIT) is widely used for investigation of primary hyperaldosteronism (PA), however, the impact of one hour sitting period prior to SSIT (as recommended by the Endocrine Society) on the test outcome remains unclear.

Patients & Methods: In 82 individuals (23 males) age 57.3 ± 12.6 years, BMI 28.3 ± 5.1 kg/m^2, with adrenal incidentalomas, we performed a SSIT (two litre of 0.9% saline/4 hours) preceded by a two hour postural test (1st protocol), or immediately after waking, ie, without any period of sitting, or standing prior to the test (2nd protocol, a cross-over design).

Results: Though aldosterone & renin concentrations before the onset of saline infusion were higher after 1st protocol (aldosterone: 16.27 ± 1.28 ng/dL (mean ± SEM) vs 9.51 ± 1.20 ng/mL, $P <$ .001, renin: 23.52 ± 2.19 µIU/mL versus 8.09 ± 0.91 µIU/mL, $P <$ .001), an overall suppression of aldosterone secretion was not different after 1st protocol versus 2nd protocol (6.34 ng/dL ± 0.68 ng/dL (mean ± SEM) vs 5.74 ± 0.66 ng/dL, P = .124). In contrast renin concentrations were lower after 2nd protocol (7.32 ± 0.74 µIU/mL vs 5.13 ± 0.45 µIU/mL, P = .027). There was, however, no significant difference between the number of individuals who had clearly non-suppressible aldosterone concentration (>10 ng/mL), ie, 9 (11%) for 1st protocol versus 8 (9.75%) (2nd protocol), P = 82, as well as for individuals in the "grey zone" (7.8-10 ng/mL), ie, five (6.1%) individuals for each protocol, P = 1.0).

Conclusions: A period of ambulation (or sitting) before SSIT does not significantly impact the chance of detection of PA, so formal recommendation of at least one hour sitting period prior to SSIT can be safely avoided.

Abstract citation ID: lvag096.667

EP58 - ECE_1318 - Risk factors and outcomes of critical illness-related corticosteroid insufficiency

Moeber Mahzari[1], Omar Alluhayyan[2], Reema Alkalefah[3], Shahad Yarkandi[3], Yara Aleidi[3], Shaden Almutairi[3], Faisal Almutawa[1], Rakan Alotaibi[1] and Husam Ardah[1,4]
[1]KSAU-HS, Riyadh, Saudi Arabia; [2]KAMC, Riyadh, Saudi Arabia; [3]COSHP-R_F, Riyadh, Saudi Arabia; [4]Riyadh, Saudi Arabia

Introduction: Critical illness-related corticosteroid insufficiency (CIRCI) refers to inadequate corticosteroid activity compared to an illness's stress severity.

Endocrine outcomes associated with critical illness, specifically relating to adrenal insufficiency and hypothalamic–pituitary–adrenal (HPA) axis dysfunction, are not adequately assessed.

To overcome these limitations, this study aims to assess the risk factors and outcomes of CIRCI.

Methodology: This retrospective cohort study included adult intensive care unit (ICU) patients treated for suspected CIRCI between 2016 and 2024. Demographic, clinical, laboratory, and treatment data were extracted from electronic medical records. Outcomes assessed included mortality, CIRCI, readmission, and continuation of steroid therapy after hospital discharge.

Results: A total of 390 critically ill patients who received glucocorticoids in an ICU during the study period were included in the analysis. The mean age was 62.5, and 57.7% of the patients were male. The most common primary reason for ICU admission was sepsis, affecting 52.5% of the patients. Among critically ill patients, 118 (32.4%) met the criteria for CIRCI, defined as a serum cortisol level of ≤275 nmol/L, while 246 (67.6%) did not meet these criteria. CIRCI was more frequently observed among patients with neurological reasons for ICU admission (13.7% vs 5.7%, P = .009) and those requiring mechanical ventilation (80.5% vs 68.7%, P = .018).

Upon follow-up, the frequency of adrenal crisis events was significantly higher among patients with a history of CIRCI compared with those without CIRCI (mean 0.96 vs 0.36, P = .034). Longer duration of post-ICU glucocorticoid therapy was associated with a higher frequency of adrenal insufficiency events over follow-up (r = 0.59, P = .002). Post–critical illness, only 10.3% of patients underwent HPA axis assessment during follow-up, indicating limited evaluation of adrenal function.

In multivariable analysis, Mortality was independently associated with older age (estimate 0.01, P = .006), longer ICU length of stay (estimate 0.01, P = .01), and the presence of cardiogenic shock (estimate 1.26, P = .02). In contrast, baseline cortisol levels (P = .92) and duration of glucocorticoid treatment (P = .59) were not associated with mortality. During follow-up, patients who had a lower baseline cortisol level during ICU were more likely to continue steroids upon discharge (estimate −0.03, $P <$ .0001).

Conclusions: CIAI is common in critical illness and reflects endocrine vulnerability rather than mortality risk. Lower baseline cortisol identifies patients at risk for prolonged steroid dependence and recurrent adrenal insufficiency events, supporting the need for targeted post-ICU endocrine follow-up and assessment of the HPA axis.

Abstract citation ID: lvag096.668

EP59 - ECE_2265 - Upregulated glutamate receptor subunit NETO2 in primary aldosteronism promotes CYP11B2 expression in human adrenocortical cells

Yingxian Pang and Tracy Ann Williams
Munich, Germany

Background: Neuropilin and Tolloid-Like 2 (NETO2) is a key auxiliary subunit of kainate-type glutamate receptors and is involved in the regulation of sodium, potassium, and calcium homeostasis in the human brain. However, its role in primary aldosteronism remains poorly understood.

Objective: We examined NETO2 expression in primary aldosteronism and investigated its effects on CYP11B2 (aldosterone synthase) expression and the underlying mechanisms in human adrenocortical cells.

Results: Spatial transcriptomic analysis of adrenal glands from patients with APA and APM revealed high expression of *NETO2* and *CYP11B2* in aldosterone-producing lesions compared to adjacent adrenal cortex. *GLUK1*, *GLUK2*, *GLUK3*, and *GLUK5* of kainate receptors were mainly expressed in the medulla, whereas *GLUK4* gene was distributed throughout the entire adrenal tissue. Western blot showed elevated NETO2 protein in APAs versus adjacent adrenal tissue (2.9-fold change, $P <$ .01). In HAC15 cells,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

NETO2, *GLUK2* and *GLUK4* were highly expressed, whereas *GLUK1* and *GLUK5* were low and *GLUK3* undetectable. *NETO2* overexpression increased *CYP11B2* mRNA (4.7-fold change, $P < .001$), *NR4A2* mRNA (6.3-fold change, $P < .001$), and modestly *CYP11B1* mRNA (1.4-fold change, $P < .05$), with no effect on *CYP11A1* and *CYP17A1* mRNA levels. *NETO2* silencing had opposite effects.

Conclusions: NETO2 is highly expressed in primary aldosteronism and promotes *CYP11B2* expression in human adrenocortical cells. Further studies are warranted to investigate the effects of NETO2 on intracellular calcium signaling.

Abstract citation ID: lvag096.669

EP60 - ECE_2611 - Evaluation of salivary cortisone and cortisol for diagnosing mild autonomous cortisol secretion in patients with adrenal incidentalomas

Nanna Thurmann Jørgensen[1], Christina Christoffersen[2], Linda Hilsted[2], Kasper Brødbæk[2], Niklas Jørgensen[2], Randi Ugleholdt[3], Claus Feltoft[3], Åse Krogh Rasmussen[1], Ulla Feldt-Rasmussen[4], Marianne Klose[1] and Stina Willemoes Borresen[1]

[1]Department of Nephrology and Endocrinology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark; [2]Department of Clinical Biochemistry, Copenhagen University Hospital, Copenhagen, Denmark; [3]Department of Endocrinology and Internal Medicine, Copenhagen University Hospital, Herlev, Herlev, Denmark; [4]Dept of Growth and Reproduction, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark

Objective: Salivary cortisol and cortisone are promising alternatives to plasma measurements. This study investigates their diagnostic accuracy in mild autonomous cortisol secretion (MACS) and assesses agreement between liquid chromatography–tandem mass spectrometry (LC-MS/MS) and the iSYS immunoassay for salivary cortisol.

Design and Methods: This cross-sectional study prospectively included patients with adrenal incidentalomas ($N = 108$) and age- and sex-matched healthy controls ($N = 101$). Saliva was collected at 0800-0900 h, 2300-2400 h, and at 0800-0900 h following a 1-mg overnight dexamethasone suppression test (DST). Salivary cortisone was measured by LC-MS/MS, and salivary cortisol by LC-MS/MS and the iSYS immunoassay. Diagnostic accuracy was assessed using the area under the receiver operation characteristic curve (ROC-AUC) with the guideline-recommended post-DST plasma cortisol cut-off value of 50 nmol/L as the gold standard for MACS. Furthermore, an alternative cut-off value for MACS was defined as the 97.5th percentile of post-DST plasma cortisol in controls (72 nmol/L). Salivary cut-off values were based on Youden's index and the 97.5th percentile of control distributions. Method agreement was evaluated using Bland-Altman plots and Passing-Bablok regression.

Results: A post-DST salivary cortisone cut-off value of 3.1 nmol/L showed the highest discriminatory ability (sensitivity and specificity 90%) compared with post-DST salivary cortisol and late-night cortisol and cortisone (sensitivities 69-79%, specificities 66-91%). Percentile-derived cut-off values were two- to threefold higher with consequently lower sensitivities (13-17%). The MACS plasma cortisol cut-off value of 72 nmol/L significantly improved the diagnostic accuracy of post-DST salivary cortisol compared with the cut-off value of 50 nmol/L (ROC-AUC 0.78 vs 0.92, $P = .006$), whereas AUCs for post-DST salivary cortisone and late-night salivary cortisol and cortisone were unchanged. The immunoassay systematically overestimated salivary cortisol compared with LC–MS/MS in controls and patients (mean bias 10.8 vs 14.6 nmol/L at 0800-0900 h, 3.0 vs 4.8 nmol/L at 2300-2400 h, and 1.6 vs 2.9 nmol/L post-DST, respectively), but demonstrated comparable diagnostic accuracy for MACS at 2300 2400 h (ROC-AUC 0.75 vs 0.77, $P = .5$) and post-DST (ROC-AUC 0.82 vs 0.78, $P = .4$).

Conclusions: Post-DST salivary cortisone showed high diagnostic accuracy, whereas post-DST salivary cortisol and late-night salivary cortisol and cortisone had lower predictive value. A cut-off value of 72 nmol/L significantly improved post-DST salivary cortisol performance compared with 50 nmol/L. Percentile-derived salivary cut-off values were inferior to those based on the Youden's index. Despite systematic overestimation by the iSYS immunoassay compared with LC-MS/MS, diagnostic accuracy for MACS was comparable.

Abstract citation ID: lvag096.670

EP61 - ECE_2814 - Characterization of diffuse CYP11B2-positivity and multiple micronodules in autopsy samples from adults without primary aldosteronism

Juhani Isojärvi[1], Antero Ylänen[1,2], Antti Virtanen[3], Helena Leijon[4], Tiina Vesterinen[4], Heini Huhtala[5], Eeva Kokko[1], Marianna Viukari[6,7], Ilkka Pörsti[1], Niina Matikainen[6,7] and Pasi Nevalainen[2]

[1]Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [2]Tampere University Hospital, Tampere, Finland; [3]Forensic Medicine Unit, Finnish Institute for Health and Welfare, Helsinki, Finland; [4]HUS Diagnostic Center, Department of Pathology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [5]Health Sciences, Faculty of Social Sciences, Tampere University, Tampere, Finland; [6]Endocrinology, Helsinki University Hospital, Helsinki, Finland; [7]University of Helsinki, Helsinki, Finland

Background: The introduction of HISTALDO consensus has revolutionised the histopathological assessment of unilateral aldosterone-producing adrenocortical findings. Less is known about the structure of the zona glomerulosa based on aldosterone synthase (CYP11B2) immunohistochemistry in healthy adults. Previous studies have identified a negative correlation between age and adrenal CYP11B2-expressing area, as well as ageing-related transition in ZG structure from continuous CYP11B2 expression into more fragmented appearance in individuals without primary aldosteronism (PA). However, these studies have been limited to unilateral adrenal samples or small, specific cohorts, preventing a comprehensive analysis of bilateral adrenal CYP11B2 expression in the general population.

Methods: We explored the characteristics, symmetry, and clinical relevance of adrenocortical findings expressing CYP11B2 in unselected adults without known primary aldosteronism. Bilateral adrenal CYP11B2 immunohistochemistry was performed on 145 consecutive autopsy cases who died from exogenic causes and analysed following the HISTALDO consensus when applicable. A four-grade classification was used: 1) diffuse CYP11B2 positivity, 2) ≥20 aldosterone-producing micronodules (APMs), 3) <20 APMs, and 4) aldosterone-producing nodules or adenomas

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(APNs/ APAs). Autopsy findings were documented, and ante-mortem data including diagnoses, prescriptions, and laboratory results were collected. This study was registered in ClinicalTrials.gov (NCT05446779).

Results: The cohort included 104 males and 41 females, with a median age of 53.9 years. Bilateral diffuse CYP11B2 positivity was observed in 12 subjects (8.3%). APMs were identified in 131 subjects (90.3%), with ≥20 APMs in 42 (32.1%) and <20 APMs in 89 (67.9%). Two subjects had an APN, while no APAs were detected. CYP11B2 staining patterns were symmetric between the adrenals in 72.4% of subjects. Diffuse CYP11B2 positivity was more frequent in females than in males ($P = .005$). The CYP11B2 expression groups showed no association with age, hypokalaemia, hypertension, or autopsy-identified cardiovascular pathologies, nor did they differ between individuals with or without cardiovascular disease. Detailed analyses about the diffuse positivity are under way and will be presented in ECE2026, Prague.

Interpretation: Taken together, bilateral multiple APMs were frequently found in this unselected adult population and showed considerable side-to-side symmetry, while diffuse CYP11B2 positivity, considered as normal ZG, was rare. Our results suggest that presence of bilateral CYP11B2-positive APMs without clinical signs of primary aldosteronism is a common non-pathological finding.

Abstract citation ID: lvag096.671

EP62 - ECE_3022 - Androgen profiling in adrenal incidentalomas: differentiating mild autonomous cortisol secretion from non-functioning adrenal incidentaloma

Sara Cerrato[1], Filippo Vignali[1], Lucia Zirilli[2], Bruno Madeo[2], Laura Roli[3], Maria Cristina De Santis[3], Giulia Canu[3], Tommaso Fasano[3], Sara De Vincentis[1] and Vincenzo Rochira[1,2]

[1]Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [2]Endocrinology, Department of Specialty Medicine, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [3]Department of Laboratory Medicine and Pathology, Azienda USL Modena, Modena, Italy

Introduction: Mild autonomous cortisol secretion (MACS) is increasingly recognised among patients with adrenal incidentalomas (AI). Growing evidence suggests that adrenal androgen production is lower in MACS compared to non-functioning adrenal incidentaloma (NFAI); however, current evidence remains conflicting.

Objective: To investigate the androgen profile of AI and delineate key biochemical differences between MACS and NFAI.

Materials and Methods: We performed a retrospective monocentric study including adult patients with AI, referred to the Endocrinology Unit of the AOU-Modena (2013-2025). Patients with overt Cushing syndrome, primary aldosteronism, aldosterone–cortisol co-secretion, interfering medications, or major confounders were excluded. Morning serum values of dehydroepiandrosterone sulphate (DHEA-S), 17-hydroxyprogesterone (17OH-P), and androstenedione were measured. The DHEA-S ratio (DHEA-S divided by the age and sex-adjusted lower limit of the reference range) and DHEA-S ULN (DHEA-S divided by the upper limit of the reference range) were also calculated. Results are expressed as median and IQR.

Results: A total of 178 patients were included (60 MACS, 118 NFAI). Patients with MACS (0,39 [0,22-0,73] μg/L) showed significantly lower DHEA-S levels compared to those with NFAI (0,78 [0,40-1,33] μg/L; $P < 0,001$), as well as lower DHEA-S ULN values (0,20 [0,14-0,31] vs 0,32 [0,21-0,50]; $P < 0,005$). In contrast, the DHEA-S ratio did not differ significantly between the two groups ($P = 0,367$). ROC analysis confirmed the superiority of DHEA-S [area under the curve (AUC) 0.707] and DHEA-S ULN (AUC 0.692) over DHEA-S ratio (AUC 0.597) in discriminating MACS from NFAI. The optimal diagnostic cut-off identified for DHEA-S was ≤0.63 mg/L, and ≤0.22 for DHEA-S ULN, both providing the best balance between sensitivity (72,9% DHEAS; 57.6% DHEA-S ULN) and specificity (62,7% DHEAS; 74,6% DHEA-S ULN) in discriminating MACS from NFAI. No significant differences were observed for 17OH-P levels (0,90 [0,50-1,38] ng/mL in MACS vs 1,00 [0,70-1,30] ng/mL in NFAI; $P = 0,684$) and androstenedione (0,73 [0,50-1,50] ng/mL in MACS vs 1,08 [0,61-1,58] ng/mL in NFAI; $P = 0,462$).

Conclusions: MACS exhibit lower DHEA-S levels compared to NFAI, reflecting the inhibitory effect of autonomous cortisol on the hypothalamic-pituitary-adrenal axis. The lack of significance for the DHEA-S ratio in our cohort suggests that age-related decrease of the lower reference limit may obscure pathological androgen suppression in elderly patients. Given the advanced median age at diagnosis of AI (63 years in our results), the use of DHEA-S ULN appears to better preserve information on absolute adrenal androgen reduction and may represent a reliable biomarker of cortisol autonomy in clinical practice.

Abstract citation ID: lvag096.672

EP63 - ECE_3317 - Natural history of large adrenal tumors

Magdalena Macech[1], Maclej Stępień[1], Joanna Podgórska[2], Sadegh Toutounchi[3], Lukasz Koperski[4], Joanna Barankiewicz[5], Malgorzata Bobrowicz[1], Agnieszka Kondracka[1] and Urszula Ambroziak[1]

[1]Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland; [2]Warsaw, Poland; [3]Department of General, Vascular, Endocrine and Transplant Surgery, Medical University of Warsaw, Warsaw, Poland; [4]Department of Pathology, Medical University of Warsaw, Warsaw, Poland; [5]Laboratory of Cellular and Genetic Therapies, Center for Preclinical Research, Medical University of Warsaw, Warsaw, Poland

Objective: The aim of this study was to characterize large adrenal tumors (LATs), assess the accuracy of imaging diagnostics in detecting malignant LATs, and determine whether further follow-up of seemingly benign LATs is necessary.

Patients and Methods: We investigated the clinical, biochemical, and imaging characteristics at presentation and follow-up in a retrospective single-center cohort of patients with adrenal tumors ≥4 cm in diameter during the period from June 2013 to June 2023.

Results: Of 1473 patients with adrenal tumors, 269 (18.3%) had adrenal masses measuring ≥4 cm in diameter, 220 patients were included in the study. Among LATs 34.6% were

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

adrenocortical adenomas, 27.3% other benign adrenal tumors, 17.3% adrenocortical carcinomas, 11.4% other malignant tumors, 9.6% pheochromocytomas. 44.7% of tumors were non-functioning and 37.8% were producing corticosteroids.

Sensitivity of an unenhanced computed tomography attenuation in detecting malignancy was 100% using the threshold >10 Hounsfield Units and 89.5% for >20 Hounsfield Units (with specificity 66.1% and 81.4% respectively). Magnetic resonance with chemical shift analysis also had high sensitivity (94.4%), but low specificity (56.8%). ^{18}F-fluorodeoxyglucose-positron emission tomography integrated with computed tomography had 100% sensitivity using adrenal liver ratio >1, when the maximum standardized uptake value >5 cutoff was employed, sensitivity remained high (100%) while specificity improved (82.1% vs 100%).

87 tumors remained under follow-up. The mean follow-up was 30.1 months. Significant tumor growth was observed in 4 cases (4.6%). 3 of these tumors were myelolipomas, 1 was indeterminate mass in a patient with extraadrenal malignancy. Adrenalectomy was performed in 6 patients (6.9%). While they were initially assessed as adrenocortical adenomas, in 5 of them histopathology revealed benign lesions and in one an adrenocortical carcinoma. The risk of developing mild autonomous cortisol secretion among non-functioning lesions was 6.7%. No progression to overt Cushing's syndrome was observed.

Conclusions: While the risk of malignancy increases with tumor size, most large adrenal tumors are benign. Imaging sensitivity for detecting malignancy is high in LATs. No malignancy was diagnosed in lesions with certain benign features (homogenous <10 HU). LATs that do not meet these criteria **s**hould be assessed by a multidisciplinary team and be subjected to continued follow-up.

Abstract citation ID: lvag096.673

EP64 - ECE_3408 - Evaluating variability in 24-hour urine free cortisol measurements: impact of sample collection errors

Ömer Ozcan[1], Karlijn Koops[1], Jacquelien Hillebrand[1], Antonius van Herwaarden[2], Annenienke van de Ven[3], Peter Bisschop[4], Wendy den Elzen[5] and Annemieke C. Heijboer[1]

[1]Endocrine Laboratory, Amsterdam UMC, Amsterdam, The Netherlands; [2]Laboratory Medicine, Radboud UMC, Nijmegen, The Netherlands; [3]Department of Internal Medicine, Division of Endocrinology, Radboud UMC, Nijmegen, The Netherlands; [4]Endocrinology, Amsterdam UMC, Amsterdam, The Netherlands; [5]Laboratory Specialized Diagnostics & Research, Amsterdam UMC, Amsterdam, The Netherlands

Introduction: Twenty-four hour urine free cortisol (UFC) reflects systemic cortisol exposure. It shows high variability and therefore requires multiple collections for Cushing's syndrome (CS) screening. This variability arises from both inherent biological variation and variation introduced by collection errors. Importantly, UFC results are interpreted using a cut-off based on the 24-hour collection, rather than per liter or normalized to creatinine, making the accuracy of urine collection volume critical for correct interpretation. This study aimed to determine the proportion of inaccurately collected samples and evaluate the impact on UFC variability.

Methods: Two 24-hour UFC measurements from the same subjects ($n = 552$) from two Dutch academic hospitals were evaluated retrospectively. The UFC results were considered inaccurately collected when they met 1) a creatinine difference of more than 4.0 mmol/24 hours and 2) a volume discrepancy of more than 55% between the two collections.

Results: 19% of 24-hour urine samples were inaccurately collected. Notably, UFC concentrations between the two collections varied less ($P < .001$) among accurately collected samples (Coefficient of variation; 17%), than among inaccurate collected samples (Coefficient of variation; 33%).

Conclusions: This study demonstrates that there is a substantial amount of incorrectly collected samples. These errors contribute considerably to the total variability of 24-hour UFC measurements. This highlights the importance of patient instruction and adherence to collection protocols for reproducibility of UFC measurements.

Abstract citation ID: lvag096.674

EP65 - ECE_1827 - Transient Thyroiditis as a Confounding Feature in Autoimmune Polyglandular Syndrome Type 2

Vijay Ramadoss, Ryan Goindoo, Lisa Owen and Michael Pierides

Leicester, United Kingdom

Background: Autoimmune Polyglandular Syndrome type 2 (APS-2) is characterised by autoimmune adrenal insufficiency (AI) with autoimmune thyroid disease and/or type 1 diabetes mellitus or primary ovarian insufficiency. Thyroid dysfunction most commonly manifests as Graves' disease or Hashimoto's thyroiditis. We describe a case of APS-2 presenting with primary AI and a transient thyrotoxic phase most consistent with thyroiditis, highlighting important diagnostic and therapeutic considerations.

Case Presentation: A 45-year-old woman presented with a 12-month history of salt craving, postural dizziness, nausea, vomiting and fatigue. Examination revealed generalised hyperpigmentation. She was clinically euvolaemic with otherwise unremarkable cardiovascular, respiratory and abdominal examinations. Ocular examination demonstrated lid lag without features of Graves' ophthalmopathy. There was no goitre or thyroid tenderness.

Her medical history included attention deficit hyperactivity disorder treated with lisdexamfetamine. She had three successful pregnancies and one termination at 15 weeks' gestation without excessive bleeding. She reported secondary amenorrhoea for 18 months and had no family history of autoimmune disease.

Initial investigations demonstrated hyponatraemia (123 mmol/L), borderline hyperkalaemia (5.3 mmol/L), low serum osmolality (266 mOsm/kg), elevated urine osmolality (556 mOsm/kg) and elevated urine sodium (83 mmol/L). Thyroid function tests suggested biochemical thyrotoxicosis (TSH < 0.01 mIU/L, FT4 29.5 pmol/L). Gonadotropins were elevated with low oestradiol, consistent with primary ovarian failure.

Morning cortisol was 417 nmol/L, inappropriately normal for the clinical context. Given the high pre-test probability of AI, a short Synacthen test was performed, demonstrating suboptimal peak cortisol of 306 nmol/L, without any rise, and with markedly elevated ACTH (914 ng/L), confirming primary AI.

Management: The patient was commenced on hydrocortisone (10/5/5 mg) and fludrocortisone 100 micrograms daily. Antithyroid therapy was deferred until steroid repletion to avoid

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

precipitating adrenal crisis. At four-week follow-up, there was biochemical resolution of hyponatraemia and hyperkalaemia with significant symptomatic improvement. Thyroid function normalised spontaneously (FT4 12.8 pmol/L, TSH 1.31 mIU/L) without specific therapy. TSH receptor and anti-TPO antibodies were negative, while adrenal and ovarian antibodies were positive, confirming APS-2 with primary AI and ovarian failure.

Conclusions: This case highlights the importance of dynamic adrenal testing despite an adequate baseline cortisol when clinical suspicion is high. Thyroid dysfunction in APS-2 may be transient, and thyroid-directed therapy should be deferred until patients are steroid replete. To our knowledge, this adds to the limited literature describing APS-2 presenting with features most consistent with painless thyroiditis, raising the possibility of an unusual temporal association in the context of prolonged untreated AI.

Abstract citation ID: lvag096.675

EP68 - ECE_3024 - Clinical outcomes of patients with adrenocortical carcinoma—a single centre experience

Theodora Nistor[1], Monalisa Preda-Ivascu[1], Roxana Enachescu[1], Cristina Coman[2], Roxana Nita[3], Radu Iorgulescu[2], Roxana Dusceac[1], Dan Niculescu[1,4], Simona Galoiu[1,4], Serban Radian[1,4] and Catalina Poiana[1,4]
[1]Institutul Național de Endocrinologie CI Parhon, București, Romania; [2]Spitalul Clinic de Urgență Sfântul Ioan București, București, Romania; [3]Spitalul de Boli Cronice Sfântul Luca București, București, Romania; [4]Ramnicu Valcea, Romania

Background: Adrenocortical carcinoma (ACC) is a rare endocrine malignancy with aggressive clinical behaviour and poor prognosis, due to limited therapeutic options. Management relies on a multidisciplinary approach, in order to improve outcomes.

Methods: A retrospective, observational study was conducted in a tertiary endocrine centre. Clinical findings, hormone secretion, histopathological characteristics, treatment modalities and outcomes were reviewed. Overall survival (OS) and progression- free survival (PFS) were analyzed using the Kaplan-Meier method.

Results: Thirteen patients were included, predominantly female (76.9%), median age at diagnosis 49 years (range 22-76). 76.9% of tumors were functional, 40% of these having mixed glucocorticoid and androgen secretion. The mean axial tumor diameter at diagnosis was of 8.3 cm. The median Weiss score was 6 (range 4-8) and median Ki-67 index was 17.5% (range 5-80). All patients underwent surgical resection of primary tumors, with selected patients undergoing resections of metastases. Adjuvant therapy was used in most patients: Mitotane (76.9%), chemotherapy (53.8%) and radiotherapy (30.8%).

Metastatic disease was present at diagnosis in 4 patients and developed during follow-up in five. Median follow-up was 18 months (1-84) and median survival was 13.5 months (10-17), for the deceased patients. Median OS was not reached, while median PFS was 24 months.

Conclusions: In routine clinical practice, aggressive surgical management combined with individualized adjuvant treatment is associated with significant survival in selected patients with ACC, ideally provided in a multidisciplinary setting.

Abstract citation ID: lvag096.676

EP69 - ECE_3356 - When adrenal masses are not metastasis: a Primary Adrenal Lymphoma

Beatriz R. Pereira[1], Joana Vinhais[1], David Verissimo[1], Catarina Ivo[1], Ana Cláudia Martins[1], D'jalma Soulé[2], Miguel Valente[2], Ascension Lopez[2], Luis Lopes[1], Dolores Passos[1], Mafalda Marcelino[1], João Jácome de Castro[1] and João Nunes Silva[1]
[1]Endocrinology, Hospital Das Forças Armadas, Lisboa, Portugal; [2]Lisboa, Portugal

Introduction: Primary adrenal lymphoma is rare, accounting for less than 1% of non-Hodgkin lymphomas. It typically manifests as bilateral adrenal masses, often associated with adrenal insufficiency.

Case-Report: An 83-year-old male was admitted to the emergency room with fatigue, vomiting, progressive abdominal distension and a 16 kg weight loss over two months. His medical history included type 2 diabetes, hypertension and dyslipidemia, managed with once a day metformin 1000 mg, carvedilol 6.25 mg and simvastatin 20 mg. On examination no differentiating features were found other than distended painless abdomen.

Initial laboratory tests showed hypoglycemia (61 mg/dL), hypercalcemia (11.9 mg/dL) and hyponatremia (126 mmol/L), which improved with intravenous fluids. Abdominal CT revealed two large solid adrenal masses (14 cm on the right and 11 cm on the left), with adjacent lymphadenopathy, suggesting lymphoproliferative disease. Hence, he was admitted with suspected bilateral adrenal neoplasm.

Complementary evaluation showed low-to-normal cortisol (10.9 ug/dL), elevated ACTH (137 pg/mL), low PTH (3.8 pg/mL), elevated 1,25-dihydroxyvitamin D (117 pg/mL), and suppressed PTHrP (<1.2 pmol/L). Remaining adrenal function and its precursors were within normal range. Due to presumed adrenal insufficiency along with $1,25(OH)_2D$ mediated hypercalcemia prednisolone was initiated.

FDG PET/CT revealed bulky upper-abdominal disease with extensive visceral and perivascular lymphadenopathy. An inguinal node was biopsied, confirming diffuse large B-cells lymphoma. Despite sustained correction of sodium, calcium and glucose, the patient died of disease progression on day 20 of admission.

Discussion/Conclusions: This is a rare case of primary adrenal lymphoma, presenting with bilateral adrenal masses and adrenal insufficiency. Also exhibiting calcitriol-mediated hypercalcemia, the predominant mechanism in lymphoma, although an uncommon cause of malignancy-related hypercalcemia.

Despite metastases accounting for most adrenal masses, the fulminant course requires a high index of suspicion for primary adrenal lymphoma. Targeted therapy requires timely diagnosis, which was not possible due to rapid clinical decline. When adrenal insufficiency is suspected, prompt glucocorticoid therapy is needed to mitigate acute complications that contribute to mortality. Given its distinctive features and aggressiveness, primarily adrenal lymphoma should remain in the differential diagnosis of bilateral adrenal masses.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.677

EP70 - ECE_3476 - ACTH-producing pheochromocytomas

Barbora Holá, Michal Krsek, Tomáš Zelinka, Ondrej Petrák, Zuzana Krátká and Václav HánaJr
Prague, Czech Republic

Background: Adrenocorticotropic hormone (ACTH) secreting pheochromocytoma is a rare and severe cause of ACTH-dependent Cushing syndrome (CS) that is associated with high morbidity.

The aim of this study is to describe clinical and biochemical characteristics of patients with ACTH-secreting pheochromocytoma.

Methods: This is a retrospective case series of patients with the diagnosis of pheochromocytoma associated with biochemical evidence of ACTH excess production, collected from one centre between the years 1994 and 2024. The data included demographic characteristics, tumour size, presence of clinical signs of CS, metabolic and electrolyte disturbances, catecholamine secretion and cortisol parameters.

Results: In total, there were 7 patients included (4 women, 3 men), with a median age at diagnosis of 51 years (range 26–72). Median size of tumour was 52 mm (range 26-95). At the time of diagnosis, hypertension and diabetes mellitus or impaired glucose metabolism were present in 6 (86%) patients, and hypokalaemia in all patients. Cushingoid phenotype was apparent in 4 patients (57%). ACTH levels were markedly elevated in most patients (up to 40 of upper limit of normal), accompanied by elevated urinary free cortisol reaching over 100 of upper limit of normal in few cases. Cortisol levels remained high in dexamethasone suppression test performed in 4 patients. Catecholamine excess production was measured in all 7 patients but varied greatly, in 5 patients (70%) adrenergic type of pheochromocytoma was confirmed and 2 patients (30%) had noradrenergic type of pheochromocytoma.

Conclusions: This case series confirms that ACTH-secreting pheochromocytomas frequently present with severe hypercortisolism, hypokalaemia, diabetes and hypertension. Our findings are consistent with available published data and further support the need to consider ectopic ACTH secretion in patients with clinical and laboratory signs of Cushing syndrome and adrenal masses.

Abstract citation ID: lvag096.678

EP72 - ECE_1861 - Mixed corticomedullary tumor of the adrenal gland with component of cortical adenoma, pheochromocytoma and ganglioneuroma: a rare case report

Marie Cornec[1], Emmanuel Sonnet[1], Vincent Joulin[2], Jean-Romain Risson[3], Laurent Doucet[4] and Philippe Thuillier[1]
[1]*Department of Endocrinology, University Hospital of Brest, Brest, France;* [2]*Department of Urology, University Hospital of Brest, Brest, France;* [3]*Department of Radiology, University Hospital of Brest, Brest, France;* [4]*Department of Pathology, University Hospital of Brest, Brest, France*

Background: Mixed corticomedullary tumors (MCMTs) of the adrenal gland are extremely rare lesions containing both medullary and cortical cells within a single mass. First documented in 2011, we describe an even rarer adrenal MCMT case with cortical adenoma, pheochromocytoma and ganglioneuroma components.

Case Presentation: A 77-year-old man, under medical follow-up in urology for elevated prostate-specific antigen, was referred to our clinic in 2025 after the discovery of a left adrenal incidentaloma on MRI. Clinical assessment highlighted labile hypertension associated with malaise, palpitations and flushes. Cardiac echography showed a left ventricular hypertrophy without heart failure.

Biological findings ruled out primary hyperaldosteronism, hypercortisolism and androgen excess. Both the 24-hour urine and plasma normetanephrine levels were elevated (respectively 4.08 µmol (0.2–1.5) and 0.86 nmol/L (<0.36)), while metanephrine levels remained normal.

Computed tomography revealed a left hypervascular heterogeneous mass (46 mm) with necrosis and spontaneous density of 18 Hounsfield Units. The patient underwent an 18F-DOPA PET/CT which revealed intense radiotracer uptake by the lesion.

The association of his clinical presentation, biological and imaging findings raised a high suspicion of pheochromocytoma and surgery was scheduled. Patient received alpha-blocker treatment (Urapidil) preoperatively, which was poorly tolerated (severe hypotension that required volume expansion). A robot-assisted laparoscopic left adrenalectomy was performed without complication.

Gross and microscopic examination revealed a 40×20 mm mass, composed of cortical adenoma (50%), pheochromocytoma (25%) and ganglioneuroma (25%).

The areas were topographically distinct, within the same non-encapsulated lesion. Immunohistochemistry confirmed SF1, inhibin and Calretinin positivity on the cortical component, Chromogranins A & B positivity on pheochromocytoma cells and neurofilament and calretinin on ganglioneuroma component. Ki67 was <1%, PASS score 2/20 and WEISS score 0/9.

NGS did not detect any pathogenic variants or mutations associated with pheochromocytoma. Additional analyses are ongoing.

Discussion: This case represents an extremely rare adrenal tumor, confirmed by immunohistochemistry. To our knowledge, this is only the fourth case ever reported.

The pathogenesis of MCMTs remains unclear, as medullary and cortical cells derive from different embryonic lineages. Two previously reported cases presented with Cushing's syndrome, and the third case showed both catecholamine and cortisol excess. In contrast, our patient experienced isolated catecholamine excess without hypersecretion from the cortical adenoma component.

The existence of MCMTs seems to be rare, and suggests screening for hypercortisolism in some cases of patients with a strong suspicion of pheochromocytoma.

Abstract citation ID: lvag096.679

EP73 - ECE_1335 - From trauma to tumour: incidental giant left adrenal myelolipoma in congenital adrenal hyperplasia

Emily Mayar, Anna Crown and Sing Yang Sim
University Hospitals Sussex NHS Foundation Trust, Brighton, United Kingdom

Background: Adrenal myelolipomas are rare, benign tumours with an estimated prevalence of 0.08-0.4%. With increasing

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

utilisation of CT scans, these lesions are being detected more often, accounting for about 6% to 16% of all adrenal incidentalomas. Patients with congenital adrenal hyperplasia (CAH) are predisposed to adrenal hyperplasia and, occasionally, giant or bilateral myelolipomas due to persistent ACTH stimulation which induces tumorigenesis. Giant myelolipomas (>10 cm) involve a 3-6% risk of spontaneous rupture. CAH patients are 30 times more likely to develop myelolipomas compared to the general population.

Case history: A 49-year-old female with CAH underwent a CT scan after sustaining a stab wound to her abdomen, which demonstrated a superficial abdominal wall injury. There was an incidental finding of a 12 cm encapsulated left adrenal lesion containing fat, soft tissue, and calcification, suggestive of a giant myelolipoma. She was diagnosed with CAH at birth due to the presence of ambiguous genitalia. Her brother has CAH and bilateral adrenal myelolipomas.

The patient was reviewed in an endocrine clinic and reported good adherence to hydrocortisone 10 mg twice daily and fludrocortisone 200 mcg daily. However, her persistently elevated androstenedione, 17-OHP and renin levels indicated possible non-compliance with medication.

Biochemistry:

Parameter	Result	Reference ranges
17-hydroxyprogesterone	117.5	1-8.7 nmol/L
Androstenedione	18.8	2-5.4 nmol/L
Renin	191.0	5.4-60 mU/L
Testosterone	4.3	0.29-1.67 nmol/L
Sodium	135	136-145 mmol/L
Potassium	4.9	3.5-5.1 mmol/L
eGFR	>60	60-90 mL/min

Given the size of the adrenal myelolipoma and potential risk of spontaneous rupture the case was reviewed in the adrenal MDT meeting and a left adrenalectomy was offered to her.

Discussion: Giant lesions may rupture and usually need surgical excision, preferably at a specialist centre because of operative complexity. It is important to integrate clinical history, biochemical markers and imaging to effectively risk stratify. In CAH, bilateral adrenal involvement is a result of ACTH overstimulation. This leads to adrenal hyperplasia, which later undergoes metaplastic transformation into hematopoietic tissue, resulting in the formation of myelolipomas. Multidisciplinary management is paramount to determine if surgery is required, arrange steroid cover and monitor the contralateral adrenal gland.

Conclusions: Our case illustrates a rare giant myelolipoma in a CAH patient emphasizing the importance of biochemical and imaging surveillance. Multidisciplinary management will help guide management. Future research could help establish imaging protocols for early detection to reduce risk of spontaneous rupture.

Abstract citation ID: lvag096.680

EP74 - ECE_1908 - Acute dilated cardiomyopathy revealing oncocytic adrenocortical adenoma induced ACTH-independent Cushing's syndrome in a young adult harbouring an ARMC5 variant

Fatma Alshamsi, Budoor Alemadi, Elamin Abdelgadir and Fatheya Alawadi
Dubai Hospital, Dubai, United Arab Emirates

Background: ACTH-independent Cushing's syndrome (CS) due to adrenocortical adenomas is uncommon, and acute cardiomyopathy is a rare initial manifestation. Excess cortisol impairs myocardial contractility and metabolism. Pediatric-onset CS guidelines recommend genetic testing directed at the source of hypercortisolemia, and genomic testing is advised for patients with bilateral adrenal masses and ACTH-independent cortisol excess. Guidelines for young adults with unilateral adenomas is limited.

Case Presentation: A 22-year-old man presented with progressive obesity, uncontrolled type 2 diabetes mellitus requiring insulin, and hypertension, culminating in acute heart failure. Echocardiography demonstrated severe left ventricular dysfunction with an ejection fraction of 25%. Causes of non-ischemic cardiomyopathy were excluded. Cushingoid features prompted endocrine evaluation, confirming ACTH-independent hypercortisolemia. Laboratory results included: 24-hour urinary free cortisol >570 µg/24 h (11.5–102), AM cortisol 614 nmol/L; repeat 24-hour urinary free cortisol 262 µg/24 h; salivary cortisol 6.37 µg/L (late evening <1.1 µg/L); ACTH <1.5 pg/mL; AM cortisol 579 nmol/L; DHEAS 5.48 µmol/L; subsequent 24-hour urinary free cortisol 324 µg/24 h; and salivary cortisol 7.08 µg/L.

CT imaging demonstrated a benign-appearing right adrenal mass with wedge compression fractures of the D10–D12 vertebral bodies. Bone densitometry confirmed osteoporosis. Given the patient's young age and a brother with obesity, poorly controlled diabetes, and erectile dysfunction in his twenties, germline genetic testing was performed, identifying a heterozygous ARMC5 variant of uncertain significance, previously associated with ACTH-independent macronodular adrenal hyperplasia.

The patient underwent right adrenalectomy. Gross examination revealed a $5.0 \times 4.0 \times 4.0$ cm well-circumscribed nodular adrenal mass with a well-defined capsule. Histopathology confirmed a benign oncocytic adrenocortical adenoma. Postoperatively, serum cortisol normalized, insulin therapy was discontinued following improved glycemic control, and left ventricular function improved to an ejection fraction of 47%.

Discussion: Severe, reversible cardiomyopathy may be the presenting feature of ACTH-independent CS. Current guidelines recommend genetic testing in pediatric-onset disease and bilateral adrenal pathology; however, this case suggests that young adults with unilateral adenomas may also harbor clinically relevant genetic variants. Identification of germline mutations is essential for individualized management, genetic counselling, and family screening. Early recognition and surgical intervention can allow cardiac recovery.

Conclusions: This abstract reports a case of severe decompensated cardiomyopathy due to genetically mediated ACTH-independent Cushing's syndrome in a 22-year-old man and describes an ARMC5 variant associated with a unilateral oncocytic adrenal

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

adenoma. Genetic testing beyond current guidelines may be warranted in young patients with ACTH-independent hypercortisolism. Timely adrenalectomy can reverse cardiovascular and metabolic complications.

Abstract citation ID: lvag096.681

EP75 - ECE_2199 - Incidental adrenal angiomyolipoma revealing primary hyperaldosteronism

Hamza El Fekih[1], Eya Zorai[2], Wiem Saafi[2], Sawsen Nouira[2], Ayoub Gasmi[3], Imen Halloul[2], Ach Taieb[1], Ghada Saad[2] and Yosra Hasni[2]

[1]Faculty of Medicine of Sousse, Department of Endocrinology and Diabetology/ Laboratory of Exercise Physiology and Pathophysiology (LR19ES09), Farhat Hached University Hospital, University of Sousse, Sousse, Tunisia; [2]Department of Endocrinology and Diabetology, Farhat Hached University Hospital, Sousse, Tunisia; [3]Department of Radiology, Farhat Hached University Hospital, Sousse, Tunisia

Introduction: Angiomyolipoma is an extremely rare mesenchymal tumor without malignant characteristics composed, in varying proportions, of blood vessels, smooth muscle cells, and adipocytes. It usually affects the kidney. Extra-renal angiomyolipoma is rarein clinical practice, particularly in the adrenal gland-which limits our understanding of the disease.We herein report the case of a patient with an incidentally discovered adrenal angiomyolipoma, who was diagnosed with primary hyperaldosteronism during the diagnostic workup.

Case Presentation: A 58-year-old woman, with grade I arterial hypertension, had an abdominal ultrasoundfor diffuse abdominal pain which revealed a right adrenal mass of 4 cm, with a heterogeneous and hypoechoic appearance. The patient had manysuggestive clinical features of essential hypertension: family history of hypertension, her age, class II obesity, no target organ damage, nor clinical signs suggestive of hormonal hypersecretion. Serum potassiumlevels were normal. Computed tomography scan confirmed the presence of a right adrenal incidentaloma measuring 50 × 32 mm, with radiological features suggesting an angiomyolipoma. Hormonal assessmentwas systematically done confirming primary hyperaldosteronism, with elevated plasma aldosterone levels (561 pmol/L) and aldosterone-to-renin ratio.

Discussion: Adrenal angiomyolipoma is a rare benign tumor, commonly discovered incidentally during radiological investigations. Although usually considered non-functioning, hormonal hypersecretion may be foundin a few cases of patients with adrenal angiomyolipoma. This association should alert clinicians to the possibility of a potentially curable cause of secondary hypertension requiring specific treatment.

Abstract citation ID: lvag096.682

EP76 - ECE_2610 - Adult-onset X-linked adrenoleukodystrophy with ABCD1 gene mutation

Zehra Irshad and Pratibha Natesh

Coventry, United Kingdom

X-linked adrenoleukodystrophy (X-ALD) is a progressive neurodegenerative disorder associated with mutation of ABCD1 gene encoded protein adrenoleukodystrophy protein (ALDP). This results in accumulation of very long chain fatty acids which damages the myelin sheath in the brain, spinal cord and adrenal glands causing adrenal insufficiency and neurology. Here we describe a case of delayed diagnosis of adult-onset X-ALD.

A 50-year-old gentleman was referred to Neurology with progressive poor mobility and spasticity which started in his 20s. He had a strong family history of neurological conditions. His mother was diagnosed with late-onset peripheral neuropathy and his maternal uncle passed away in early 30s with poor mobility. He was diagosed as Hereditary spastic paraparesis and was managed with Baclofen and physiotherapy under Neurology. However, his symptoms continued to progress and further investigations (EMG, nerve conduction studies, MRI head and spine and ERG) did not show any supportive findings. He was sent for further gene analysis which identified mutation in ABCD1 and was hence referred to Endocrine to review adrenal involvement. He denied symptoms of fatigue, dizziness, weight-loss, headaches, palpitation or sweating. His observations showed blood pressure of 158/81 and BMI of 30. There was absence of stigmata of adrenal disease. His 9am biochemical profile showed elevated plasma ACTH (435 ng/L ref <30 ng/L) with normal sodium, potassium, serum aldosterone, plasma renin and cortisol (357 nmol/L; ref 145-619). His plasma metnephrines and normetnephrines were also within normal range. He was referred for urgent short synacten test which confirmed adrenal insufficiency and hence he was started on hydrocortisone.

X-ALD manifests as adrenal insufficieny in 90% of the patients independently of the neurological affection which affects 50% of the males.[1] Diagnosis is usually confirmed with gene analysis. Treatment requires multidiscliplinary involvement for symptoms management. Our case highlights the importance of early gene analysis in patients with strong family history of neurodegeneration to support early diagnosis and management in absence of overt adrenal symptoms.

Reference

1. Paláu-Hernández S, Rodriguez-Leyva I, Shiguetomi-Medina JM. Late onset adrenoleukodystrophy: a review related clinical case report. *Eneurologicalsci*. 2019;14:62-67. https://doi.org/10.1016/j.ensci.2019.01.007

Abstract citation ID: lvag096.683

EP77 - ECE_2193 - An insidious case of food-dependent Cushing's syndrome associated with a germline KDM1A variant in Bilateral Macronodular Adrenal Disease (BMAD)

Dorota Leszczynska[1], Julia Latocha[2], Alicja Duquenne[2,3,4], Beata Woźniak[3], Wojciech Zgliczyński[3] and Piotr Glinicki[3,4]

[1]Centre of Postgraduate Medical Education, Endocrinology, Warsaw, Poland; [2]Centre of Postgraduate Medical Education, Student Scientific Group at the Department of Endocrinology, Warsaw, Poland; [3]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [4]Centre of Postgraduate Medical Education, EndoLab Laboratory, Warsaw, Poland

Background: Bilateral Macronodular Adrenal Disease (BMAD) is characterized by the presence of benign bilateral adrenal lesions larger than 10 mm and by variable degrees of cortisol overproduction. It may account for up to 30% of cases of bilateral

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

adrenal incidentalomas. Cortisol secretion in BMAD is regulated by aberrantly expressed adrenal receptors.

Case Presentation: A 44-year-old woman was referred to a tertiary endocrine center because of incidentally detected bilateral adrenal nodules. The patient reported unintentional weight gain of 4 kg over six months and sleep disturbances. Physical examination revealed central obesity and easy bruising, and her medical history was notable for well-controlled hypertension on monotherapy. Laboratory evaluation revealed low morning serum cortisol (4.8 µg/dL) with suppressed plasma ACTH levels, loss of circadian cortisol rhythm, lack of cortisol suppression in the 1 mg overnight dexamethasone suppression test and elevated 24-hour urinary free cortisol excretion.

Computed tomography demonstrated bilateral macronodular adrenal hyperplasia with a dominant lesion in the right adrenal gland. Magnetic resonance imaging revealed signal drop on out-of-phase sequences in all adrenal lesions, consistent with lipid-rich nodules.

Receptor stimulation testing was performed with cortisol and ACTH measurements at baseline and at 60 and 120 minutes. The diagnostic work-up included supine-to-upright posture testing, stimulation with octreotide, metoclopramide, desmopressin, gonadotropin-releasing hormone (GnRH), tetracosactide (ACTH 1–24), oral glucose tolerance test, and a mixed meal. A greater than 50% increase in serum cortisol following the mixed meal, oral glucose tolerance test, and GnRH stimulation was interpreted as a positive response, suggesting gastric inhibitory polypeptide (GIP)- and GnRH-dependent hypercortisolaemia.

Molecular testing identified a heterozygous *KDM1A* variant (c.982G>A; p.Glu328Lys, exon 7), classified as potentially pathogenic. The patient's family history was notable for her mother, who had bilateral adrenal lesions and underwent bilateral adrenalectomy because of ACTH-independent hypercortisolaemia. The patient's only daughter was tested negative for the *KDM1A* variant.

Conclusions: The presented case underlines the necessity of including bilateral macronodular adrenal disease (BMAD) in the differential diagnosis of bilateral adrenal incidentalomas. The mild and insidious clinical course of hypercortisolaemia in most patients may lead to delayed diagnosis. Germline KDM1A variants are the most prevalent genetic cause of BMAD associated with food-dependent Cushing's syndrome (FDCS). Loss of KDM1A, a tumour suppressor gene, results in aberrant adrenal GIP receptor expression and postprandial stimulation of cortisol secretion. Identification of FDCS should prompt biochemical and genetic screening of relatives.

Abstract citation ID: lvag096.684

EP78 - ECE_2622 - Baseline cortisol as a predictor of adrenal insufficiency and the value of the 60-minute post-synacthen cortisol

Simon Mifsud[1], Jacob Cassar[2] and Charlton Agius[2]
[1]*Department of Diabetes and Endocrinology, Mater Dei Hospital, Msida, Malta;* [2]*Department of Pathology, Clinical Chemistry Section, Mater Dei Hospital, Msida, Malta*

Introduction: The short synacthen test (SST) evaluates the integrity of the hypothalamic-pituitary-adrenal axis. The study aimed to evaluate (1) the diagnostic performance of morning baseline serum cortisol for adrenal insufficiency (AI) and (2) the agreement between the 30- and 60-minute cortisol measurements.

Method: Adult SSTs performed using the Siemens IMMULITE® 2000 cortisol immunoassay between January 2024 and August 2025 were retrospectively analyzed. AI was defined as peak cortisol <500 nmol/L.

Results: The cohort included 282 adults (mean age 50.6 years [SD 16.5]) with a female predominance (59.2%). AI was diagnosed in 45 patients (16.0%).

Patients with AI had a significantly lower baseline cortisol compared to those with adrenal sufficiency (median 192 nmol/L [IQR:144.5–249.5] vs 255 nmol/L [IQR:198–331], $P < .001$). Baseline cortisol demonstrated moderate discrimination for AI (AUC 0.728, 95% CI 0.653–0.803). A baseline cortisol threshold ≤124 nmol/L achieved 95.4% specificity (sensitivity 22.2%) for AI, whereas a threshold >291 nmol/L excluded AI with 95.6% sensitivity (specificity 36.7%). In this cohort, baseline cortisol thresholds of ≤89.5 nmol/L and >376.5 nmol/L provided 100% specificity and 100% sensitivity, respectively.

Median cortisol increased from 241.5 nmol/L (IQR:180.5–309) at 0-minutes to 528.5 nmol/L (IQR:464-590) at 30-minutes and 605.5 nmol/L (IQR:541-683.3) at 60-minutes post-synacthen. Wilcoxon signed-rank tests confirmed statistically significant increases for all pairwise comparisons (0 vs 30 min: $Z = -14.492$; 30 vs 60 min: $Z = -14.180$; 0 vs 60 min: $Z = -14.473$, all $P < .001$; Bonferroni-adjusted $\alpha = 0.0167$). The largest increase occurs between 0 vs 30 minutes, but the 30 vs 60 minutes also shows a significant rise, capturing late responders.

When examining consistency across the 30- and 60-minute intervals within our cohort, 168 patients passed at both time intervals, 68 passed at 60-minutes only, and 1 passed at 30-minutes only ($\kappa = 0.435$, $P < .001$). These findings indicate moderate agreement between the 30- and 60-minute classifications.

McNemar's test demonstrated significant asymmetry ($P < .001$), with substantially more individuals passing the SST at 60-minutes but failing at 30-minutes than the reverse. Reliance on the 30-minute cortisol alone would have misclassified 28.6% ($n = 68/237$) as adrenal insufficient despite passing at 60-minutes.

Conclusions: Morning baseline cortisol was associated with SST outcome and demonstrated moderate discrimination for AI in our cohort. In addition, cortisol continued to increase significantly between 30 and 60-minutes post-synacthen. This supports inclusion of the 60-minute cortisol measurement to identify late-responders and reduce false-positive diagnoses of AI compared with relying solely on the 30-minute cut-off.

Abstract citation ID: lvag096.685

EP79 - ECE_2709 - Adrenal incidentalomas: 1 mg dexamethasone test result in the context of cardiometabolic risk

Alicja Hubalewska-Dydejczyk[1], Joanna Kokoszka[2], Marta Opalinska[1], Magdalena Kolasa[2], Katarzyna Sitarz[3], Anna Matrejek[2], Aleksandra Banas[1], Gabriela Pabian[1], Karol Musial[1], Aleksandra Gilis-Januszewska[1] and Krystyna Sztefko[4]
[1]*Jagiellonian University Medical College, Cracow, Poland;* [2]*University Hospital, Cracow, Poland;* [3]*Department of Clinical Genetics and Rare Diseases, Medical University of Silesia, Katowice, Poland;*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[4]Department of Clinical Biochemistry, Jagiellonian University Medical College, Institute of Paediatrics, Cracow, Poland

Introduction: Mild autonomous cortisol secretion (MACS) represents the most common hormonal abnormality in patients with adrenal incidentalomas. The 1 mg dexamethasone suppression test (DST), using a cortisol cutoff value of 1.8 µg/dL, is currently recommended to exclude hypercortisolism. However, growing evidence suggests that adrenal tumors classified as non-functioning may still secrete low amounts of cortisol that remain below the established cutoff yet contribute to an increased cardiometabolic risk. This observation raises concerns that the currently accepted cutoff value may underestimate clinically relevant cortisol excess.

Objectives: The aim of this study was to reassess the cortisol cutoff value in the 1 mg DST for identifying increased cardiometabolic risk in patients with adrenal incidentalomas.

Methods: This retrospective, cross-sectional observational study included patients with adrenal incidentalomas treated at a tertiary endocrinology center between 2017 and 2020. Of 1077 initially screened patients, 807 met the inclusion criteria based on complete hormonal evaluation, adrenal CT imaging, and histopathological confirmation in surgically treated cases. All patients underwent a 1 mg DST. Receiver operating characteristic (ROC) curve analysis and area under the curve (AUC) calculations were used to evaluate the ability of post-DST cortisol concentrations to predict cardiometabolic diseases. Multivariable logistic regression models adjusted for age, sex, obesity, and smoking status were applied.

Results: Post-DST cortisol concentrations were significantly higher in patients with hypertension, coronary heart disease (CHD), chronic heart failure (CHF), diabetes mellitus, chronic obstructive pulmonary disease (COPD), and chronic kidney disease (CKD) compared with patients without these conditions. In multivariable analyses, cortisol thresholds lower than the conventional 1.8 µg/dL were significantly associated with increased disease risk: 1.46 µg/dL for CHD, 1.64 µg/dL for CHF, 1.20 µg/dL for diabetes mellitus, and 1.37 µg/dL for CKD. A common cortisol threshold of 1.35 µg/dL was identified, above which the risk of CHD, diabetes mellitus, and CHF increased significantly.

Conclusions: The findings of this study suggest that the currently recommended DST cutoff value of 1.8 µg/dL may fail to detect clinically relevant cortisol excess in patients with adrenal incidentalomas. Lower cortisol thresholds may better identify individuals at increased cardiometabolic risk and could improve clinical risk stratification and management.

Abstract citation ID: lvag096.686

EP80 - ECE_2865 - Circadian profiling of steroid hormones and metabolites in dried blood spots (DBS) by Liquid Chromatography-Mass Spectrometry (LC-MS/MS): a pilot study

Greta Galante[1,2], Mathieu Galmiche[2,3], Valentina Bissi[1], Federico Mao[1,4], Gianmarco Pizza[1,4], Alessia Gennai[1], Laura Tribotti[1,4], Francesca Donnarumma[1,4], Guido Di Dalmazi[1,4], Uberto Pagotto[1,4], Serge Rudaz[2,3] and Flaminia Fanelli[1]

[1]Center for Applied Biomedical Research, CRBA, University of Bologna, Bologna, Italy; [2]School of Pharmaceutical Sciences, University of Geneva, CMU- Rue Michel-Servet 1, Geneva, Switzerland; [3]Institute of Pharmaceutical Sciences of Western Switzerland, University of Geneva, CMU - Rue Michel-Servet 1, Geneva, Switzerland; [4]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Introduction: Altered steroid hormone levels have been reported in a wide range of endocrine and non-endocrine disorders. However, the investigation of perturbation of circadian steroid secretion remains challenging, mainly due to the need for frequent blood sampling and highly sensitive analytical methods. DBS from finger-prick allows autonEomous and non-invasive home sampling. In parallel, recent advances in LC-MS/MS provides high sensitivity for measurements of small blood volumes, while quantitation based on internal calibration enhances throughput and ensures accuracy.

Aim: To assess the feasibility of DBS sampling combined with LC-MS/MS and internal calibration quantitation as a tool to investigate steroid circadian fluctuation.

Methods: DBS were collected from 6 healthy subjects (3 males, 3 females) at nine time points of an ordinary day (07:00, 08:30, 10:00, 12:30, 14:00, 16:00, 19:30, 21:00 and 23:00). After the addition of isotopically labelled internal calibrants, cortisol, cortisone, 11-deoxycortisol, 11-deoxycorticosterone, 17OH-progesterone, androstenedione and testosterone were quantified by LC-MS/MS from extracts of two 6 mm DBS punches. Data were reported in ng/mL and analysed by non-parametric tests. The analytical method also included a relative quantitation of a broad panel of steroids and related metabolites. For the latter, normalized peak areas were used for exploratory analyses to evaluate global temporal metabolic patterns.

Results: Cortisol, cortisone, and 11-deoxycortisol showed the expected circadian fluctuation (all $P < .001$), with higher levels in the morning and a progressive decline throughout the day. When spit by sex, these trends remained significant within both males and females (cortisol $P < .001$ and 0.037; cortisone $P < .001$ and .005; 11-deoxycortisol $P = .006$ and .003 respectively). 17OH-progesterone ($P < .001$), androstenedione ($P < .001$) and testosterone ($P = .014$) showed a circadian modulation in males but not in females. 11-deoxycorticosterone and progesterone showed no fluctuations either in males or females. Exploratory analyses showed that several glucocorticoid metabolites (20α- and 20β-dihydrocortisol, 5β-dihydrocortisol, 18-hydroxycortisol, and 11-dihydrocorticosterone) followed the same circadian pattern as their parent compound cortisol, displaying a significant decrease from morning to evening (all $P < .005$). In contrast, androgen-related metabolites, including androstenediol ($P = .027$), androsterone-3α-glucuronide ($P = .003$), and 11β-hydroxyetiocholanolone ($P = .023$), showed increasing trends over the day.

Conclusions: These preliminary findings in a small control group demonstrate the feasibility of using DBS combined with internal calibration LC-MS/MS quantitation to explore circadian steroid patterns, paving the way for future studies in larger cohorts and diverse physiological states.

Funding: PRIN2020ERLB52_001.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.687

EP82 - ECE_2910 - Clinical characteristics, diagnosis, and treatment of Cushing's syndrome: analysis of a multicenter registry in Antioquia, Colombia

Alejandro Roman-Gonzalez[1], Wilfredo Rivera[1], Maria Ramirez[1], Stefania Cruz[2], Nestor Diaz[2], Johnayro Gutierrez Restrepo[1,3], Natalia Aristizabal[2,4], Pablo Castano[3], Catalina Tobon[3], Nestor Lopez[3], Jorge Donado[5] and Carlos Builes Montaño[1,5]
[1]*Endocrinology, Universidad de Antioquia, Medellín, Colombia;* [2]*Universidad Pontificia Bolivariana, Medellín, Colombia;* [3]*Clinica Somer, Rionegro, Colombia;* [4]*Clínica Las Américas Auna, Medellin, Colombia;* [5]*Hospital Pablo Tobón Uribe, Medellín, Colombia*

Introduction: Cushing's syndrome (CS) is an endocrine disorder characterized by chronic hypercortisolism, leading to multiple comorbidities and complications. This research sought to characterize the clinical, diagnostic, and therapeutic features of patients with CS and to assess the results of surgery for Cushing's disease according to the surgical team's expertise at six medical centers in the department of Antioquia, Colombia, between 2010 and 2024.

Methods: We conducted a retrospective observational study through a review of electronic medical records. Demographic, clinical, diagnostic test data, treatment modalities, and postoperative outcomes were gathered.

Results: A total of 130 patients with CS were included; 86.9% were women, with a mean age of 50.7 years (SD: 15.04). The most common clinical presentation was weight gain (79.2%). The most frequent etiology was Cushing's disease (74.6%), then adrenal CS (16.9%) and ectopic CS (1.5%). Hypertension (66.2%) and obesity (61.5%) were the most prevalent comorbidities. Urinary free cortisol and the low-dose dexamethasone suppression test had the highest proportion of positive results at diagnosis. Transsphenoidal resection was the most commonly used treatment for pituitary disease (81.4%). The overall postoperative remission rate was 63.3%, with no significant differences according to neurosurgical expertise (68.2% with expert surgeons vs. 59.1% with others). Similarly, no differences were observed in recurrence, persistence, or postoperative complication rates.

Conclusions: This study emphasizes the diversity in symptoms, diagnosis, and therapy for CS, with a high prevalence of comorbidities and a considerable rate of postoperative recurrence. Using both use of late-night salivary cortisol and low-dose dexamethasone suppression testing may improve diagnostic accuracy in Colombia. Surgical outcomes for Cushing's disease in Antioquia are comparable to those reported by specialized pituitary centers worldwide.

Keywords Cushing's syndrome, registry, epidemiology, surgery

Abstract citation ID: lvag096.688

EP84 - ECE_3411 - Can the monocyte-to-HDL cholesterol ratio predict cardiovascular risk in patients with primary aldosteronism?

Gökhan Rıza Baykal[1], Muzaffer Serdar Deniz[1], Şefika Burçak Polat[2], Samet Senel[3], Abbas Ali Tam[2], Oya Topaloglu[2], Reyhan Ersoy[2] and Bekir Cakir[2]
[1]*Department of Endocrinology and Metabolism, Ankara Bilkent City Hospital, Ankara, Türkiye;* [2]*Department of Endocrinology and Metabolism, Endocrinology and Metabolism, Ankara Yıldırım Beyazıt University Faculty of Medicine, Ankara Bilkent City Hospital, Ankara, Türkiye;* [3]*Department of Urology, Ankara Bilkent City Hospital, Ankara, Türkiye*

Background: Primary aldosteronism (PA) is associated with a disproportionately high cardiovascular (CV) risk. The monocyte-to-HDL cholesterol ratio (MHR) is an emerging inflammatory marker, but its role in PA is unclear. We aimed to evaluate the relationship between MHR and estimated 10-year CV risk and to explore differences across PA subtypes.

Methods: In this single-centre retrospective study, we included 56 patients with biochemically and radiologically confirmed PA (mean age 53.5 ± 7.6 years, 66% women). Demographic and clinical data, blood pressure, lipid profile, and full blood count were retrieved from medical records. MHR was calculated as monocyte count ($\times 10^9$/L) divided by HDL-cholesterol (mg/dL). Neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII) were derived from the same blood tests. Ten-year CV risk was estimated using SCORE2 according to ESC recommendations. Correlations between MHR, inflammatory indices and SCORE2 were assessed, and MHR was compared between unilateral and bilateral PA.

Results: Median MHR was 8.29 (IQR 5.95–10.29). Mean SCORE2 was 5.87 ± 3.84%, and 34% of patients had SCORE2 ≥7.5%. MHR correlated positively with SCORE2 (Spearman $\rho = 0.48$, $P = .0002$) and increased stepwise across MHR tertiles, paralleled by higher SCORE2 values (median 2.6%, 5.2% and 7.6% in the lowest, middle and highest tertiles; P for trend = 0.00013). MHR also correlated with NLR ($\rho = 0.38$, $P = .0035$) and SII ($\rho = 0.43$, $P = .0009$). Patients with bilateral PA had higher MHR than those with unilateral disease (9.97 ± 3.92 vs 7.48 ± 2.54; $P = .031$).

Conclusions: In patients with PA, higher MHR is associated with greater estimated 10-year CV risk and higher inflammatory burden and is more pronounced in bilateral disease. MHR may represent a simple, inexpensive adjunct marker for CV risk stratification in PA, warranting confirmation in larger, prospective cohorts.

Abstract citation ID: lvag096.689

EP85 - ECE_2015 - Hair cortisol in dogs with congenital portosystemic shunts: a potential marker of chronic stress

Joelle Leiwy[1], Emily Stacey[1], Alex Chan[2], Victoria Lipscomb[3], Rhiannon Strickland[3], Michael Tivers[4] and Rob Fowkes[5]
[1]*Comparative Biomedical Sciences, Royal Veterinary College, University of London, London, United Kingdom;* [2]*Bristol Vet Specialists, Bristol, United Kingdom;* [3]*Clinical Sciences & Services, Royal Veterinary College, University of London, Hatfield, United Kingdom;* [4]*Paragon Veterinary Referrals, Wakefield, United Kingdom;* [5]*Small Animal Clinical Sciences, Michigan State University College of Veterinary Medicine, East Lansing, United States*

Congenital portosystemic shunts (cPSS) are vascular abnormalities that affect the development and function of the liver. In companion animals, cPSS are serious disorders that can present as a failure to thrive, metabolic abnormalities, neuronal complications and in severe cases, coma and death. Associated conditions such as hyperammonaemia and hepatic encephalopathy present increased morbidity in affected animals, as well as

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

causing deleterious quality of life issues. In this study, we examined the use of hair cortisol concentrations (HCC) as a potential marker of chronic stress and hypercortisolism in dogs with cPSS. Hair samples were collected from a cohort ($n = 75$) of dogs with cPSS recruited from two referral hospitals for attenuation surgery to treat either intrahepatic (IHPSS) or extrahepatic (EHPSS) shunts, along with samples from 15 healthy dogs. HCC in affected dogs was significantly higher than those without hepatic disease, regardless of shunt origin (0.730 ± 0.12 μg/dL in cPSS dogs vs 0.16 ± 0.02 μg/dL in healthy dogs, $P < .001$). However, in dogs that required a second attenuation surgery, HCC was not significantly altered following their initial attenuation surgery. Furthermore, HCC did not correlate with serum bile acid ($P = .9$) and ammonia ($P = .93$) concentrations for dogs where these parameters were available. Hair colour did not significantly affect HCC. These data indicate that dogs with cPSS exhibit hypercortisolism which could indicate chronic stress, as determined by elevated HCC. HCC has potential in future cPSS studies in assessing severity and outcome as a minimally-invasive Quality of Life indicator.

Abstract citation ID: lvag096.690

EP86 - ECE_2180 - 11-Oxygenated androgens and endocrine disruptors in women with Polycystic ovary syndrome or Idiopathic hirsutism

Anežka Varausová[1], Jana Vitku[1], Tereza Skodova[1], Lucie Kolatorova[1], Michala Vosátková[2], Josef Vcelak[3], Jana Vrbikova[4], Markéta Šimková[1] and Michaela Svojtková[1]
[1]*Department of Steroids and Proteofactors, Institute of Endocrinology, Prague, Czech Republic;* [2]*Department of Clinical Biochemistry, Institute of Endocrinology, Prague, Czech Republic;* [3]*Prague, Czech Republic;* [4]*Department of Clinical Endocrinology, Institute of Endocrinology, Prague, Czech Republic*

Introduction: Polycystic ovary syndrome (PCOS) and idiopathic hirsutism (IH) represent androgen excess disorders traditionally diagnosed using conventional androgen measurements. The contribution of 11-oxygenated androgens and endocrine disruptors (EDs) to these conditions remains incompletely defined.

Aim: This study investigates the role of less common steroid hormones, endocrine disruptors, and cytokines in polycystic ovary syndrome and idiopathic hirsutism to provide a comprehensive understanding of their pathophysiology.

Methods: 25 steroid hormones and 18 EDs were measured by using liquid chromatography–tandem mass spectrometry, biochemical markers were analyzed using routine methods on a Cobas® 6000 analyzer and 27 cytokines were determined with a Bio-Plex Pro™ Human Cytokine 27-plex assay kit Comparisons included non-obese women with PCOS ($n = 10$), women with IH ($n = 12$) and controls ($n = 20$), and non-obese PCOS women were compared to obese women with PCOS ($n = 9$).

Results: Levels of 11-oxygenated androgens were higher in women with PCOS compared with women with IH, with no statistically significant difference compared to controls. Women with IH exhibited lower 11-oxygenated androgen levels compared with controls. Cytokine concentrations did not differ between women with IH and controls. BPA levels were higher in obese women with PCOS than in non-obese women with PCOS. Bisphenol S was detected more frequently in women with PCOS (90%) than in controls (65%) and women with IH (50%). Significant correlations were observed between 11-ketotestosterone, androstenedione, and testosterone and insulin levels and HOMA-IR, and between immunomodulatory 7-oxygenated DHEA metabolites and nine interleukins. Our data confirms that PCOS is a multiendocrine gland disorder. Higher BPA levels in obese women with PCOS might exacerbate metabolic abnormalities. IH was not associated with inflammatory markers or altered ED levels, however it was associated with decreased 11-oxygenated androgens.

Conclusions: 7-oxygenated DHEA metabolites were associated with inflammatory cytokines, supporting their immunomodulatory role, while androgens correlated with insulin resistance and metabolic parameters, indicating a link between androgen excess and metabolic dysfunction. PCOS was confirmed as a complex disorder involving both ovarian and adrenal steroidogenesis, with a prominent contribution of 11-oxygenated androgens, low-grade inflammation driven mainly by obesity, and a potential aggravating role of BPA in obese women. In contrast, idiopathic hirsutism differed in the profile of androgens of adrenal origin without evidence of systemic inflammation or BPA involvement, suggesting differing pathophysiological mechanisms from PCOS.

Acknowledgement: The work was supported by MH CZ—DRO, Institute of Endocrinology EÚ, 00023761.

Abstract citation ID: lvag096.691

EP87 - ECE_1759 - Primary adrenal insufficiency and subclinical hypothyroidism induced by immune checkpoint inhibitors: a rare endocrine immune-related adverse event

Roxana Novac
CLINICA DR. NOVAC, Bacau, Romania

Background: Immune checkpoint inhibitors (ICIs), including CTLA-4 monoclonal antibodies, are increasingly used in oncology and are associated with immune-related endocrine adverse events. While hypophysitis with secondary adrenal and thyroid insufficiency is relatively common, primary adrenal insufficiency remains extremely rare, with only isolated cases reported in the literature.

Case Presentation: We report the case of a 58-year-old male diagnosed with right renal cell carcinoma, treated with an immune checkpoint inhibitor in combination with a CTLA-4 monoclonal antibody. After approximately 8 months of therapy, the patient developed progressive asthenia and recurrent episodes of hypotension, leading to multiple emergency department admissions. Despite repeated evaluations, no definitive diagnosis was established until August 2025, when the patient was referred to the endocrinology department.

Endocrine assessment revealed primary adrenal insufficiency, confirmed by low cortisol levels with elevated ACTH (>1300 pg/mL), and subclinical hypothyroidism, characterized by elevated TSH (8,6 uUI/mL n.v. 0,4-4,2) with normal free thyroxine levels. No clinical or biochemical evidence of hypopituitarism was identified. Adrenal imaging excluded metastatic involvement. Hormone replacement therapy resulted in significant clinical improvement.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Discussion: Primary adrenal failure induced by ICIs is exceptionally rare, particularly in contrast to secondary adrenal insufficiency due to hypophysitis. The coexistence of primary adrenal insufficiency with hypothyroidism is noteworthy, as immune checkpoint–related endocrine toxicity typically involves pituitary dysfunction leading to combined secondary adrenal and thyroid deficiencies. This case highlights an unusual pattern of endocrine immune-related adverse events and emphasizes the importance of early endocrine referral in patients receiving ICIs with nonspecific symptoms such as fatigue and hypotension.

Conclusions: This case underscores the need for increased awareness of rare endocrine immune-related adverse events associated with immune checkpoint inhibitors. Early recognition and prompt endocrine evaluation are essential to prevent diagnostic delay and potentially life-threatening complications.

Abstract citation ID: lvag096.692

EP88 - ECE_3576 - Not everything is as it seems—drug-induced endocrinopathy?

Jana Lešková[1,2], Helena Urbankova[1,2], Juliana Gregova[1,2], Martin Straka[1,2] and Peter Vanuga[1,2]
[1]*National Institute of Endocrinology and Diabetology, L'ubochňa, Slovakia;* [2]*5th Department of Internal Medicine, Faculty of Medicine, Clinical Research Unit in Endocrinology and Osteology, Comenius University and University Hospital, Bratislava, Slovakia*

Case Report: A 72-year-old female patient is followed up at an endocrinology outpatient clinic for autoimmune thyroiditis in the stage of hypothyroidism on thyroxine replacement therapy. Her past medical history: recurrent breast carcinoma (surgery in 2006 and 2021; treated with an aromatase inhibitor therapy, currently in remission), seronegative rheumatoid arthritis, osteopenia, sick sinus syndrome (bradycardia–tachycardia syndrome) with a pacemaker implanted, paroxysmal atrial fibrillation (AF) on oral anticoagulation, arterial hypertension (antihypertensive therapy affecting the renin–angiotensin–aldosterone system—RAAS), and chronic heart failure (eplerenone therapy).

The patient was newly diagnosed with diffuse large B-cell Non-Hodgkin lymphoma and received immunochemotherapy due to incomplete remission of the disease. She presents for endocrinological examination after the 9th administration of a monoclonal antibody. She complains of weakness, fatigue, dyspnoea, tremor, hair loss, weight loss, frequent stools, memory impairment and darkening of the skin, which she reports over the last month. Based on the clinical picture, Addison's disease was strongly suspected.

Hypocorticism was not confirmed after evaluation of laboratory parameters (renin > 500 mIU/L, aldosterone: 2.77 nmol/L, ACTH: 20.1 pg/mL, cortisol: 754.5 nmol/L, TSH: 28.1 mIU/L, fT4: 14.0 pmol/L, K+: 2.87 mmol/L, Na+: 135.0 mmol/L, Cl-: 96 mmol/L, WBC: 3.11 × 10^9/l).

Differential diagnosis of hyperpigmentation with a high renin level and mineral imbalance:

- Hyperpigmentation within a paraneoplastic syndrome (increased melanotropin or fragments of proopiomelanocortin)
- Loncastuximab tesirine, as a monoclonal antibody, contains a pyrrolobenzodiazepine cytotoxic payload, which causes DNA damage not only in tumour cells but may also affect healthy skin, which may lead to increased melanin production
- Secondary hyperaldosteronism in congestive heart failure
- Adverse effects of drugs affecting RAAS

Conclusions: The coexistence of malignancies and their targeted therapies in the patient complicated the assessment of the hypothalamic–pituitary–adrenal axis. We concluded that the patient's clinical picture and laboratory findings were most likely attributable to adverse drug effects (eplerenone, ACE inhibitor, diuretic, and the monoclonal antibody loncastuximab tesirine) and/or within a paraneoplastic syndrome.

Abstract citation ID: lvag096.693

EP89 - ECE_2606 - A rare endocrine duo: concurrent pheochromocytoma and hyperparathyroidism in neurofibromatosis-1

Shebina Liz Mathews, Muhammad Akhtar, David Lopez-Lazaro and Cornelius Fernandez
Diabetes and Endocrinology, Pilgrim Hospital, Boston (United Lincolnshire Hospitals NHS Trust), Boston, United Kingdom

Introduction: We present a young woman with Neurofibromatosis-1 (NF1) with incidentally detected bilateral pheochromocytomas (PCCs) and primary hyperparathyroidism (PHPT) following evaluation for flank pain.

Case Presentation: A 47-year-old woman presented with left flank pain, found to have a right adrenal mass. Dedicated adrenal CT revealed a large heterogeneous right adrenal mass 7.6 × 6.9 × 5.6cm with irregular necrotic areas and pre-contrast density of 50HU, suspicious for an aggressive lesion. An indeterminate left adrenal 1 cm nodule was also noted. Compared to the CT aortogram done 6 years ago, which showed bilateral adrenal nodules, though overlooked, the right adrenal lesion had grown. In retrospect, she reported occasional palpitations and headache, but remained normotensive.

Plasma Metanephrines 16 746 (0-509), Normetanephrines 10 553 (0-1179) and 3-Methoxytyramine <60 (0-179) in pmol/L. Calcium was elevated at 3.12 mmol/L with PTH of 17.9 (1.6-6.9 pmol/L), suggestive of PHPT with asymptomatic moderate hypercalcemia, for which Cinacalcet was initiated.

Further to the discussion in Adrenal MDT, MIBG confirmed bilateral PCCs. Although USS Neck wasn't contributory, SESTAMIBI revealed a left inferior parathyroid adenoma. A syndromic association was considered, and genetic test results are awaited, with ongoing input from the adrenal MDT.

Discussion: Given the patient's young age and concurrence of two endocrine neoplasia, it is important to think of genetic syndromes. Hereditary PCC may be associated with VHL, MEN2A or NF1. While MEN2A could explain this concurrence, MTC (70-100% by 70 years) was not present in this patient. Incidence of PCC and PHPT in MEN2A is ≤50% and ≤30%, respectively.

Nearly 1-5% of NF1 patients can develop PCCs; however, they are usually solitary, benign, rarely bilateral, and often asymptomatic or present atypically. This is due to a "two-hit mutation" leading to somatic loss of the second NF1 allele in adrenal chromaffin cells.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

It is also possible that there may be no syndromic association between the two endocrine neoplasia. However, given bilateral PCCs, genetic association is highly likely.

Conclusions: Genetic testing is paramount here to guide further management, especially surveillance for associated tumours. In asymptomatic patients with NF1, there are no guidelines that mandate screening for PCC; however, missing a diagnosis of PCC may lead to untoward outcomes. Keeping a high index of suspicion is crucial, screening ideally all patients with NF1.

Reference

1. Shinall MC, Solórzano CC. Pheochromocytoma in neurofibromatosis type 1: when should it be suspected? *Endocr Pract*. 2014;20(8):792-796. doi: https://doi.org/10.4158/EP13417.

Abstract citation ID: lvag096.694

EP91 - ECE_1558 - Adrenocortical response during HUT test in patients with vasovagal syncope

Barbora Pavlovič Bačkorová[1], Zora Lazúrová[2], Peter Mitro[3] and Ivica Lazúrová[1]

[1]Department of Internal Medicine 1, Medical Faculty P.J. Šafárik University, Košice, Slovakia; [2]4th Department of Internal Medicine, Medical Faculty P.J. Šafárik University, Košice, Slovakia; [3]Department of Cardiology 1, Medical Faculty P.J. Šafárik University, Košice, Slovakia

The objective of this prospective observational study was to evaluate the effect of head-up tilt (HUT)–induced vasovagal syncope on adrenocortical hormones (cortisol and aldosterone) and their relationship to hemodynamic changes.

Subjects and Methods: Blood samples from 79 patients who underwent the HUT test (48 women and 31 men, aged 19–73 years) were analyzed for serum aldosterone and cortisol levels. Based on their response to the HUT test, patients were divided into two groups: 50 HUT-positive (HUT+) and 29 HUT-negative (HUT−) individuals.

Results: Patients in the HUT+ group exhibited significantly lower baseline aldosterone levels compared to the HUT− group (203.1 ± 78.8 vs 266.2 ± 76.3 pg/mL, $P = .0009$). Similarly, post-HUT aldosterone levels were lower in HUT+ patients than in HUT− patients (249.5 ± 101.3 vs 351.4 ± 98.1 pg/mL, $P < .0001$). In contrast, no significant differences in serum cortisol levels were observed between the two groups. In response to the HUT test, aldosterone levels increased in both groups. Furthermore, aldosterone concentrations showed a positive correlation with systolic and diastolic blood pressure as well as heart rate. The integration of aldosterone measurement with clinical assessment and additional laboratory parameters may improve diagnostic accuracy and risk stratification in patients with syncope.

Conclusions: HUT+ patients were characterized by lower serum aldosterone concentrations and associated hemodynamic changes during orthostatic stress induced by the HUT test. These findings suggest a potential role of aldosterone in the pathophysiology of vasovagal syncope. Serum cortisol levels showed no discriminatory value between HUT-positive and HUT-negative patients.

Abstract citation ID: lvag096.695

EP92 - ECE_2235 - The effect of cyclic transdermal 17-β-estradiol on glucose metabolism and cardiovascular risk factors in postmenopausal women: a secondary analysis

Rona Brokkelkamp[1], Esther M. Speksnijder[1], Dirk Jan Stenvers[1,2], Peter Bisschop[1] and Sarah Siegelaar[1]

[1]Endocrinology and Metabolism, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands; [2]Endocrinology and Metabolism, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

Background: Menopausal hormone therapy (MHT) is widely used to manage menopausal symptoms, but its impact on cardiovascular risk remains debated. Many different regimens and doses of transdermal MHT are available; however, randomized controlled trials evaluating their cardiometabolic effects are scarce, and transdermal estrogen is typically administered continuously rather than in a more physiological, cyclic pattern. Therefore, we investigated the effect of cyclic 17-β-estradiol, compared to continuous 17-β-estradiol on glucose metabolism and cardiovascular risk factors in postmenopausal women.

Methods: This was a randomized, controlled, open-label trial involving 42 postmenopausal women. Participants were randomly assigned to receive one of the following treatments for 16 weeks: cyclic transdermal 17-β-estradiol (alternating 25 μg/24 h and 50 μg/24 h 17-β-estradiol in a four-week cycle), continuous 25 μg/24 h transdermal 17-β-estradiol or continuous 50 μg/24 h transdermal 17-β-estradiol. In all treatment arms, 17-β-estradiol therapy was combined with continuous 100 mg oral micronized progesterone daily. The primary outcome of the study was the effect of 17-β-estradiol on bone turnover markers. In this secondary analysis, the following outcomes are presented: glucose metabolism assessed with an oral glucose tolerance test (OGTT), body mass index (BMI), waist circumference, controlled attenuation parameter (CAP) score of the liver, lipid profile and blood pressure before and after the allocated intervention.

Results: The mean age of participants was 53.3 ± SD 3.3 years, with a median age at final menstrual period of 51.0 (IQR 48.0–53.3) years. Median BMI was 25.0 (IQR 23.2–27.9) kg/m^2 and mean HbA1c level was 37.4 ± SD 2.5 mmol/mol. Mean Greene Climacteric Scale (GCS) scores were 17 ± SD 7. After 16 weeks of treatment, no differences were found between the three treatment groups in terms of change in fasting glucose and insulin, glucose, and insulin levels 2 h post-OGTT, HOMA-IR, BMI, CAP-score, HDL, LDL-C, total cholesterol, and triglyceride levels. After 16 weeks of treatment, the continuous 25 μg/24 h group showed a greater reduction in waist circumference compared to the continuous 50 μg/24 h group (mean difference: −3.7 cm, SE 1.3, [95% CI -6.8,-0.5], $P = .018$), and the continuous 50 μg/24 h group showed a greater reduction in diastolic blood pressure compared to the continuous 25 μg/24 h group (mean difference: 10 mmHg, SE 3, [95% CI 2,18], $P = .011$).

Conclusions: Cyclic transdermal 17-β-estradiol combined with continuous progesterone showed similar effects to standard-dose and low-dose continuous transdermal 17-β-estradiol therapies regarding cardiovascular risk factors. All three treatment regimens showed a neutral effect on glucose metabolism, lipid profile, and blood pressure in healthy postmenopausal women.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.696

EP93 - ECE_2628 - Atypical presentation of silent pheochromocytoma in a young patient

Alexandra Mirica[1], Georgiana Taujan[1], Mihaela Rosu[2] and Iconaru Laura[3]
[1]Kraainem, Belgium; [2]CHU Brugmann, Bruxelles, Belgium; [3]CHU Brugmann Site Victor Horta, Bruxelles, Belgium

Title: A biochemically silent pheochromocytoma in a young patient

Background: Pheochromocytoma is a catecholamine-secreting tumor originating from chromaffin cells of the adrenal medulla. The majority of tumors that secrete catecholamines are sporadic. The catecholamine-secreting tumors are more likely to be bilateral adrenal pheochromocytomas or paragangliomas in about 40% of people who have the condition as part of a hereditary disorder.

Aim: To describe an atypical presentation of pheochromocytoma as an adrenal incidentaloma in a young adult and to emphasize the importance of recognizing hereditary tumor syndromes.

Methods: A 25-year-old asymptomatic man of Guinean origin was found to have a right adrenal mass during abdominal ultrasound performed for abnormal liver function tests. Clinical evaluation, biochemical investigations, multimodal imaging (adrenal MRI, PET-DOTANOC), and surgical management were undertaken. In this case of a young patient with an adrenal tumor showing imaging signs of pheochromocytoma, we also performed genetic testing.

Results: Adrenal MRI revealed a right adrenal mass measuring approximately 3 cm. Urinary catecholamines were normal, and blood tests showed only a slight elevation of neuron-specific enolase. PET-DOTANOC revealed an adrenal lesion with marker uptake at the tumor site. No lymphadenopathy or other visceral lesions were detected. Right adrenalectomy was performed. Histopathology confirmed a completely excised pheochromocytoma without capsular invasion, with one mitosis per 10 mm^2 and a low Ki-67 index of 1%.The genetic panel performed indicated the presence of the VHL gene mutation, confirming Von Hippel Lindau syndrome.

Conclusions: This case highlights the diagnostic challenges of biochemically silent pheochromocytomas in young patients. Genetic testing including VHL gene mutations should be strongly considered in such cases to allow early diagnosis, appropriate surveillance, and family screening.

Abstract citation ID: lvag096.697

EP94 - ECE_2718 - LINC CARE Phase IV study design: Efficacy and safety of osilodrostat in patients with hypertension caused by Cushing's syndrome with mean urinary free cortisol ≤2× the upper limit of normal

Irina Bancos[1], Javed Butler[2], Richard Auchus[3], Oksana Hamidi[4], Amir Hamrahian[5], Andrea Piacentini[6], Massimo Casi[6], Michal Sarnecki[7] and Martin Reincke[8]
[1]Division of Endocrinology, Metabolism and Nutrition, Mayo Clinic, Rochester, MN, United States; [2]Department of Medicine, Baylor Scott and White Research Institute and University of Mississippi, Dallas, TX and Jackson, MS, United States; [3]Department of Pharmacology and Division of Metabolism, Endocrinology and Diabetes, University of Michigan, Ann Arbor, MI, United States; [4]Division of Endocrinology, University of Texas Southwestern Medical Center, Dallas, TX, United States; [5]Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Johns Hopkins University, Baltimore, MD, United States; [6]Recordati SpA, Milan, Italy; [7]Recordati AG, Basel, Switzerland; [8]Department of Medicine IV, LMU Hospital, Ludwig-Maximilians-Universität München, Munich, Germany

Introduction: Hypertension and dysglycaemia are common comorbidities in patients with Cushing's syndrome (CS), driven by cortisol excess of varying severity. Data from a pooled analysis of two Phase III studies (LINC 3, LINC 4) highlight that 66.7% and 47.4% of patients with Cushing's disease and mean urinary free cortisol (mUFC) ≤2× the upper limit of normal (ULN) had hypertension and dysglycaemia at baseline, respectively. In LINC 3 and LINC 4 analyses, osilodrostat, a potent inhibitor of 11β-hydroxylase and aldosterone synthase, decreased blood pressure and glycaemic parameters in patients with CS and comorbid hypertension and/or diabetes mellitus. LINC CARE (NCT07247162) will evaluate the efficacy and safety of osilodrostat in patients with hypertension caused by CS with mUFC≤2xULN.

Methods: ~63 CS patients (aged ≥18 years) with uncontrolled hypertension despite medication (systolic blood pressure [SBP] ≥135 mmHg or diastolic blood pressure [DBP] ≥85 mmHg) and mUFC>1–≤2xULN will enrol across ~75 sites (Europe, USA, Canada, Latin America). Following a ≤3-week (W) screening period, the 30W randomised, double-blind, placebo-controlled study will comprise an 18W dose-titration and 12W dose-maintenance phase. Patients will be randomly allocated to osilodrostat 1 mg once daily (evening) or matching placebo (2:1 ratio). During the dose-titration phase, treatment will be titrated every 3W according to serum cortisol levels and clinical response. In the dose-maintenance phase, patients will continue on the dose received at the end of the titration phase unless there is a need to reduce or discontinue the medication for safety reasons. The primary endpoint is the proportion of patients with mUFC≤ULN at W30. The key secondary endpoint is the proportion of blood pressure responders (≥5 mmHg reduction in mean SBP and/or DBP, assessed by ambulatory blood pressure monitoring) at W30. Other secondary endpoints (assessed at W21 and W30 unless otherwise specified) include: proportion of responders in glycaemia (≥25% reduction in glucose from baseline during oral glucose tolerance test in patients with baseline glycated haemoglobin ≥6%) and body weight (≥5% decrease from baseline); change from baseline in SBP, glycaemic parameters, and antihypertensive and antidiabetic medication; change in body weight and proportion of patients with mUFC≤ULN over time; and occurrence of adverse events, including hypocortisolism.

Conclusions: LINC CARE will provide valuable data on the efficacy, safety and dosing of osilodrostat in patients with hypertension caused by CS and with mUFC ≤ 2xULN.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.698

EP95 - ECE_2721 - Adrenal masses in advanced cutaneous melanoma: prevalence, clinical features, and prognostic implications in a large retrospective cohort

Erika Messina[1], Francesca Dughera[1], Giuseppe Ferruzza[2], Gabriele Roccuzzo[2], Emanuele Koumantakis[1], Soraya Puglisi[1], Marianna Torchio[1], Massimo Terzolo[1], Pietro Quaglino[2] and Giuseppe Reimondo[1]
[1]*Orbassano, Italy;* [2]*Department of Medical Sciences, Section of Dermatology, University of Turin, Turin, Italy*

Background: Cutaneous melanoma frequently metastasizes to the adrenal glands, but radiological data on adrenal involvement and its clinical significance in advanced melanoma remain limited.

Objective: To evaluate the prevalence, radiological characteristics, and prognostic impact of adrenal lesions, both metastatic and non-metastatic, in patients with stage III–IV cutaneous melanoma.

Methods: We retrospectively studied 680 patients with stage III-IV melanoma followed at the Dermatology Unit of the "Città della Salute e della Scienza" of Turin through December 2023. All patients underwent at least one CT scan for disease staging. Adrenal findings were classified as: no lesions, metastasis, or non-metastatic lesions. Clinical, cardiometabolic, and genetic data (BRAF and NRAS mutational status) were collected.

Results: The cohort had a mean age at diagnosis of 61 years and a male predominance (57.4%). Stage IV disease was more common than stage III (64.3% vs 35.7%). Compared with stage III patients, those with stage IV melanoma were older ($P = .025$), had a higher prevalence of hypertension ($P = .036$), and higher mortality during follow-up ($P < .001$), while sex distribution and diabetes prevalence were similar. No significant differences in BRAF or NRAS mutational status were observed between stages.

Overall, adrenal lesions were detected in 13.5% of patients, including 8.1% non-metastatic and 5.4% metastatic lesions. Adrenal involvement was strongly associated with disease stage. Metastatic adrenal lesions were rare in stage III (0.8%) but occurred in 8% of stage IV patients; non-metastatic lesions were also more frequent in stage IV than in stage III (10.1% vs 4.5%).

Patients with non-metastatic adrenal lesions tended to be older and showed a higher prevalence of hypertension without an increase in cardiovascular mortality.

Five-year overall survival worsened with advancing stage, reaching 90% in stage III and 76% in stage IV melanoma. When stratified by adrenal CT findings, five-year survival was similar in patients with metastatic (72%) and non-metastatic adrenal lesions (74%), and lower than in patients without adrenal involvement (81%). Survival curves for metastatic and non-metastatic adrenal lesions largely overlapped, suggesting that adrenal metastases did not confer additional prognostic impairment beyond advanced disease stage.

Conclusions: In advanced melanoma, adrenal involvement is more frequent in stage IV disease. Non-metastatic adrenal lesions are associated with a prognosis comparable to that of adrenal metastases, despite representing a condition with low intrinsic mortality. This unexpected overlap in survival suggests that non-metastatic adrenal lesions warrant careful identification and clinical characterization, as they may be associated with mild autonomous hormonal activity.

Abstract citation ID: lvag096.699

EP96 - ECE_3316 - Differences in renal outcomes in ethnic groups and between surgical and medical treatment in primary aldosteronism: a retrospective cohort study

Yuliya Manova[1], Russell Senanayake[1,2], Anand Velusamy[1], Johnathan Hubbard[1] and Paul Carroll[1]
[1]*Departments of Endocrinology and Endocrine Surgery, Guy's and St Thomas' NHS Foundation Trust, Endocrine Clinic, London, United Kingdom;* [2]*School of Biomedical Engineering & Imaging Science, King's College, London, United Kingdom*

Background: Primary aldosteronism (PA) is associated with impaired renal function. Treatment with surgery (adrenalectomy) or medical treatment with mineralocorticoid receptor antagonists (MRAs) leads to a change in eGFR by eliminating aldosterone-induced hyperfiltration. However, data comparing renal outcomes by treatment modality across different ethnic groups remain limited.

Objectives: To compare renal outcomes between treatment modalities and ethnic groups.

Methods: We conducted a single-centre retrospective cohort study using electronic health records of patients aged >18 years old with a confirmed diagnosis of PA between January 2000 and December 2024, based on Endocrine Society 2016 guidelines. Variables collected included demographics (age, sex, ethnicity), treatment modality, and renal outcomes (creatinine and eGFR). Statistical calculations were performed on SPSS including Wilcoxon signed rank for comparison of non-parametric data sets.

Results: A total of 121 patients were identified. Mean age was 53.9 years; 63 (52.1%) were male and 69 (57.0%) were of Black ethnicity. Adrenalectomy for suitable patients with unilateral disease was performed in 53 patients (43.8%), and 68 (56.2%) received medical treatment with MRAs.

In the total cohort of 121 patients, the average eGFR at baseline was 77.7 mL/min (±19.2) and after intervention 67.3 mL/min (±18.1, $P < .001$). Within the treatment groups, there was no change in the average decline in eGFR (mL/min) in the surgical (−9.4,11.8%) and medical treatment group (−11.2,14.7%) ($P = .23$, $\alpha = 0.05$). There was no difference in eGFR between black and other ethnicity ($P = .082$). There was no significant difference in creatinine change between surgical (+13.2 umol/L, 15.9%) and medical treatment (+15.0 umol/L, 17.3%) groups ($P = .4$), and no difference between Black and other ethnicities ($P = .8$). The average increase in renin mass 18.4 mU/L (579%) in the surgical group and 15.4 (438%) in the medical group, with no significant difference ($P = .19$). Average K was 3.4 mmol/L (±0.44) at baseline and 5.0 mmol/L (±7.44) after treatment. Aldosterone demonstrated a positive correlation with pre- and post-treatment creatinine ($r = 0.179$ and 0.048, respectively) and an inverse correlation with pre- and post-treatment eGFR ($r = -0.223$ and −0.160, respectively).

No ethnic differences were observed with changes in renin ($P = .28$), potassium ($P = .18$), systolic BP ($P = .11$), or diastolic BP ($P = .08$) between treatment groups.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: eGFR fell significantly following both surgical and medical treatment of PA, regardless of ethnicity. Clinicians should be aware that successful treatment of PA may be associated with a reduction in eGFR, which pre-treatment may be falsely reassuring because of PA induced hyperfiltration.

Abstract citation ID: lvag096.700

EP97 - ECE_3460 - Preoperative CT-derived abdominal fat volume predicts clinical outcome in patients with primary aldosteronism undergoing unilateral adrenalectomy

Matthias Oettle[1], Markus Kroiss[1], Raphael Hirner[1], Erik Petersenn[1], Felix Herr[2], Isabel Stüfchen[1], Petra Zimmermann[3], Tracy Ann Williams[1], Nicole Reisch[1], Martin Reincke[1], Jens Ricke[2], Lalith Kumar Shiyam Sundar[2], Christine Schmid-Tannwald[2], Wolfgang Kunz[2], Lukas Gold[2] and Nabeel Mansour[2]

[1]Department of Medicine IV, LMU University Hospital, LMU Munich, Munich, Germany; [2]Department of Radiology, LMU University Hospital, LMU Munich, Munich, Germany; [3]Department of General, Visceral and Transplantation Surgery, LMU University Hospital, LMU Munich, Munich, Germany

Purpose: Lateralized primary aldosteronism (PA) represents a potentially curable cause of secondary hypertension, yet, clinical outcomes following unilateral adrenalectomy vary substantially. Beyond conventional anthropometric measures, computed tomography (CT)-derived assessments of visceral fat volume and body fat distribution may provide additional prognostic information in patients with lateralized PA.

Methods: This retrospective study included 70 patients with lateralized PA from the German Conn Registry, Ludwig-Maximilian-University Hospital Munich, who underwent unilateral adrenalectomy. Preoperative non-contrast CT-based body composition parameters, including visceral fat volume (VFV), subcutaneous fat volume (SFV), the VFV/SFV ratio, and the VFV-to-skeletal muscle volume (VFV/SMV) ratio, were analyzed at the third lumbar vertebral (L3) level using a fully automated software tool (Visage Imaging GmbH, Berlin, Germany). Associations between body composition parameters and preoperative plasma aldosterone concentrations (PAC) were assessed by linear regression models using log-transformed PAC. PAC was measured using Chemiluminescent Immunoassay. Clinical outcomes after adrenalectomy were classified according to the PASO criteria, and their association with body composition parameters analyzed using ordinal logistic regression models. Effect sizes were reported as odds ratios per standard deviation increase.

Results: No significant associations were observed between preoperative PAC ($n = 70$; median 227.5 ng/L, IQR 157.0–363.8 ng/L) and body composition parameters, including VFV, SFV and distribution-based ratios (all $P > .05$). Postoperative clinical outcome data were available for 52 patients (23 female; median age 49 years), including 11 with absent, 31 with partial, and 10 with complete clinical success. Higher body mass index (BMI) was associated with a lower likelihood of achieving a better clinical outcome (OR 0.37 per SD increase, 95% CI 0.19–0.71). Similar, higher VFV and SFV were each associated with a lower likelihood of a better clinical outcome (OR 0.51 per SD increase, 95% CI 0.28–0.92 and OR 0.46 per SD increase, 95% CI 0.25–0.83 respectively). In contrast, neither the VFV/SFV ratio (OR 0.77 per SD increase, 95% CI 0.45–1.31) nor the VFV/SMV ratio (OR 0.63 per SD increase, 95% CI 0.35–1.11) was associated with clinical outcome.

Conclusions: Fully automated CT-based body composition analysis enables rapid and standardized quantification of visceral adiposity. In patients with lateralized PA, CT-derived visceral and subcutaneous fat volume were predictive of clinical outcomes following unilateral adrenalectomy, while distribution-based ratios showed no associations. However, BMI was more strongly associated with clinical outcome, suggesting that the incremental clinical value of CT-based body composition assessment beyond conventional measures was limited in our cohort.

Abstract citation ID: lvag096.701

EP98 - ECE_3554 - Cushing Syndrome's lipid and amine metabolic peripheral blood signatures are partially reflected in other states of cortisol excess and insufficiency

Flaminia Fanelli[1], Greta Galante[1], Carlo Mengucci[2], Lorenzo Tucci[1,3], Kimberly Coscia[1,3], Valentina Bissi[1], Giacomo Colombin[1,3], Alessandro Perrone[1], Valentina Vicennati[1,3], Uberto Pagotto[1,3], Francesco Capozzi[2] and Guido Di Dalmazi[1,3]

[1]Center for Applied Biomedical Research, CRBA, University of Bologna, Bologna, Italy; [2]Department of Agricultural and Food Sciences, DISTAL, University of Bologna, Bologna, Italy; [3]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Introduction: Cushing's syndrome (CS), adrenal insufficiency under replacement therapy (AIRT), and adrenocortical tumours with mild autonomic cortisol secretion (MACS) display different alterations of cortisol rhythm. Circadian alterations of metabolic pathways in these diseases were not characterized yet.

Objective: To identify peripheral blood molecular patterns characterizing CS, and verify their dysregulation in AIRT and MACS.

Methods: We enrolled 10 healthy subjects (HS), 9 newly diagnosed CS, 8 AIRT taking dual-release hydrocortisone and 12 MACS patients. All followed 7-days standardised isocaloric Mediterranean diet. On day seven, they collected dried blood spots from finger-prick 30 min before and 2 h after breakfast, lunch and dinner, and at 11 pm. We used a targeted metabolomic LC-MS/MS method measuring 42 amino acids and biogenic amines, 40 acylcarnitines, 15 sphingomyelins and 90 glycerophospholipids. A BORUTA algorithm was trained to separate HS and CS, as the most divergent phenotypes, and defined the most informative features. These were reduced by Factor Analysis (FA). The circadian fluctuation of molecular patterns was evaluated by combining molecule concentrations and FA-coefficients along the 7 time-points. Resulting patterns were analyzed within AIRT and MACS groups. Kinetics for each class were fit using second (SOP) or third order polynomial (TOP), or power law ($y = Axk + c$).

Results: Two patterns distinguished CS patients from HS, with top 5 informative molecules being phosphatidylcholines (PC) aa-C38:0, ae-C44:3, aa-C38:6, ae-C42:5 and aa-C36:0 (PCs) for pattern A; and carnitine, histidine, creatinine, asparagine and spermidine for pattern B. Pattern A PC levels and fluctuation

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

were markedly divergent in HS and CS ($P < .05$ at each time point): HS showed a U-shaped (SOP) rhythm with minimum levels before lunch, whereas CS displayed low levels reaching a plateau in the evening (TOP). HS exhibited a U-shaped rhythm also for pattern B amines. Conversely, CS showed persistently high amine levels ($P < .05$ from 9:30 to 23:00), with maximal divergence from HS in early afternoon. AIRT exhibited pattern A and B levels resembling CS and HS, respectively, with pronounced morning oscillations. MACS showed pattern A levels similar to CS, with U-shaped fluctuation similar to HS, and pattern B levels intermediate to HS and CS, with TOP oscillation.

Conclusions: PC and amines in CS displayed deranged rhythms and opposite dysregulation of levels. In AIRT, PC and amines were overall low, with marked morning oscillation probably derived by glucocorticoid intake after awakening. PC dysregulation in MACS was similar to CS, while amine imbalance displayed an intermediate pattern.

Funding: 2017HRTZYA_002.

Abstract citation ID: lvag096.702

EP99 - ECE_3694 - Mild Autonomous Cortisol Secretion (MACS)—silent autonomy or hidden danger? Predictors and metabolic consequences: a multidimensional comparison of functional adrenal incidentaloma phenotypes

Ksenia Janas[1], Janusz Strzelczyk[1], Krzysztof Bylok[2], Adrian Bukała[3], Wiktoria Borowska[4], Oliwia Jewuła[5] and Natalia Aleksander[2]

[1]Department of Endocrinology and Neuroendocrine Tumours, Medical University of Silesia, Katowice, Poland; [2]Student Scientific Society at the Clinic of Endocrinology and Neuroendocrine Tumors of the Department of Pathophysiology and Endocrinology of the Silesian Medical University in Zabrze, Medical University of Silesia in Katowice, 35 Ceglana St., Katowice 40-514, Poland; [3]Student Scientific Society at the Clinic of Endocrinology and Neuroendocrine Tumors of the Department of Pathophysiology and Endocrinology of the Silesian Medical University in Zabrze, Medical University of Silesia in Katowice, 35 Ceglana St., Katowice 40-514; [4]Student Scientific Society at the Clinic of Endocrinology and Neuroendocrine Tumors of the Department of Pathophysiology and Endocrinology of the Silesian Medical University in Zabrze, Medical University of Silesia in Katowice, 35 Ceglana St., Katowice 40-514, Poland; [5]Student Scientific Society at the Clinic of Endocrinology and Neuroendocrine Tumors of the Department of Pathophysiology and Endocrinology of the Silesian Medical University in Zabrze, Medical University of Silesia in Katowice, 35 Ceglana St., Katowice 40-514, Poland

Introduction: Adrenal incidentalomas (AI) are found in 4-10% of adults. Mild autonomous cortisol secretion (MACS) is the most frequent functional abnormality, associated with increased cardiometabolic risk. This study aimed to characterize Polish patients with AI, focusing on identifying independent predictors and metabolic consequences of the MACS phenotype.

Material and Methods: This retrospective observational study analyzed 404 consecutive patients (73.5% female, mean age 62.5 years) hospitalized at a tertiary endocrine center (2024-2025). MACS was defined as cortisol >1.8 µg/dL after a 1-mg dexamethasone suppression test (DST) in patients without overt Cushing's syndrome (CS), according to ESE/ENSAT 2023 guidelines. Subjects were categorized into: non-functioning AI (NFAI, 69.6%), MACS (20.8%), pheochromocytoma (PCC, 5.7%), CS (2.7%), and primary aldosteronism (PA, 1.2%). Hormonal profiles (8:00/23:00 serum cortisol, ACTH) and metabolic status were evaluated. Statistical analysis included Kruskal-Wallis tests and multivariable logistic regression using backward stepwise selection; glucose levels were centered to the mean to mitigate collinearity in interaction models. Due to small sample sizes in the CS and PA groups, comparisons involving these phenotypes were treated as exploratory.

Results: MACS patients were significantly older (66.6 ± 10.8 years) than NFAI patients ($P = .007$). The multivariable regression model showed high discriminatory power (AUC = 0.836) and identified age (OR = 1.042) and late-night serum cortisol (OR = 1.685; $P < .001$) as independent predictors of MACS. Exploratory ROC analysis established cutoff points for late-night cortisol (>4.07 µg/dL, NPV = 89.1%) and ACTH (<10.32 pg/mL, NPV = 85.0%), though these require validation in independent cohorts. Regarding metabolic impact, the multivariable model revealed that MACS tripled the risk of hypertension (OR = 2.957). A significant interaction between hypertension and fasting glycemia was found (OR = 1.097, $P = .002$); each 1 mg/dL increase in glucose intensified the association between MACS and hypertension by 9.7%. Lipid parameters were not independent predictors in the multivariable model.

Conclusions: MACS risk increases with age, which is consistent with the hypothesis of progressive functional evolution of adrenal adenomas. The identified synergistic effect of glycemia on hypertension highlights that MACS patients with impaired glucose metabolism represent a particularly high-risk cardiovascular group. Late-night serum cortisol and ACTH levels show high negative predictive values, suggesting their potential utility in excluding MACS, although standardized collection and external validation are necessary.

Abstract citation ID: lvag096.703

EP100 - ECE_2028 - Apparent bilateral aldosterone suppression during non-stimulated adrenal vein sampling: an artifact of the Liaison immunoassay and other causes

Christina Pamporaki[1], Carmina Teresa Fuss[2], Ralph Kickuth[3], Lydia Kuerzinger[3], Mirko Peitzsch[4], Sybille Fuld[4], Manuel Schulze[5], Jun Yang[6], Martin Reincke[7], Sven Gruber[8], Felix Beuschlein[8], Jacques Lenders[9] and Graeme Eisenhofer[4]

[1]Medical Clinic III, University Hospital Carl Gustav Carus Dresden, Dresden, Germany; [2]Würzburg University Hospital, Würzburg, Germany; [3]Würzburg University Hospital Straubmühlweg Heliport, Würzburg, Germany; [4]University Hospital Carl Gustav Carus Dresden, Dresden, Germany; [5]Technische Universität Dresden Medizinische Fakultät, Dresden, Germany; [6]Monash Institute of Medical Research, Clayton, Australia; [7]Ludwig Maximilian University, Munich, Germany; [8]University Hospital, Zürich, Switzerland; [9]Radboud Universiteit, Nijmegen, The Netherlands

Objective: Subtyping of primary aldosteronism usually requires adrenal vein sampling (AVS). Interpretation can be compromised by apparent bilateral aldosterone suppression (ABAS), which we hypothesized reflects an artifact of the Liaison immunoassay of aldosterone. We therefore compared measurements of aldosterone by liquid chromatography-tandem mass spectrometry (LC-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

MS/MS) with measurements by the Liaison immunoassay and a different immunoassay.

Design: retrospective cross-sectional multicenter study.

Patients: The study involved 222 patients who underwent bilaterally selective non-stimulated AVS.

Measurements: Adrenal and peripheral venous plasma aldosterone concentrations were measured by Liaison and iSYS immunoassays in 112 and 110 respective samplings compared to LC-MS/MS in all samplings. Ratios of aldosterone to cortisol below 1.0 in adrenal versus peripheral vein samples defined suppression of aldosterone secretion.

Results: Among all AVS procedures, 9.5% (21/222) of samplings with immunoassay measurements showed ABAS, 3-fold more ($P = .0004$) than the 3.2% (7/222) with LC-MS/MS measurements. Rates of ABAS were particularly high with the Liaison immunoassay compared to LC-MS/MS (14.2% vs 0.9%, $P < .0001$) and remained higher after substitution of LC-MS/MS measurements of cortisol in the ratio with immunoassay measured aldosterone (9.8% vs 0.9%, $P = .0064$). Among 110 procedures involving iSYS immunoassay measurements, rates of ABAS at 4.6% were a third ($P = .0132$) those of the Liaison immunoassay and did not differ from LC-MS/MS measurements (5.5%). ABAS confined to LC-MS/MS measurements in one patient was resolved with a second right adrenal vein sampling.

Conclusions: ABAS occurs more frequently using the Liaison immunoassay of aldosterone than the iSYS immunoassay and LC/MS-MS measurement. In addition to this artefact, ABAS can also reflect adrenal vein catheter placement.

Abstract citation ID: lvag096.704

EP101 - ECE_2354 - The silent emergency: acute adrenal crisis in the emergency department—experience from a Moroccan tertiary center

Mohamed Nhili[1] and Mohamed Amine Elhasnaoui[2]
[1]*Endocrinology, Diabetology and Metabolic Diseases Department, Mohammed VI University Hospital of Tangier, Tangier, Morocco;* [2]*Emergency Department, Mohammed VI University Hospital of Tangier, Tangier, Morocco*

Background: Acute adrenal crisis (AC) is a rare but life-threatening endocrine emergency, with reported mortality rates ranging from 6% to 15% despite appropriate treatment. Diagnosis is frequently delayed due to nonspecific clinical presentation, including digestive, neurological, and cardiovascular symptoms. Early recognition and prompt initiation of glucocorticoid replacement are key determinants of prognosis.

Objective: To describe diagnostic delays, management strategies, and outcomes of patients presenting with acute adrenal crisis in a Moroccan emergency department, and to identify areas for improvement in early recognition and prevention.

Methods: We conducted a retrospective, descriptive, single-center study at the emergency department of Mohammed VI University Hospital, Tangier, between November 2023 and August 2025. We included patients admitted for acute adrenal crisis as well as those who were diagnosed during hospitalization for another condition in the emergency department. Data were collected from electronic medical records using a standardized data extraction form and analyzed descriptively.

Results: Thirteen patients were included (mean age 43.7 years, range 21-65), with a female predominance (9 women, 4 men; F/M ratio 2.25). Chronic adrenal insufficiency was previously known in 8 patients (61.5%), while AC was inaugural in 5 cases (38.5%). Diagnostic delay was markedly longer in patients without known adrenal insufficiency, with a median pre-hospital symptom duration of 15 days, compared with less than 24 hours in known patients. Triggering factors included infections, corticosteroid withdrawal or non-adherence, and metabolic disturbances. Hyponatremia was observed in 58% and hyperkalemia in 42% of cases. In all patients (100%), AC management was started immediately upon clinical suspicion, without waiting for cortisol assay results, using intravenous hydrocortisone and fluid resuscitation. Vasopressors were required in one patient (7.7%). Eleven patients had a favorable outcome, one left against medical advice, and one died in intensive care, resulting in an in-hospital mortality rate of 7.7%.

Conclusions: Acute adrenal crisis remains a major diagnostic challenge in the emergency setting, particularly in patients without known adrenal insufficiency. Early treatment based on clinical suspicion allows outcomes comparable to international series. Improving frontline healthcare provider awareness, standardizing emergency protocols, and strengthening preventive strategies during hospitalization are essential to further reduce mortality.

Abstract citation ID: lvag096.705

EP102 - ECE_3642 - Optimizing patient selection for adrenal vein sampling in primary hyperaldosteronism

Meir Frankel, Gabriel Munter, Gavriel Lichewitz, Noa Sylvetsky and Anthony Verstandig
Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel

Background: Primary hyperaldosteronism (PA) is caused by excessive aldosterone production from one or both adrenal glands. Diagnostic evaluation includes biochemical testing, imaging, and in most patients requires adrenal vein sampling (AVS) to differentiate unilateral disease, which may benefit from surgical treatment, from bilateral disease, which is managed medically. According to 2025 Endocrine Society guidelines, screening for PA is recommended in all patients with hypertension, a strategy that is expected to increase PA detection. Following biochemical confirmation, AVS is generally recommended for patients with a moderate/high likelihood of unilateral disease, while those with a low probability are managed with medical therapy as first-line treatment. Identifying clinical predictors of unilateral aldosterone secretion may therefore optimize patient selection for AVS.

Methods: We retrospectively analyzed all patients with confirmed PA who underwent AVS at Shaare Zedek Medical Center during 2019-2025, with successful determination of unilateral or bilateral aldosterone secretion according to accepted criteria. Baseline demographic, clinical, and imaging variables were evaluated using statistical analyses to identify predictors of unilateral disease and to develop a predictive model for AVS outcomes.

Results: During the study period, 85 patients with PA underwent AVS with definitive classification of aldosterone secretion as unilateral or bilateral. Unilateral aldosterone secretion was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

identified in 55 patients (65%), while 30 (35%) had bilateral disease. In univariable analysis, hypokalemia was strongly associated with unilateral aldosterone secretion (odds ratio [OR] = 16.7), as was a lowest recorded serum potassium level <3.3 mEq/L (OR = 8.3). An aldosterone-to-renin ratio (ARR) >10 was also significantly associated with unilateral disease (OR = 4.5). Chronic kidney disease was significantly associated with bilateral aldosterone secretion (OR = 0.3). Baseline low renin levels demonstrated a borderline association with unilateral disease (OR = 1.9). Age, Gender, age at hypertension diagnosis, serum aldosterone level and adrenal mass (uni or bilateral) in imaging were not significantly associated with AVS results. In multivariable logistic regression analysis, a lowest serum potassium level <3.3 mEq/L and ARR >10 remained independently and strongly associated with unilateral aldosterone secretion. A predictive model based on the variables achieved an overall accuracy of approximately 80% in predicting AVS outcomes.

Conclusions: Patients with PA and unilateral aldosterone secretion exhibit distinct baseline clinical and biochemical characteristics compared to patients with bilateral disease. These findings, together with the predictive model developed in this study, may assist clinicians in determining whether to initiate medical therapy as first-line treatment or to proceed with AVS to evaluate candidacy for surgical management of unilateral disease.

Abstract citation ID: lvag096.706

EP103 - ECE_3176 - Evaluation of hypokalaemia correction practices in hospitalised patients: a retrospective audit of guideline compliance and monitoring in renal impairment

Aparna Ravikumar[1], Seth King[1], Rubern Rajasivam[1], Sarath Vayolipoyil[1] and Tadeusz Pawlak[2]
[1]*York and Scarborough Teaching Hospitals NHS Foundation Trust, Scarborough, United Kingdom;* [2]*Endocrinology and Diabetes, York and Scarborough Teaching Hospitals NHS Foundation Trust, Scarborough, United Kingdom*

Background: Hypokalaemia affects up to 20% of hospitalised patients and is associated with significant cardiovascular morbidity and mortality. Potassium homeostasis is largely regulated by renal handling, and patients with acute or chronic renal impairment are particularly vulnerable to over-correction due to impaired clearance and altered intracellular–extracellular potassium shifts. Safe correction requires cautious replacement supported by biochemical and cardiac monitoring, including post-infusion checks.

Objective: This Retrospective audit evaluated adherence to local guidelines for safe hypokalaemia correction in hospitalised patients, with particular focus on monitoring during replacement therapy in those with renal impairment.

Methods: A retrospective audit was conducted over one year including adult medical inpatients with serum potassium <3.5 mmol/L admitted to a UK district general hospital. Data collected included hypokalaemia severity, documented aetiology, presence of acute kidney injury (AKI) or chronic kidney disease (CKD), appropriate route of potassium replacement, ECG monitoring during replacement, post-infusion serum potassium monitoring, serum magnesium monitoring (given its role in potassium homeostasis), and time to correction. Practice was assessed against local hypokalaemia management guidelines.

Results: Fifty-five patients were included. Hypokalaemia was predominantly mild (73%), with moderate (24%) and severe (3%) cases. An underlying cause was documented in 49% of patients, most commonly gastrointestinal potassium loss (33%). Renal impairment (AKI or CKD) was present in 49%. Among patients with mild to moderate hypokalaemia, oral potassium replacement was used in 68%, consistent with guideline recommendations. However, 35% received intravenous potassium, with documented severity or symptoms supporting IV use in only 16%. ECG's were performed in 45% of mild, 69% of moderate, and 100% of severe cases; among those receiving IV potassium, Continuous Cardiac monitoring occurred in 37% receiving IV Potassium. Post-correction potassium checks were undertaken in 84% patients. In renal impairment, daily serum potassium monitoring during active replacement was documented in 36% of patients with CKD & 54% with AKI. Median time to correction was 2 days in patients without renal impairment and 3 days in those with renal dysfunction. Magnesium levels were checked in 78% of patients with renal impairment.

Conclusions: Although hypokalaemia correction was generally achieved, variability in monitoring practices has important patient-safety implications, particularly in renal impairment. Inconsistent ECG surveillance and incomplete daily biochemical monitoring during replacement may increase the risk of arrhythmias and over-correction. These findings support the need for cautious, closely monitored correction strategies and improved adherence to guidelines through structured monitoring prompts.

Abstract citation ID: lvag096.707

EP104 - ECE_3291 - oxLDL and early launch of menopausal hormone replacement therapy among women with vasomotor syndrome

Iryna Muryzina
Obstetrics and Gynaecology, ABC Clinic, Kharkiv National Medical University, Kharkiv, Ukraine

Introduction: Menopausal vasomotor syndrome is a well-known risk factor for future cardiovascular events (CVE). Endothelial dysfunction (ED) is viewed as a favourable ambience for rebuilding cascade in subepithelial layer triggered by binding oxidized LDL (oxLDL) to scavenger receptors of macrophages. Obviously at first estrogen decline weakens natural repair work spurring up impairment of an arterial wall, as well as oxLDL-related suppression of NO release. On the other hand menopausal hormone replacement therapy (MHRT) turns into a foe, if it is prescribed when intima-media impairment becomes evident. The question is whether VMS are associated with raised oxLDL and if MHRT is capable to curb oxLDL production.

Objective: The study aimed to evaluate serum oxLDL in women experienced VMS and if oxLDL is affected by MHRT.

Methods: The study accrued 51 women 46-54 y.o. with VMS debut (1 group) and 30 pts without VMS otherwise matching (control). The 1st group was split into two arms: MHRT (23 pts) and without MHRT (28 pts). They were tested twice (at accrual, in 1 year) for serum oxLDL, lipoproteins, C-reactive protein (CRP),

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

IL6, TNFα, ApoB, brachial artery dilation, coronary CT angiography, cross-sectional associations were examined.

Results: It turned out that VMS-patients showed raised oxLDL in comparison with control group. Then MHRT-women experienced drop in oxLDL (still a bit higher than in control but not significantly, $P > .05$), whereas non-MHRT-patients were recognized with staggering trend to grow despite improvement in VMS course attained by non-hormonal treatment ($P < .0001$), lower vasodilation response, higher total plaque burden with remodeling index >1 comparatively to the women MHRT.

Conclusions: Earlier launch of MHRT is associated with slower pace of ED considering the fluctuations of oxLDL as a very sensitive high risk of CVE.

Abstract citation ID: lvag096.708

EP106 - ECE_3567 - Hidden congenital adrenal hyperplasia in APS-2: a case of non-classical 21-hydroxylase deficiency

Emma Capparelli, Luca Manetti, Elisabetta Sciarroni, Giulia Marconcini, Claudio Urbani, Maurizio Carbonari, Martina Parenti, Alessio Basolo, Ferruccio Santini and Isabella Lupi
Department of Clinical and Experimental Medicine, Unit of Endocrinology 1, Pisa University Hospital, Pisa, Italy

Background: Primary adrenal insufficiency (PAI) is most frequently caused by autoimmune adrenalitis (70%-80%), followed by tuberculosis and rare genetic disorders. Autoimmune Addison's disease may occur within Autoimmune Polyendocrine Syndrome type 2 (APS-2), in association with autoimmune thyroid disease and type 1 diabetes mellitus. Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is a rare genetic condition resulting from impaired steroidogenesis and may present as classical or non-classical disease. The non-classical form is typically characterized by late-onset hyperandrogenic manifestations. Standard therapy for primary adrenal insufficiency consists of glucocorticoid and mineralcorticoid (fludrocortisone) replacement; in CAH, tailored glucocorticoid timing may be required to control androgen excess.

Case Presentation: A 28-year-old woman with APS-2, diagnosed at 14 years of age, was referred to our Endocrinology Unit. She was treated with modified-release hydrocortisone (Plenadren®) 40 mg/day and fludrocortisone 0.2 mg/day. Menarche occurred at 13 years; she reported secondary amenorrhea for eight months. Biochemical evaluation showed normal electrolytes and HbA1c of 7.1%. Suspecting glucocorticoid overtreatment, hydrocortisone was progressively reduced to 20 mg/day, leading to the resumption of menstrual cycles, although oligomenorrhea persisted. Hormonal assessment excluded premature ovarian insufficiency but revealed markedly elevated 17-hydroxyprogesterone levels (15.54 µg/L). Genetic analysis identified a heterozygous c.955C>Tp.(Gln319*) mutation in the CYP21A2 gene, without gene deletion or conversion, leading to the diagnosis of non-classical 21-hydroxylase deficiency. Glucocorticoid therapy was switched to modified-release hydrocortisone specifically approved for CAH (Efmody®), administered as 10 mg in the morning and 15 mg in the evening. After four months, significant biochemical improvement was observed, with normalization of 17-hydroxyprogesterone (0.54 µg/L) and androstenedione (0.61 µg/L). Menstrual regularity improved, and the patient achieved spontaneous pregnancy. Partner genetic screening was negative.

Conclusions: This case highlights the importance of considering coexisting genetic adrenal disorders in patients with APS-2. Identification of non-classical 21-hydroxylase deficiency enabled personalized glucocorticoid therapy, resulting in improved biochemical control, restoration of reproductive function, and safe pregnancy planning.

Abstract citation ID: lvag096.709

EP108 - ECE_2322 - Diagnostic and therapeutic challenges in a patient with acute pain and a large adrenal mass

Christina Lymniati[1], Anastasia Filippidou[1], Georgios Kyriakopoulos[2], Eleni Statiri[1], Anastasios Chatzinikolaou[1] and Charalampos Tsentidis[1]
[1]*Endocrinology, Diabetes Mellitus and Metabolism Department, General Hospital of Nikaia Piraeus "Ag. Panteleimon", Piraeus, Greece;* [2]*Department of Pathology, Evangelismos Hospital, Department of Biological Chemistry, Medical School, National and Kapodistrian University of Athens, Athens, Greece*

Aim: To highlight the diagnostic challenges and clinical decision-making process in a patient presenting with acute pain and a large adrenal mass, emphasizing the importance of considering silent pheochromocytoma and metastatic disease despite inconclusive biochemical and imaging findings.

Summary/Methods: We report the case of a 51-year-old male who presented to the emergency department with acute right-sided flank pain. Initial clinical assessment suggested renal colic; however, abdominal computed tomography revealed a heterogeneous right adrenal mass measuring 6 cm, with attenuation values exceeding 20 Hounsfield units. Although the scan was not performed using a dedicated adrenal protocol, the lesion's size and imaging characteristics prompted further investigation. Magnetic resonance imaging demonstrated a large adrenal mass with heterogeneous signal intensity on T1- and T2-weighted sequences and atypical imaging and hemodynamic features. Differential diagnoses included pheochromocytoma, adrenocortical carcinoma, and metastatic disease. **Preoperative imaging did not demonstrate any evident metastatic lesions or pulmonary primary focus.** Comprehensive endocrinological evaluation showed normal cortisol, ACTH, renin–aldosterone axis, sex steroids, steroid precursors, and 24-hour urinary free cortisol. Chromogranin A was mildly elevated, while plasma normetanephrine levels were borderline increased. No hypertensive episodes were recorded on 24-hour blood pressure monitoring, cardiac evaluation was unremarkable, and MIBG scintigraphy was negative. Despite the absence of classical symptoms or definitive biochemical evidence of catecholamine excess, a silent pheochromocytoma could not be excluded. In accordance with international guidelines, preoperative alpha-adrenergic blockade with doxazosin was administered prior to adrenalectomy.

Results: The patient underwent right adrenalectomy with an uncomplicated perioperative course. Histopathological and immunohistochemical analysis revealed a highly proliferative metastatic neuroendocrine neoplasm of pulmonary origin.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Postoperatively, a rapid and marked clinical and radiological deterioration was observed, with PET imaging confirming widespread metastatic disease, including involvement of the contralateral adrenal gland and brain. Partial adrenal insufficiency was diagnosed postoperatively, and glucocorticoid replacement therapy was initiated. Despite prompt oncological management, the disease followed an aggressive course, and the patient ultimately died from complications of advanced metastatic cancer.

Abstract citation ID: lvag096.710

EP109 - ECE_2637 - Pheochromocytoma with catecholamine-induced Takotsubo cardiomyopathy: a case series from a tertiary centre

Sabahat Ahmad[1], Umesha Wijenayake[1], Bahram Jafar-Mohammadi[1], Radu Mihai[1], Shahab Khan[1], El-Muhtadi Saeed Biallah[2] and Christine May[1]
[1]*Endocrinology and Diabetes, Churchill Hospital, Oxford, United Kingdom;* [2]*Royal Berkshire Hospital, Reading, London, United Kingdom*

Pheochromocytomas (PCC) are classically associated with symptoms of headache, palpitations and diaphoresis. Rarely, they can present as Catecholamine-induced Takotsubo cardiomyopathy. The initial presentation maybe difficult to distinguish from ischemic cardiomyopathy. We discuss 5 patients with pheochromocytoma presenting with cardiomyopathy at our tertiary centre.

Case 1: A 40-year-old female, presented with severe LVF (LV failure) and cardiogenic shock but had unobstructed coronaries. Imaging revealed 6 cm adrenal Pheochromocytoma and elevated urinary metanephrines. Her Cardiac MRI revealed normal cardiac function 3 weeks post-event. Adrenalectomy was done. Patient remains under our follow-up, recurrence free for 20 years.

Case 2: A 65-year-old female, admitted with chest pain and STEMI, underwent thrombolysis, but went into cardiogenic shock with LVF, needing IABP. CT angiogram revealed normal coronaries. CT Abdomen revealed: 5 cm LT adrenal mass with 30 HU and elevated Urinary Normetadrenalines: 7.72[0-3.65 micromol/24 hours]) and metadrenalines: 15.64 (0-1.4 micromol/24 hours), leading to PCC diagnosis. Echo revealed severe biventricular dysfunction, which improved quickly. She underwent adrenalectomy and Histopathology revealed PASS 5/20. She has stayed recurrence free during follow-up (15 years).

Case 3: A 75-year-old Female, admitted with central chest pain, BP 226/106, Troponin 270, ECG revealed dynamic changes, progressing to ST elevation on initiation of beta blockade. Echo: Ejection fraction (EF) 35% and inferolateral hypokinesia. PCI found no obstructive lesions. CT-angiogram revealed 5 cm adrenal lesion, and elevated urinary metadrenalines 34, nor-metadrenalines 26. She underwent adrenalectomy (PASS score 6/20).

Case 4: A 54-year-old male, admitted peri-arrest with pulmonary oedema and EF 12%. He had known heart failure secondary to PCC catecholamine exposure. Coronary angiogram revealed concomitant mild-moderate stenosis. He was stabilized medically and was able to have successful adrenalectomy with IABP. Post-operative significant improvement of cardiac status noted, with EF 45%. Histopathology revealed 9 cm tumour, PASS 2/20.

Case 5: A 55-year-old female, initially presented with severe LV impairment: Ejection fraction 30%, frequent ectopics and non-sustained Ventricular tachycardia on Holter monitoring. She was found to have Rt adrenal pheochromocytoma with normetadrenalines of 55.1(0-3.65). Cardiac MRI once stabilized revealed mild LV dysfunction with EF 51% and mitral-regurgitation. She underwent successful adrenalectomy: 75 mm tumour, benign histology and negative genetics. EF post-operatively improved to 57% with improvement in ectopics.

Conclusions: Catecholamine-induced Cardiomyopathy is a rare presenting feature of Pheochromocytoma. Early appropriate diagnosis is essential and allows establishment of alpha-blockade before beta blockade initiation. Despite initial dramatic presentation, all our patients had significant improvement of their cardiac function after removal of pheochromocytoma, indicating reversibility of cardiac impairment and good long-term outcomes.

Abstract citation ID: lvag096.711

EP112 - ECE_3340 - DHEAS levels in premenopausal versus postmenopausal women with mild autonomous cortisol secretion

Ioana Maria Posea[1], Vlad Radulescu[1,2], Beatrice Cristea[1], Roxana Fota[1], Monica Livia Gheorghiu[1,2] and Corin Badiu[1,2]
[1]*Adult Endocrinology, Endocrinology IV, National Institute of Endocrinology "C.I Parhon", Bucharest, Romania;* [2]*Department of Endocrinology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

Background: Mild autonomous cortisol secretion (MACS) represents a spectrum of subtle hypercortisolism in patients with adrenal incidentalomas. A low or low–normal circulating dehydroepiandrosterone sulfate (DHEAS) levels are one of the characteristic biochemical feature of this condition. Although the vast majority of circulating DHEAS is of adrenal origin, its secretion demonstrates a well-described physiological decline with advancing age and during the menopausal transition. Consequently, menopausal status may further exacerbate the relative hypoandrogenism already present in MACS. However, the extent to which menopausal status independently influences DHEAS concentrations in women with MACS has not been sufficiently characterized.

Objective: To compare serum DHEAS levels between premenopausal and postmenopausal women diagnosed with MACS and to evaluate whether menopausal status independently predicts DHEAS concentrations after adjustment for potential confounding factors.

Methods: We conducted a cross-sectional observational study including 98 women with MACS. Patients were stratified according to menopausal status into premenopausal and postmenopausal groups. Serum DHEAS, age, body mass index (BMI), basal adrenocorticotropic hormone (ACTH) and cortisol levels after 1-mg dexamethasone suppression (post-1 mg DST) testing were analyzed. Normality was assessed using Shapiro–Wilk and Kolmogorov–Smirnov tests, which demonstrated non-normal distribution for DHEAS and hormonal variables. Therefore, group comparisons were performed using the Mann–Whitney U test. Multivariable linear regression (ANOVA) was applied to evaluate the independent association between menopausal status and DHEAS levels, adjusting for age, BMI, lesion size, and basal ACTH.

Results: Premenopausal women ($n = 14$) demonstrated significantly higher DHEAS levels [median 76.60 μg/dL (27.87-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

123.67 ug/dL)] compared to postmenopausal women ($n = 84$) [median 36.65 μg/dL (21.6-69.6 ug/dL)]. Both groups had similar BMI, basal ACTH and cortisol levels post-1 mgDST. Mann-Whitney U test demonstrated a statistically significant difference in DHEAS levels between premenopausal and postmenopausal women ($P = .036$). Multiple linear regression analysis confirmed that menopausal status was an independent predictor of DHEAS levels ($P = .002$) after controlling for age, BMI, tumor diameter, and basal ACTH. The overall regression model was statistically significant ($P = .006$).

Conclusions: Women with MACS show significantly different DHEAS profiles according to menopausal status. Premenopausal patients exhibit higher adrenal androgen levels independent of age, BMI, lesion size, and ACTH. This phenomenon suggests endocrine interaction between ovarian decline and adrenal steroidogenesis, making the influence of menopause on DHEAS physiologically interesting despite its predominantly adrenal origin. Menopausal status should therefore be considered when interpreting DHEAS values in women with MACS, as it represents an important determinant of adrenal androgen secretion in this population.

Abstract citation ID: lvag096.712

EP113 - ECE_3355 - When an adrenal mass is not adrenal: renal vein leiomyosarcoma presenting as an adrenal incidentaloma

Danai Barlampa[1], Athanasios Fountas[1], Irini Giagourta[1], Dimitra Zerva[1], Dimitrios Bouklas[2], Marina Sassi[2], Labrini Papanastasiou[1] and Athina Markou[1]
[1]*Unit of Endocrinology and Diabetes, Department of Endocrinology, G. Gennimatas General Hospital of Athens, Athens 11527, Greece;* [2]*Surgical Pathologist Department, "G. Gennimatas" General Hospital of Athens, Athens, Greece*

Background: Adrenal incidentalomas represent a common clinical scenario and, while in most cases lesions are benign, large adrenal masses with atypical imaging features raise concern for malignancy. Herein, we present a case of a large mass initially suspected to arise from the left adrenal gland but proven to be a renal vein leiomyosarcoma.

Case Presentation: An 82-year-old woman with a history of arterial hypertension and glaucoma was referred to the Endocrinology Department for evaluation of a left adrenal incidentaloma. Patient underwent an abdominal ultrasound as part of preventive screening which revealed a hypoechoic solid mass with calcifications measuring approximately 6×4.6 cm. Non-contrast CT demonstrated a rounded adrenal lesion with soft tissue density and calcifications measuring 5.65×5.1 cm. Subsequent an adrenal MRI revealed a large, well-defined oval retroperitoneal mass, measuring $6.17 \times 6.48 \times 9.59$ mm, presumed to originate from the left adrenal gland; the lesion exhibited intermediate signal intensity on T1-weighted images, intermediate-to-high signal intensity on T2-weighted and fat-suppressed sequences and heterogeneous intense contrast enhancement. Due to its size, the mass exerted compressive effects on the left kidney with posterior displacement. Endocrine evaluation excluded cortisol and aldosterone hypersecretion while plasma free metanephrine and normetanephrine levels as well as urinary fractionated metanephrines were within normal range. Taking into account the radiological features of the adrenal mass which raised strong suspicion for malignancy an uneventful adrenalectomy was performed. Surprisingly, histopathological examination revealed a leiomyosarcoma of intermediate grade arising from the wall of the left renal vein, with no infiltration of the adrenal cortex. Immunohistochemistry was positive for SMA, desmin, and h-caldesmon, with a Ki-67 index of approximately 35%.

Conclusions: This case highlights the diagnostic complexity of large adrenal-region masses and emphasizes that non-adrenal malignancies, including vascular leiomyosarcomas, may radiologically mimic adrenal tumors.

Abstract citation ID: lvag096.713

EP114 - ECE_3413 - Is mild autonomous cortisol secretion (MACS) truly mild?

Mari Minasyan[1], Aleksandra Gamrat-Żmuda[2,3], Maria Borysowicz[4], Alicja Hubalewska-Dydejczyk[1] and Aleksandra Gilis-Januszewska[1]
[1]*Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland;* [2]*Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland;* [3]*Doctoral School of Medical and Health Sciences, Jagiellonian University Medical College, Krakow, Poland;* [4]*Students' Scientific Circle of Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland*

Introduction: Mild autonomous cortisol secretion (MACS) is a condition of mild cortisol excess due to autonomous secretion by adrenal tumor(s). Patients lack typical Cushing syndrome symptoms but face increased risks of cardiovascular, metabolic, and skeletal complications.

Materials and Methods: We reviewed clinical characteristics of MACS patients hospitalized at a reference endocrinology center in southeastern Poland from 2018-2024. Inclusion criteria: serum cortisol $\geq$1.8 μg/dL in 1 mg dexamethasone suppression test (post-DST), ACTH $\leq$ 20 pg/mL, benign adrenal lesion(s) on imaging. Exclusion criteria: active malignancy, steroid therapy, active infection, alcohol abuse.

Results: A total of 203 patients fulfilled inclusion criteria (74% women; mean age 67 ± 10 years). Mean ACTH concentration was 12.7 ± 4.4 pg/mL, and median post-DST cortisol was 2.83 μg/dL (IQR 1.8-13.9). All patients were referred for evaluation of adrenal incidentalomas. Imaging revealed bilateral adenomas in 37.5%, unilateral left adenomas in 36.5%, unilateral right adenomas in 22%, adrenal hyperplasia in 3.5%, and adrenal trunk thickening in 0.5%. ARMC5 mutations were identified in 7% of patients with bilateral adenomas. Comorbidities were highly prevalent: obesity in 40.5%, overweight in 28%, and disturbances of glucose metabolism in 48%, including poorly controlled diabetes in 23%. Hypertension was present in 84%, with poor control in 23%, dyslipidemia in 71%, and coronary heart disease in 20%. Pathological fractures occurred in 11% of patients, predominantly vertebral (73%). Osteoporosis or osteopenia of the femoral neck was detected in 12.8%, and of the lumbar spine in 13%. Hepatic complications icluded isolated steatosis in 14%, isolated elevation of liver enzymes in 15%, and both in 7.5%.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Thromboembolic events were documented in 5.4%, including deep vein thrombosis (64%), pulmonary embolism (27%) and both in 9%. Psychiatric manifestations included depression (12.8%), anxiety (4.5%), and insomnia (4.5%). Nineteen patients underwent adrenal surgery. All patients with unilateral adenomas (11) achieved remission, whereas outcomes in bilateral disease were heterogeneous (50% no remission, 25% temporary [21-276 months], 25% permanent). 9 patients were included in relacorilant trial (6 bilateral adenomas, 3 post-unilateral relapse).

Conclusions: MACS patients have significant prevalence of cardiometabolic, thromboembolic, skeletal, hepatic and psychological complications. These findings challenge the perception of MACS as a benign condition and underscore the need for refined risk stratification and prospective studies to better define morbidity and guide treatment strategies.

Abstract citation ID: lvag096.714

EP115 - ECE_3519 - Assessment of hypothalamic-pituitary-adrenal axis function in adults with sickle cell disease: a retrospective study

Kalliopi Pantelia[1], Vasiliki Antonopoulou[1], Galateia Stathori[1], Stella Tsanaxidou[1], Aikaterini Kapama[1], Andromachi Panagiotopoulou[1], Sofia Chatzi[1], Anna Louisa Chaliasou[1], Angelos Theocharis[1], Chrysa Kalkana[2], Loukia Evliati[2], Marinella Tzanela[1] and Georgia Ntali[1]
[1]*Department of Endocrinology "D. Ikkos", Diabetes Center, EndoERN-Evangelismos General Hospital, Athens, Greece;* [2]*Thalassaemia and Sickle Cell Unit, Evangelismos General Hospital, Athens, Greece*

Introduction: Sickle cell disease (SCD) is a chronic inherited hemoglobin disorder associated with recurrent pain, anemia, and multisystem complications. Endocrine involvement, including dysfunction of the hypothalamic–pituitary–adrenal (HPA) axis, has been described, but remains poorly characterized. Proposed mechanisms include pituitary siderosis in transfusion-dependent patients and hypoxic–vascular injury during sickling episodes, though data in adults with SCD are limited.

Objective: To evaluate HPA axis through basal cortisol/ACTH levels and androgen levels in patients with SCD.

Methods: We conducted a retrospective study of adult patients with SCD followed at the Mediterranean Anemia and Sickle Cell Disease Unit who underwent assessment of basal ACTH and cortisol levels between January 2019 and January 2026. Patients with borderline or low cortisol levels underwent Synacthen stimulation testing, with cortisol measured at 0, 30, and 60 minutes. Serum DHEA-s were evaluated using sex/age-adjusted reference ranges.

Results: Twenty-three patients were included (mean age 53.2 ± 10.6 years, 15 females—8 males); 20/23 (87%) had sickle cell thalassemia, and 3/23 (13%) had homozygous sickle cell disease. Basal serum cortisol levels ranged from 2.3 to 27.6 μg/dL (mean 13.9 ± 5). 3/23 (13%) patients had cortisol levels <10 μg/dL; all underwent Synacthen testing and demonstrated adequate adrenal responses (peak cortisol 21.1-26.2 μg/dL). 11/23 (48%) patients had cortisol levels between 10 and 15 μg/dL and 3/11 (27%) underwent Synacthen testing with adequate peak responses (22-26 μg/dL). 9/23 (39%) had basal cortisol levels >15 μg/dL. Basal ACTH levels ranged from <5 to 58.6 pg/mL, with a mean value (±SD) 24.1 (±14.3) pg/mL. DHEA-s levels were available for 11/23 (47.8%) patients. Reduced DHEA-s levels were noted in 8/11(73%) patients while 3/11 (27%) had levels within the reference range. One patient had DHEA-s levels below the assay detection threshold (<15 μg/dL).

Conclusions: HPA axis function appears largely preserved in patients with SCD at our center, possibly reflecting improved contemporary disease management. However, low DHEA-s levels were observed in the majority of patients, the clinical significance of this finding remains unclear. Limited data—particularly in patients with microdrepanocytic anemia, who comprised most of our cohort—highlight the novelty of this analysis and the need for further studies to better characterize endocrine function in this population.

Abstract citation ID: lvag096.715

EP116 - ECE_3742 - The effect of hepatic impairment on the pharmacokinetics of atumelnant for the treatment of congenital adrenal hyperplasia and adrenocorticotropic hormone-dependent Cushing syndrome

Xiaoli Wang[1], Rosa Luo[2], Daria Stypinski[3], Scott Brantley[1], Lei Xu[1], Eduardo De La Torre[1], Alejandro Ayala[1] and Lise Kjems[1]
[1]*Princeton, NJ, United States;* [2]*A2-Ai LLC, Ann Arbor, MI, United States;* [3]*DS Clinical Pharmacology Consulting LLC, Manson, WA, United States*

Atumelnant is a first-in-class, once-daily, oral, selective, melanocortin type 2 receptor antagonist in development for congenital adrenal hyperplasia and adrenocorticotropic hormone-dependent Cushing syndrome. The objective of this study was to compare the pharmacokinetics (PK) of a single dose of atumelnant in participants with varying degrees of hepatic impairment with that of healthy matched control participants. Safety and tolerability of a single dose of atumelnant were assessed.

This was a Phase 1 single-dose, open-label, parallel study. Male and female adults were screened and assigned to a study group according to hepatic function (mild, moderate, or severe impairment) using the Child-Pugh classification system. Healthy control participants were matched with participants with hepatic impairment of varying degrees according to sex, age (±10 years), and body mass index (±20%). All participants received a single oral dose of 10 mg atumelnant in the morning following an overnight fast of ≥10 hours. Participants remained fasted for 4 hours after dosing. Serial blood samples for PK analysis of atumelnant concentrations were collected within 15 minutes before and ≤144 hours after atumelnant administration. Area under the curve (AUC) and maximum plasma concentration (C_{max}) were determined for both total and unbound atumelnant. Adverse events were summarized.

Twenty-three participants with hepatic impairment of varying degrees were included (mild, $n = 8$; moderate, $n = 8$; severe, $n = 7$) and matched with healthy control participants ($n = 13$). Participants with mild, moderate, and severe hepatic impairment exhibited a modest decrease (25%, 57%, and 25%, respectively) in total AUC compared with healthy controls. However, 90% CIs of geometric mean ratio (GMR) of AUC for comparison of mild and severe hepatic impairment relative to normal

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

function included unity. After taking into consideration the fraction of protein binding, the unbound AUC and C_{max} were similar between hepatic impairment groups and healthy controls; GMRs for AUC in mild, moderate, and severe impairment were 0.94, 0.71, and 1.43, respectively, and 1.00, 0.74, and 0.95 for C_{max}, respectively. The 90% CIs for all unbound exposure parameters included unity. There were 5 treatment-emergent adverse events (drug related, $n = 3$, all mild; not drug related, $n = 2$, 1 severe and 1 moderate); all resolved by end of study.

Hepatic impairment did not result in clinically meaningful changes in the total or unbound atumelnant exposures; therefore, dose adjustment of atumelnant is not required in participants with mild, moderate, or severe hepatic impairment. A single 10-mg dose was well tolerated in participants with varying degrees of hepatic impairment.

Abstract citation ID: lvag096.716

EP121 - ECE_3641 - Evaluation of the high-dose dexamethasone suppression test in mild autonomous cortisol secretion: what does it add compared with the low-dose dexamethasone suppression test?

Zeynep Elüstü Belten, Ozge Sahin Kimyon, Selin Celik, Hamide Piskinpasa, Meral Mert and Sema Ciftci
Endocrinology and Metabolism, Sağlık Bilimleri Üniversitesi Bakırköy Doktor Sadi Konuk Eğitim Ve Araştırma Hastanesi, Bakırköy, Türkiye

Objective: Mild autonomous cortisol secretion (MACS) is a common hormonal abnormality in patients with adrenal incidentalomas and is characterized by biochemical hypercortisolism in the absence of the classical clinical features of Cushing syndrome. Diagnosis is based on a morning serum cortisol level >1.8 μg/dL following the 1-mg dexamethasone suppression test (DST). However, treatment strategies remain individualized, and clear criteria for adrenalectomy are still lacking. This study aimed to assess the clinical usefulness of the recently recommended high-dose (8-mg) DST in guiding adrenalectomy decisions in patients with MACS.

Methods: Seventy-four patients diagnosed with MACS based on the 1-mg DST during the evaluation of adrenal incidentalomas at a tertiary endocrinology clinic were included. All patients underwent an 8-mg DST, and post-test serum cortisol levels >1.8 μg/dL were considered indicative of a lack of suppression. The frequency of cortisol suppression with the high-dose DST, its association with metabolic and clinical features, its influence on adrenalectomy decisions, and its correlation with 1-mg DST results were analyzed.

Results: The study population comprised 5 men and 69 women, with a mean age of 57 ± 8 years. Mean basal ACTH levels were 6.2 ± 3.3 ng/L. The mean cortisol concentration after the 1-mg DST was 3.3 ± 1.3 μg/dL. Age-and sex-adjusted DHEA-S levels were suppressed in 14% of patients and were within the normal range in the others. Imaging revealed unilateral adrenal adenomas in 70% of cases and bilateral macronodular hyperplasia in the remaining 30%. Only three patients (4.1%) demonstrated cortisol suppression following the 8-mg DST. Paradoxical increases in cortisol levels after the 8-mg DST compared with the 1-mg DST were observed in 50 patients. The three patients who achieved cortisol suppression had metabolic comorbidities but no osteoporosis or osteopenia. Among the remaining patients, cardiometabolic complications were common, including obesity, diabetes or prediabetes, hypertension, dyslipidemia, and reduced bone mineral density. Adrenalectomy was performed in seven patients based on clinical judgment. None of these patients showed cortisol suppression with the 8-mg DST. All patients had suppressed ACTH levels, and DHEA-S levels were suppressed in more than half of them. Positive correlation was observed between cortisol levels after the 1-mg and 8-mg DSTs ($r = 0.656$, $P < .001$).

Conclusions: In patients with MACS, the high-dose DST largely parallels the results of the standard 1-mg DST and provides limited additional diagnostic or therapeutic guidance. Based on the present findings, its role in guiding adrenalectomy decisions remains uncertain. Larger prospective studies are required to clarify the clinical relevance of the 8-mg DST in the management of MACS.

Abstract citation ID: lvag096.717

EP122 - ECE_2324 - From cardiac crisis to endocrine diagnosis: pheochromocytoma-induced myocarditis

Ruxandra Costinescu[1], Dana Tilici[1,2,3], Adina Onofrei[1], Mirona Costea[1,2], Beatrice Grecu[1], Claudia Nacea[1], Ana-Maria Arnautu[1], Daniela Greere[1,4] and Diana Paun[1,2,4]
[1]Endocrinology, University Emergency Hospital of Bucharest, Bucharest, Romania; [2]Doctoral School, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [3]University Emergency Hospital of Bucharest, Bucuresti, Romania; [4]Bucharest, Romania

Introduction: Recent guidelines and clinical experience indicate a significant increase in the incidence of secondary hypertension. Additionally, secondary hypertension resulting from endocrine disorders is increasingly prevalent. Therefore, in patients presenting with cardiac dysfunction of unknown origin, clinicians should consider the possibility of pheochromocytoma. This approach is especially important, as the literature reports that up to 11% of these cases may develop catecholamine-induced cardiomyopathy. Myocarditis represents a potential manifestation of this form of cardiomyopathy. Given its potential to threaten patient survival, rapid diagnosis is critical for optimal outcomes. Although surgical intervention remains the standard curative approach, preoperative preparation is often challenging and does not eliminate the risk of intraoperative complications.

Purpose: A clinical case from the Bucharest University Emergency Hospital emphasizes the importance of considering pheochromocytoma in the differential diagnosis of patients presenting with unexplained myocarditis, especially when infectious, autoimmune, or toxic causes have been excluded.

Results: A 45 year-old female patient with no prior cardiovascular history presented to the emergency room with acute substernal pain, palpitations, and severe hypertension (SAP = 230 mmHg). Initial evaluation revealed negative T waves in the lateral leads, elevated cardiac troponin I (>6000 ng/L) and increased NT-proBNP (4271 pg/mL). Echocardiography demonstrated diffuse left ventricular hypokinesia with a LVEF of 30%-35%. Emergency coronary angiography showed normal coronary arteries. Cardiac MRI revealed findings consistent with acute

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

myocarditis. The differential diagnosis of acute myocarditis was performed, with infectious, toxic, and autoimmune causes excluded by specific tests. During hospitalization, a chest CT scan incidentally identified a 3.5 cm mass in the left adrenal gland. Endocrinological evaluation, including a detailed history, revealed a pattern of hypertensive episodes at home over the preceding 18 months, associated with severe headache, nausea, and vomiting. Biochemical screening for secondary hypertension demonstrated plasma metanephrine levels exceeding 1.5× ULN and plasma normetanephrine levels exceeding 4× ULN. An abdominal CT scan was done to confirm the presence of an adrenal mass and to exclude paragangliomas. Subsequently, left adrenalectomy was performed following established preoperative protocols. Despite dual therapy with alpha and beta adrenergic receptor blockers, the patient experienced an intraoperative hypertensive episode that resolved spontaneously. Histopathological analysis confirmed pheochromocytoma, and postoperative cardiac function normalized, with a LVEF of 60%.

Conclusions: This case highlights the importance of considering pheochromocytoma in young patients presenting with heart disease of unknown etiology, including myocarditis. Implementing a multidisciplinary approach and developing standardized protocols are crucial for ensuring accurate treatment and favorable long-term outcomes.

Abstract citation ID: lvag096.718

EP123 - ECE_1220 - Evolving optimism in the medical management of Cushing's syndrome

Efthymia Kallistrou, Christos Savvidis, Vasiliki Tsiama, Stella Proikaki, Konstantinos Belis, Dimitra Ragia, Dimitra Motsiou and Ioannis Ilias
Department of Endocrinology, Hippokration Hospital, Athens, Greece

Background: Cushing's syndrome (CS) is a therapeutically challenging disorder. Hypercortisolism may persist and CS-related comorbidities are numerous. While medical therapies for CS have evolved, such as with steroidogenesis inhibitors and glucocorticoid antagonists, the perception of their efficacy and safety in the medical literature remains underexplored. Sentiment analysis (SA) of the medical literature—using Artificial Intelligence (AI)—can provide a new assessment metric, which has been shown to be analogous to meta-analysis. Furthermore, SA represents an area that might project researcher attitudes toward therapeutic interventions, possibly highlighting biases or progress.

Methods: From a total of 239 relevant publications, in the years 2000-2025 (PubMed), 30 relevant abstracts were manually extracted by two expert endocrinologists and were included in the analysis. Only abstracts of original publications were retained. Each abstract was reviewed for sentiment attribution by an expert AI (ChatGPT version of October 2, 2025). Sentiments were categorized as positive (with a score of +1: emphasizing efficacy/safety), neutral (0: descriptive/protocols), or negative (−1: highlighting limitations/adverse effects). The distribution of SA scores was assessed by the chi-square test. Temporal trends in SA scores against publication year were evaluated using linear regression and the chi-square for trend across year groups (2000-2009, 2010-2019, 2020-2025).

Results: Eighteen abstracts (60%) were classified as being positive, focusing on drugs like metyrapone and osilodrostat; nine (30%) were neutral, often emphasizing trial protocols and three (10%) were negative, noting toxicity or incomplete remission. Chi-square analysis disclosed significant sentiment differences, with $x^2 = 15.8$, $df = 2$, $P < .001$, with positives being predominant. Linear regression revealed increasing positive sentiments over time, with $\beta = .12$/year, $P = .04$, $R^2 = 0.15$ (Grouped analysis: 2000-2009, $n = 15$, 7 positive, 5 neutral, 3 negative; 2010-2019, $n = 5$, 3 positive, 2 neutral, 0 negative; 2020-2025, $n = 10$, 8 positive, 2 neutral, 0 negative, confirming upward trend, $P = .03$).

Conclusions: Positive sentiments dominate the recent medical literature on CS therapy, apparently reflecting therapeutic advancements. This trend also suggests growing optimism among researchers and may influence clinical adoption. However, the underrepresentation of negatives may also suggest the presence of publication bias.

Abstract citation ID: lvag096.719

EP124 - ECE_1276 - Overnight hypoglycaemic episodes in adrenal insufficiency alleviated with modified release hydrocortisone (Efmody); a case report

Muhammad Fahad Arshad[1,2] and Miguel Debono[1,2]
[1]*Endocrinology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom;* [2]*School of Medicine and Population Health, University of Sheffield, Sheffield, United Kingdom*

Background: Hypoglycaemia is a recognised symptom of adrenal insufficiency (AI), albeit more common in children. Rarely, hypoglycaemia can occur in people with AI despite conventional immediate-release hydrocortisone, due to its inability to mimic the physiological cortisol circadian rhythm.[1]

Case Details: We present the case of a 53-year-old Caucasian female (general practitioner doctor). She was referred to endocrinology for suspected tertiary AI resulting from frequent oral glucocorticoid courses and long-term inhaled glucocorticoids for asthma. AI was confirmed with an abnormal short synacthen test (0 min cortisol 63 nmol/L; 30 min cortisol 197 nmol/L; normal response >430 nmol/L) with low plasma adrenocorticotrophic hormone (ACTH) levels (5 ng/L, reference range 7.2-63.3). Rest of the pituitary function tests and magnetic resonance imaging (MRI) scan of pituitary gland were normal. She was started on hydrocortisone 15 mg per day in divided doses as per her body weight (60.3 kg). However, she started to notice symptoms suggestive of hypoglycaemia, especially around late night and early morning. Low glucose readings were confirmed on capillary glucose testing as well as continuous glucose monitoring (CGM) using Dexcom G6® and Freestyle Libre®. She also underwent a 72-hour fast which ruled out hyperinsulinaemia. Hydrocortisone dose was then increased to total 20 mg/day, but this did not alleviate the symptoms. A trial of increasing the dose beyond 20 mg resulted in manic episodes and therefore abandoned. In view of the timing of symptoms, it was decided to try off-label use of modified-release hydrocortisone, Efmody® 20 mg at nighttime followed by 10 mg in the morning. Efmody® instantly resulted in complete resolution of her symptoms and the low

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

glucose readings on CGM. The dose was then subsequently successfully reduced to 10 mg nocte and 5 mg on waking while under careful monitoring to maintain euglycaemia.

Conclusions: Efmody® mirrors the physiological early morning rise in cortisol compared to conventional glucocorticoid regimens.[1] Though it is currently licensed for patients with congenital adrenal hyperplasia, it can be used in some patients with other causes for AI with inadequate response to standard hydrocortisone treatment.

Reference

1. Arshad MF, Debono M. Current and future treatment options for adrenal insufficiency. *Curr Opin Endocrinol Diabetes Obes*. 2021;28(3):303-311. https://doi.org/10.1097/MED.0000000000000637

Abstract citation ID: lvag096.720

EP125 - ECE_2541 - The views and experiences of adult women with congenital adrenal hyperplasia on childhood genital surgery: a qualitative study

K Lynette James[1], Nicola Parkin[2], Sue Elford[3], Faisal Ahmed[4], Nils Krone[5], Michael W. O'reilly[6], Sofia Llahana[7], Jeremy Tomlinson[8] and Aled Rees[9]

[1]Cardiff, United Kingdom; [2]Cardiff University, Cardiff, United Kingdom; [3]Living with CAH Patient Support Group, Cambridge, United Kingdom; [4]Royal Hospital for Children, University of Glasgow, Glasgow, United Kingdom; [5]Division of Clinical Medicine, School of Medicine and Population Health, University of Sheffield, Sheffield, United Kingdom; [6]Royal College of Surgeons in Ireland (RCSI), Dublin, Ireland; [7]School of Health and Medical Sciences, City St George's, University of London, London, United Kingdom; [8]Oxford Centre for Diabetes, Endocrinology and Metabolism, NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, United Kingdom; [9]Neuroscience and Mental Health Innovation Institute, School of Medicine, Cardiff University, Cardiff, United Kingdom

Introduction: There is ongoing debate over the timing of genital surgery in girls with congenital adrenal hyperplasia (CAH), with calls to delay surgery until the girl can consent. However, research suggests patients and parents prefer early surgery with minimal regret.

Aim: To explore adult women's experiences of childhood genital surgery in CAH.

Methods: Virtual semi-structured interviews were conducted with adult women with CAH who had childhood genital surgery and/or their parents, recruited via the Living with CAH support group. Interviews were audio-recorded, transcribed verbatim and analysed using inductive thematic analysis. Ethical approval was obtained.

Results: Twelve women with CAH (aged 20-62 years) and two mothers were interviewed. Most women ($n = 10$) had multiple surgeries in childhood and adolescence, with three undergoing additional adult surgery. Early childhood surgery was not recalled. Three women described trauma from later surgery (>6 years) relating to hospital care (eg, cannulation, exposure to child's death). Ten women were unaware of the procedure performed, while others had a clitoral reduction ($n = 1$) with vaginoplasty ($n = 1$). Eight women reported adverse surgical and psychosexual effects (eg, vaginal stenosis, urinary tract infections, scar tissue, dyspareunia, low libido, genital dysmorphia), with distress limited to two women with incontinence and labial infections. Views on childhood feminising surgery were polarising. Both women distressed by surgical outcomes opposed childhood surgery, reporting their parents were *"forced"* by clinicians. The participants mothers reported acting in their daughter's best interest based on medical advice, with one stating surgery was medically necessary for urogenital sinus. The mothers and daughters blamed clinicians, citing inadequate information about surgery and long-term complications. All other participants felt surgery had been in their best interests, describing it as sex-affirming and medically necessary. They viewed surgery as complementing their female sex and reproductive anatomy, with early surgery perceived to reduce psychological trauma from awareness of the procedure, bullying and male rearing. These women were concerned that labelling CAH as intersex and gender-identity activism were negatively influencing surgical decision for what they viewed an endocrine disorder rather than gender dysphoria. Others supported childhood surgery for medical indications, with *"cosmetic"* feminising procedures delayed until the girl could make an informed decision.

Discussion: Views on genital surgery timing in CAH are varied, with most supporting early surgery despite psychosexual impact. Irrespective of timing, patients and their parents require comprehensive information on surgical treatment and psychological support to enable informed decision making. Larger studies are needed to explore temporal trends.

Abstract citation ID: lvag096.721

EP127 - ECE_3655 - Endoscopic ultrasound-guided trans-gastric radiofrequency ablation: an effective and safe alternative treatment for left-sided unilateral aldosterone-producing adenoma

Furnica Raluca, Deprez Pierre, Loubet Antoine and Dominique Maiter

Endocrinologie, Cliniques Universitaires Saint Luc, Brussels, Belgium

Background: Unilateral aldosterone-producing adenomas (APAs) are a potentially curable cause of hypertension through laparoscopic adrenalectomy. However, surgery may not be appropriate for all patients, especially those with significant comorbidities or preferences for less invasive management. Endoscopic ultrasound (US)-guided trans-gastric (TG) radiofrequency ablation (RFA) offers a minimally invasive alternative to treat left-sided APAs which are in close proximity with the stomach.

Methods: This novel approach was successfully performed at our center in two patients with confirmed left-sided APAs and a preference for minimally invasive curative treatment with preservation of left adrenal tissue. Prior to the procedure, co-secretion of cortisol was excluded. Both patients underwent medical preparation with spironolactone (50 mg/day) and an alpha-blocker (terazosin 2.5 mg twice daily for two weeks). Under general anesthesia, the left adrenal nodule was ablated using a 10 mm STARMed needle (Taewoong Medical, Seoul, South Korea) and a generator set at 30 W. No immediate complications were noted post-procedure. Case 1: A 35-year-old woman with familial adenomatous polyposis and a history of total colectomy was diagnosed with a left-sided APA. Abdominal CT-scan imaging

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

showed bilateral adrenal nodules (left: 23 × 16 mm and right: 17 × 12 mm), both evoking benign adenomas. Adrenal vein sampling showed a clear lateralization ratio (10.0) of aldosterone secretion from the left side. Within one week after the procedure, she achieved complete clinical remission of hypertension, allowing discontinuation of spironolactone. At one-month follow-up, her blood pressure remained normal without medication, biochemical cure of PA was confirmed, and CT imaging showed a stable left adrenal lesion with focal areas of necrosis but no delayed complications. Case 2: A 52-year-old woman with a 20-year history of hypertension and a 12 × 19 mm left-sided APA confirmed by adrenal vein sampling, experienced improvement in blood pressure after the procedure. Follow-up is ongoing.

Conclusions: EUS-RFA was an effective and safe alternative treatment for left-sided APAs, devoid of major immediate complications. Long-term follow-up is essential to assess the sustained effectiveness and safety of this innovative technique.

Abstract citation ID: lvag096.722

EP128 - ECE_2357 - Autoimmune Addison's disease mimicking tuberculous pleuro-pericardial effusions: a rare presentation and diagnostic pitfall

Mohamed Nhili[1], Aziouaz Fatima[1] and Benkacem Mariem[1]
[1]*Endocrinology, Diabetology and Metabolic Diseases Department, Mohammed VI University Hospital of Tangier, Tangier, Morocco*

Introduction: Primary adrenal insufficiency is a rare but potentially life-threatening condition with nonspecific manifestations. In tuberculosis-endemic regions, its association with pleuro-pericardial effusions often suggests disseminated tuberculosis, representing a major diagnostic pitfall.

Clinical Case: A 51-year-old man with no significant medical history was admitted for severe asthenia, weight loss, anorexia, and hemodynamic instability. Echocardiography revealed a large pericardial effusion requiring urgent drainage. Pericardial fluid analysis showed a hemorrhagic exudate with neutrophil predominance, elevated LDH, and sterile cultures. Laboratory tests revealed normochromic normocytic anemia, neutrophilic leukocytosis, elevated C-reactive protein, and mild hypoalbuminemia. Chest X-ray showed bilateral pleural effusions and upper-lobe opacities. CT scan (CTAP) demonstrated bilateral pleural effusions, apical pulmonary micronodules-highly suggesting tuberculosis-, mild ascites, and a tumefied medial limb of the left adrenal gland without destructive lesions. Pleural fluid analysis revealed a lymphocytic exudate with negative bacteriology and GeneXpert testing. Blood, urine, and sputum cultures were negative. In the setting of hypotension with hyponatremia and hyperkalemia, morning cortisol was markedly low with elevated ACTH levels. Anti-21-hydroxylase antibodies were positive, confirming autoimmune Addison's disease. Hormonal replacement with hydrocortisone and fludrocortisone led to rapid clinical and biological improvement.

Conclusions: Autoimmune Addison's disease may rarely present with pleuro-pericardial effusions and closely mimic disseminated tuberculosis. This association should be considered in patients with unexplained serous effusions and biological features of adrenal insufficiency.

Abstract citation ID: lvag096.723

EP129 - ECE_3967 - Primary hyperaldosteronism: a rare cause of hypertension in pregnancy

Georgiana Taujan, Alexandra Mirica, Mihaela Rosu and Iconaru Laura
Department of Endocrinology, CHU Brugmann, Bruxelles, Belgium

Background: Primary hyperaldosteronism is one of the main causes of secondary hypertension, but remains a rare cause of hypertension during pregnancy, with less than 80 cases described in the literature. It presents significant diagnostic and therapeutic challenges, as the physiological activation of the renin–angiotensin–aldosterone system during pregnancy may mask biochemical abnormalities and complicate interpretation of standard diagnostic tests. It also associates an increase risk of maternal and fetal complications.

Case Report: We present the case of a 34 years old pregnant patient with severe hypertension and hypokalemia suggestive of mineralocorticoid excess. The patient associated a history of severe pre-eclampsia during her previous pregnancy, with residual hypertension after the birth. No endocrinological evaluation was done between the pregnancies. The patient presented in the obstetrical clinic at 20 weeks of pregnancy for low abdominal pain. The initial evaluation showed a high-normal blood pressure despite triple therapy and severe growth restriction in the foetus. The laboratory evaluation revealed severe hypokalemia (1.5 mmol/L), with very high aldosterone level (2350 ng/dL) and a low-normal renin (5.4 mUI/L), haemolytic anemia (Hb 9.2 g/DL, LDH 870 U/L) and elevated liver enzymes (ALT 167 U/L, GGT 367 U/L). The abdominal IRM confirmed the presence of a right 2.2 cm adrenal adenoma, with all data supporting the diagnosis of primary hyperaldosteronism with severe preeclampsia and HELPP syndrome. Unfortunately, the baby did not survive. The hypokalemia was corrected with iv and oral supplementation and the patient maintained a high-normal blood pressure despite quadruple therapy. She underwent a right adrenalectomy 1 month later, with complete resolution of hypertension and hypokalemia.

Conclusions: Primary hyperaldosteronism is uncommon in pregnancy and early recognition and individualized management are essential to reduce maternal and fetal morbidity. Multidisciplinary collaboration is crucial for optimal outcomes.

Abstract citation ID: lvag096.724

EP131 - ECE_1743 - Adverse cardio-metabolic risk profile and epicardial adiposity in patients with adrenal adenoma: a cross-sectional study

Helena Niziolek[1], Anna Tosin[1], Ivica Just[1], Clemens Baumgartner[1], Oliver Koldyka[1], Paul Fellinger[1], Hannes Beiglboeck[1], Luise Bellach[1], Anton Luger[1], Siegfried Trattnig[2], Alexandra Kautzky-Willer[1], Michael Leutner[1], Hansjörg Habisch[3], Greisa Vila[1], Oliver Domenig[4], Maximilian Zeyda[5], Tobias Madl[3,6], Michael Krebs[1], Martin Krssak[1] and Peter Wolf[1]
[1]*Department of Internal Medicine III, Division of Endocrinology and Metabolism, Medical University of Vienna, Vienna, Austria;* [2]*Department of Biomedical Imaging and Image Guided Therapy, Medical University of Vienna, Vienna, Austria;* [3]*Medical University of*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Graz, Graz, Austria; [4]Vienna, Austria; [5]Department of Pediatrics and Adolescent Medicine, Division of Pediatric Pulmonology, Allergology and Endocrinology, Medical University of Vienna, Vienna, Austria; [6]BioTechMed-Graz, Graz, Austria

Research Question: Adrenal incidentaloma are common in the general population. Mild autonomous cortisol secretion (MACS) is associated with an increased cardiovascular mortality, but even patients with non-functioning adrenal adenoma (NFA) might be at risk for cardio-metabolic comorbidities compared to a control group with absence of an adrenal tumor (CON).

Materials and Methods: Seventy-four patients were included in cross sectional analysis [MACS: $n = 25$ (84% females), age: 63 (55-67) years, BMI: 27.00 (24.20-30.50); NFA: $n = 25$ (84% females), age: 61 (54-68) years, BMI: 28.50 (27.50-32.20) and CON: $n = 24$ (75%females), age: 58 (51-64) years, BMI: 27.39 (22.03-30.17). Visceral and ectopic fat stores, as well as heart function were assessed by magnetic resonance imaging and spectroscopy. Orthostatic blood pressure regulation was measured by Schellong tests. Blood was drawn in the fasting state and during an oral glucose tolerance test to assess glucose and lipid metabolism.

Results: The prevalence of hypertension (MACS: 84% vs NFA: 76% vs CON: 43.5%), dyslipidemia (MACS: 96% vs NFA 80% vs CON 62.5%) and prediabetes (MACS: 56% vs NFA 72% NFA vs CON 29.17%) was significantly different between the groups, being highest in MACS. HbA1c ($P = .0429$), HOMA_IR ($P = .007$), fasting insulin ($P = .014$) and c-peptide ($P = .018$) were highest in MACS, indicating worse insulin sensitivity. Epicardial adipose tissue was markedly increased in MACS patients, followed by NFA, with lowest values in CON (MACS: 1159 [930, 1454] mm^2 vs NFA: 873 [638, 1195] mm^2 vs HC: 672 [549, 890] mm^2; $P < .001$). No between-group-differences in cardiac function, intramyocardial fat or intrahepatic fat were observed.

Conclusions: MACS is associated with epicardial adiposity and an adverse cardio-metabolic risk profile, but even NFA might be at higher risk compared to CON.

Abstract citation ID: lvag096.725

EP133 - ECE_2419 - Basal cortisol as a predictor of short Synacthen test outcome in a 16-month outpatient audit

Du Soon Swee, Ling Zhu, Shao Ting Lim, Lih Ming Loh and Peng Chin Kek
Department of Endocrinology, Singapore General Hospital, Singapore, Singapore

Background: Outpatient short Synacthen testing (SST) is labour-intensive and capacity-limited. Basal cortisol thresholds that reliably predict SST outcome may support more efficient triage and reduce unnecessary testing. Interpretation of SST results is also influenced by assay methodology. The cortisol assay used at our institution is the Beckman Coulter Access platform, for which a lower pass threshold of 450 nmol/L has been shown to be comparable to the traditional 500 nmol/L criterion. We evaluated the predictive performance of basal cortisol using 500 nmol/L as the reference standard, and explored the potential impact of applying a 450 nmol/L cutoff.

Methods: We conducted a retrospective audit of all outpatient SSTs performed over 16 months (Aug 2024-Dec 2025) at a tertiary centre. Data included SST dose (1 µg vs 250 µg), clinical indication, diagnosis, basal cortisol (SSTbasal, 0 min), and peak cortisol (SSTpeak, 1 µg: 15, 30 or 45 min; 250 µg: 30 or 60 min). Predictive performance of SSTbasal was assessed using receiver operating characteristic (ROC) analysis, using the conventional definition of pass (SSTpeak ≥500 nmol/L) as the primary endpoint, with a secondary exploratory analysis using SSTpeak ≥450 nmol/L. In addition to Youden index thresholds, clinically oriented cutoffs prioritising high sensitivity and high specificity were derived.

Results: A total of 600 outpatient SSTs were analysed (1 µg: 64%; 250 µg: 36%). Using the standard ≥500 nmol/L definition, 314 tests (52.3%) passed; applying the exploratory ≥450 nmol/L definition, 417 tests (69.5%) would be classified as normal, thereby reclassifying 103 (17.2%) as pass. SSTbasal showed good discrimination for predicting outcome under both ≥500 and ≥450 nmol/L criteria: AUC 0.793 and AUC 0.816 respectively, with consistent performance across doses (AUC 0.804-0.848). For SSTpeak ≥500 nmol/L, a basal cortisol ≥338 nmol/L predicted pass with 95% specificity, while <165 nmol/L identified likely failures with 95% sensitivity. For SSTpeak ≥450 nmol/L, corresponding thresholds were ≥320 nmol/L (95% specificity) and <160 nmol/L (95% sensitivity). Basal values between approximately 160-330 nmol/L constituted an indeterminate zone where SST remained most informative.

Conclusions: Basal cortisol provides robust prediction of SST outcome. Exploratory analysis suggests that a 450 nmol/L threshold potentially avoids further evaluation in close to one-fifth of patients. Clinically oriented basal cortisol thresholds enable rational triage of testing, and incorporation of basal cortisol-guided pathways may improve utilisation of limited SST capacity and streamline outpatient endocrine workflows.

Abstract citation ID: lvag096.726

EP135 - ECE_1782 - Diurnal maternal progesterone exposure in third trimester added to higher PW and BW in male offspring. Odense child cohort

Hajir Al-Jorani[1,2], Richard Christian Jensen[1,3], Tina Kold Jensen[3,4], Henrik Christesen[2,4], Jan Jørgensen[4], Lucas Bacmeister[5], Ralf Dechend[6,7], Dorte Glintborg[1,2], Boye Lagerbon Jensen[2,8] and Marianne Andersen[1,2]
[1]Department of Endocrinology, University Hospital Odense, Odense, Denmark; [2]Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark; [3]Department of Clinical Pharmacology, Pharmacy and Environmental Medicine, University of Southern Denmark, Odense, Denmark; [4]Odense Child Cohort, Hans Christian Andersen Children's Hospital, Odense University Hospital, Odense, Denmark; [5]Clinic for Cardiology and Angiology, University Heart Center Freiburg–Bad Krozingen, Medical Center–University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany; [6]Experimental and Clinical Research Center, a cooperation between the Max-Delbrück-Center for Molecular Medicine in the Helmholtz Association and the Charité–Universitätsmedizin Berlin, Berlin, Germany; [7]Department of Cardiology and Nephrology, HELIOS Clinic Berlin-Buch, Berlin, Germany; [8]Institute for Molecular Medicine, University of Southern Denmark, Odense, Denmark

Background: Sexual dimorphism in maternal-fetal-placental interactions contributes to higher placental (PW) and birth weights

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(BW) in boys compared to girls; potentially, maternal progesterone may add to this sexual dimorphism. Progesterone levels increase during healthy pregnancy and promote plasma volume expansion. Diurnal urine (u-) progesterone metabolite pregnanediol-3-glucuronide (PdG) provides a more integrated estimate of overall progesterone exposure compared to serum (s-) progesterone.

Objective: To investigate associations between maternal third trimester progesterone exposure and PW or BW in offspring, including potential effects of fetal sex. Secondarily, to examine associations between 24-hour (h) u-PdG and 24 h u-sodium retention, as well as maternal blood pressure (BP).

Methods: This prospective observational study included 1503 mother-child dyads (786 boys and 703 girls) from the Odense Child Cohort. Maternal progesterone exposure was assessed in gestational week 28 by measurement of fasting morning s-progesterone ($n = 1503$) and 24 h u-PdG ($n = 566$). 24 h u-sodium retention was estimated from 24 h u-sodium excretion. Progesterone and sodium concentrations were quantified using liquid chromatography-tandem mass spectrometry.

Results: In boys, 1 µmol/day increase in maternal u-PdG was associated with higher PW and BW (β = 1.11 g [95% CI: 0.61; 1.39]) and (β = 2.14 g [95% CI: 0.97; 3.31]), respectively; there was no significant association in girls. Higher maternal 24 h u-PdG was associated with higher PW and BW (β = .69 g [95% CI: 0.41; 0.96]) and (β = 1.49 g [95% CI: 0.65; 2.33]), respectively, in the whole cohort. In boys, 1 nmol/L increase in maternal s-progesterone was associated with higher PW and BW of 0.42 g (95% CI: 0.27; 0.56) and 0.73 g (95% CI: 0.31; 1.15), respectively; correspondingly in girls, s-progesterone associated with higher PW and BW of 0.44 g (95% CI: 0.28; 0.61) and 0.95 g (95% CI: 0.46; 1.44), respectively. Higher maternal s-progesterone was positively associated with higher PW and BW (β = .43 g [95% CI: 0.32; 0.54]) and (β = .82 g [95% CI: 0.49; 1.15]), in the whole cohort. One mmol/day increase in maternal 24 h u-PdG was associated with more retention of diurnal u-sodium of −0.21 mmol/day (95% CI: −0.30; −0.11). No significant association was found between u-PdG or s-progesterone and maternal BP.

Conclusions: Maternal diurnal progesterone exposure may add to the higher PW and BW in boys compared to girls. Furthermore, higher progesterone exposure was associated with more sodium retention, but there was no association between progesterone exposure and maternal BP.

Funding: NNF20OC0063280.

Abstract citation ID: lvag096.727

EP136 - ECE_2691 - The impact of exogenous corticosteroids on outcomes in medical admissions

Jessica Mangion[1], Rebecca Attard[2], Brett Grech[2], Jasmine Borg[2], Jade Borg[2] and Mark Gruppetta[1]
[1]*Endocrinology & Diabetes Division, Department of Medicine, Mater Dei Hospital, Msida, Malta;* [2]*Department of Medicine, Mater Dei Hospital, Msida, Malta*

Introduction: Glucocorticoids are commonly prescribed; however, the impact of chronic corticosteroid use on outcomes during medical admissions is less studied. This case-control study aims to evaluate their effects on mortality, re-hospitalization rates, biochemical markers, blood count indices and serum inflammation-based scores.

Method: A retrospective analysis of 5565 medical admissions from October 2021, February 2022 and June 2022 was performed. Among these, 230 patients who were on chronic corticosteroids were matched with controls based on age, sex, and diagnosis. Clinical and biochemical data were collected, and patients were followed up until June 2025 or death. Univariate analysis identified differences between cases and controls.

Results: 22.8% ($n = 105$) of cases were males, and the median age was 72 years (IQR 64-81). Inhaled corticosteroids were the most common in 67.0% ($n = 154$), followed by oral prednisolone in 17.8% ($n = 41$) and oral dexamethasone in 9.6% ($n = 22$). Respiratory diseases accounted for 73.9% ($n = 170$) of corticosteroid indications, followed by malignancy in 10.9% ($n = 25$). The type of corticosteroid was associated with mortality at 90 days ($P < .001$) and at 1 year ($P < .001$). Statistically significant differences were noted in the neutrophil-lymphocyte ratio (NLR) (P .001), lymphocyte-monocyte ratio (LMR) (P .001), platelet-lymphocyte ratio (PLR) (P .004) and systemic immune-inflammation index (SIII) (P .019). Patients on corticosteroids had a significantly higher 1-year mortality compared to controls (9.3% vs 4.6%, $P = .003$). Cases had lower serum urea (P .027) and serum chloride (P .001). These remained significant when those on oral corticosteroids were compared to their controls (1 year mortality $P = .022$; urea $P = .004$; chloride $P < .001$). Additionally, patients on oral corticosteroids also had a higher NLR ($P = .007$). Patients on dexamethasone and prednisolone had lower serum sodium (P .008) and chloride ($P < .001$) and elevated NLR (P .002) compared to their controls. Additionally, they also exhibited a lower LMR ($P = .038$) and higher SIII ($P = .027$). Sodium, chloride, NLR and SIII remained significant even after malignancy was excluded. Inhaled corticosteroid users showed no significant biochemical or haematological differences but showed a significantly higher 1-year mortality than their controls ($P = .049$).

Conclusions: These results indicate distinct biochemical and inflammatory profiles in patients on chronic corticosteroids, particularly those on higher potency, which may correlate with poorer prognosis during medical admissions. However, larger studies are required to validate these associations and clarify underlying mechanisms.

Abstract citation ID: lvag096.728

EP137 - ECE_1773 - Twenty-one years of cardiometabolic risk evolution in women with NCCAH: a longitudinal cohort analysis

Jéssica Me Lin Ie, Ana Carolina Maués de Oliveira, Nicholas Silvestre de Souza Trigueiro, Guiomar Madureira, Larissa Gomes, Ana Claudia Latronico, Berenice Bilharinho de Mendonça, Marisa Passarelli and Tania Bachega
Division of Endocrinology and Metabolism, Laboratory of Hormones and Molecular Genetics (LIM/42), Hospital das Clínicas, Faculty of Medicine, University of São Paulo, São Paulo, Brazil

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Context: Evidence of cardiometabolic risk in nonclassical congenital adrenal hyperplasia (NCCAH) is still limited and largely derived from cross-sectional or mixed cohorts. The long-term metabolic impact of glucocorticoid (GC) therapy and hyperandrogenic exposure remains unclear.

Objective: To characterize long-term trajectories of metabolic markers and the influence of GC use and hyperandrogenic exposure in women with NCCAH.

Design, Setting, and Participants: Longitudinal cohort of 31 women with NCCAH at a tertiary reference center, contributing up to 21 years of follow-up (477 patient-years). Annual assessments included body mass index (BMI), blood pressure (BP), HDL-c, fasting plasma glucose (FPG), triglycerides (TG), 17-hydroxyprogesterone (17O HP) and total testosterone levels. Longitudinal determinants were evaluated using linear mixed-effects models.

Results: BMI increased progressively over time and showed the strongest associations across cardiometabolic parameters. Higher BMI was associated with lower HDL-c ($P = .001$), higher FPG ($P = .007$), and higher systolic and diastolic BP ($P = .001$). Current GC use was associated with lower BMI ($P = .01$) and higher HDL-c ($P = .015$), whereas cumulative duration of GC therapy correlated with higher BMI and lower HDL-c, largely reflecting between-subject differences rather than within-individual effects. The intraclass correlation indicated that most BMI variability reflected inter-individual differences rather than changes over time within the same individual. Testosterone showed no independent metabolic associations except for an inverse relationship with HDL-c ($P = .039$). HDL-c and TG shifted unfavorably over time but remained within reference ranges; no independent predictors of TG trajectories were identified.

Conclusions: In this cohort, long-term cardiometabolic trajectories were mainly characterized by progressive increases in BMI. Current physiological GC use was not associated with adverse changes in the metabolic parameters evaluated. However, a negative impact of hyperandrogenism on HDL-c levels was observed.

Abstract citation ID: lvag096.729

EP138 - ECE_2888 - Higher frequency of meningiomas in patients with pathogenic variants of the ARMC5 gene predisposing to primary bilateral macronodular adrenal hyperplasia

Victoria De Wit[1], Lucas Bouys[1], Anna Vaczlavik[1], Laurence Guignat[1], Anne Jouinot[1], Lionel Groussin[1], Guillaume Assié[1], Albain Chansavang[2] and Jérôme Bertherat[1]

[1]Reference Center for Rare Adrenal Diseases, Endocrinology Department, Cochin Hospital, Paris 75014, France; [2]Oncogenetic Unit, Genetic Department, Cochin Hospital, Paris 75014, France

Context: Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH) is a rare etiology of Cushing syndrome. Inactivating pathogenic germline variants in *armadillo repeat-containing 5 (*ARMC5) gene are responsible for 20%-25% of PBMAH. ARMC5 is expressed in many organs and previous findings suggest an association of PBMAH due to *ARMC5* mutations with specific clinical characteristics, as the presence of meningiomas. This study aims to assess the prevalence of meningiomas in patients with pathogenic *ARMC5* mutations.

Results: This retrospective monocentric study included fifty-five individuals with *ARMC5* pathogenic variant (38 index cases and 17 related cases). Thirty-five (64%) were women and the median age was sixty years old (21-93). Thirty-one patients underwent a neuroimaging. Among those, five had a radiological diagnosis of meningioma (3 index cases and 2 related cases). Four of them had unique lesions and one patient had two localizations. One patient underwent surgical treatment, another received radiotherapy and three had neuroimaging follow-ups.

Conclusions: We report a higher prevalence of meningiomas in patients with pathogenic *ARMC5* mutations (16%) than in the general population (0.5%-2%). Larger studies are needed to confirm our data. A systematic neuroimaging to exclude the presence of meningiomas in patients with *ARMC5* pathogenic variants should be considered. Use of treatment known to favor meningiomas (cyproterone acetate or Nomégestrol/Chlormadinone acetate) should also be cautious in such patients.

Abstract citation ID: lvag096.730

EP139 - ECE_3392 - Assessment of HPA axis in adult patients with β-thalassemia: a retrospective study

Kalliopi Pantelia[1], Vasiliki Antonopoulou[1], Galateia Stathori[1], Stella Tsanaxidou[1], Aikaterini Kapama[1], Andromachi Panagiotopoulou[1], Sofia Chatzi[1], Sofia Georgiadi[1], Chrysa Kalkana[2], Loukia Evliati[2], Marinella Tzanela[1] and Georgia Ntali[1]

[1]Department of Endocrinology "D. Ikkos", Diabetes Center- EndoERN-Evangelismos General Hospital, Athens, Greece; [2]Thalassaemia and Sickle Cell Unit, Evangelismos General Hospital, Athens, Greece

Introduction: β-thalassemia is a chronic inherited hemoglobin disorder characterized by ineffective erythropoiesis, chronic anemia, and iron overload, particularly in transfusion-dependent patients. Endocrine complications are well recognized and are largely attributed to iron deposition in endocrine organs. Impairment of the hypothalamic–pituitary–adrenal (HPA) axis has been described, although its prevalence and clinical relevance in adults remain incompletely defined. In addition, adrenal androgen production, as reflected by serum DHEA-S is frequently reduced despite preserved HPA axis function, suggesting dissociation of cortisol and adrenal androgen secretion.

Objective: To evaluate cortisol/ACTH and adrenal androgen levels in adult patients with β- thalassemia.

Methods: This retrospective study included adult patients with β-thalassemia followed at the Mediterranean and Sickle Cell Anemia Unit of our hospital who underwent assessment of basal ACTH and cortisol between January 2019 and January 2026. Patients with borderline or low morning cortisol levels underwent dynamic testing with Synachten with cortisol measured at baseline, 30, and 60 minutes. DHEA-S levels were interpreted according to sex and age-adjusted reference ranges.

Results: A total of 60 patients with β-thalassemia were included (mean age 51.3 years, SD: 10.3), the majority of whom were transfusion-dependent. Basal cortisol levels ranged from 7.8 to 41 μg/dL, with a mean value (±SD) of 15.1 (±5.8) μg/dL. 6/60 (10%)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

patients had morning cortisol levels <10 μg/dL and Synachten was performed in two of them. 28/60 (47%) demonstrated morning cortisol between 10-15 μg/dL and Synachten was performed in 6 of them. 26/60 (43%) had morning cortisol >15 μg/dL. Dynamic testing resulted in adequate cortisol responses in all cases. Basal ACTH levels ranged from <5 to 127 pg/mL, with a mean value (±SD) of 28 (±25.6). DHEA-S levels were available in 51 patients and were interpreted according to sex and age-adjusted reference ranges. DHEA-S levels were decreased in 30/51(59%) and normal in 21/51 (41%) patients.

Conclusions: In this cohort of adult patients with β-thalassemia, adrenal responsiveness was largely preserved despite longstanding disease and transfusion exposure. These findings may reflect improved iron chelation strategies and contemporary multidisciplinary care. Nevertheless, low DHEA-S levels were observed in a subset of patients. DHEA-S could theoretically represent a sensitive marker of subtle adrenal dysfunction in this population. Further prospective studies are needed to better define HPA axis function and its relationship with iron burden and other endocrine abnormalities in thalassemia.

Abstract citation ID: lvag096.731

EP140 - ECE_3179 - Android/gynoid fat ratio correlates with atherogenic and insulin resistance indices after 6 months of testosterone therapy in trans men

Gökçen Ünal Kocabaş[1], Ezgi Ulaş[1], Banu Sarer Yurekli[1], Hüseyin Cihan[2,3], Mehmet Yigit[1], Melih Bektas[1], Aysel Mammadyarzada[1], Esma Pehlivan[1], F. Kübra Gülpınar[1], Sercan Kamalak[1] and Murat Tozman[1]
[1]*Izmir, Türkiye;* [2]*University of Basel, Basel, Switzerland;* [3]*Department of Endocrinology, University Hospital Zürich, Zurich, Switzerland*

Background: Testosterone used as gender-affirming hormone therapy (GAHT) in trans men may alter regional fat distribution and cardiometabolic risk. We evaluated DXA-derived adiposity indices and their associations with the atherogenic index of plasma (AIP) and triglyceride–glucose (TyG) index during early testosterone therapy.

Methods: Twenty-one trans men initiating intramuscular testosterone esters (every 3 weeks) were assessed at baseline and month 6. Anthropometrics, fasting glucose/insulin and lipid parameters were obtained; body composition was measured by DXA. AIP was calculated as log(triglycerides/HDL-C), HOMA-IR was derived, and TyG index was calculated as log(triglycerides [mmol/L] × glucose [mg/dL]).

Results: Mean age was 27.43 ± 4.98 years. HOMA-IR did not change significantly (baseline 1.9 [IQR 2.65] vs month 6 2.07; $P = .156$). DXA demonstrated decreased trunk fat percentage (37.47 ± 9.04-35.00 ± 9.10; $P = .007$) and total fat percentage (39.84 ± 7.58-36.26 ± 7.68; $P < .001$), with increased trunk lean + BMC (20 140.55 ± 3418-22 581 ± 4193.7 g; $P < .001$). Android/gynoid ratio increased (0.924 ± 0.14-0.97 ± 0.14; $P < .001$) and correlated positively with AIP ($r = 0.653$, $P = .003$) and TyG index ($r = 0.512$, $P = .03$) at month 6.

Conclusions: DXA-derived android/gynoid ratio is associated with AIP and TyG index in trans men receiving testosterone GAHT, suggesting that regional fat distribution may serve as an early marker of cardiometabolic risk during therapy.

Parameter	Testosterone (Month 0)	Testosterone (Month 6)	*P* value
Arm fat (g)	2761.5 (2122.5)	2627.5 (1579.75)	.011
Arm lean + BMC (g)	3161.5 (1175.25)	3747.0 (563.25)	.011
Arm total (g)	5481.0 (2557.75)	6232.5 (2528.25)	.011
Leg fat (g)	10 102.0 (5188.0)	8522.0 (5839.5)	.008
Leg lean (g)	11 680.0 (2862.0)	12 548.5 (3583.0)	.193
Leg total (g)	21 578.0 ± 6386.57	20 893.0 ± 6217.61	.567
Trunk fat (g)	13 183.0 ± 6112.26	13 253.44 ± 6487.54	.930
Trunk lean + BMC (g)	20 140.55 ± 3418.00	22 581.00 ± 4193.70	<.001
Trunk total (g)	33 323.0 ± 9202.00	35 834.0 ± 10 034.19	.003
Android fat (g)	1977.50 ± 1059.42	1900.16 ± 1030.12	.417
Android lean (g)	2487.05 ± 499.98	2618.66 ± 492.23	.033
Android total (g)	4464.50 ± 1505.18	4518.72 ± 1457.35	.668
Gynoid fat (g)	4912.35 ± 1900.90	4593.72 ± 2034.78	.090
Gynoid lean (g)	5877.15 ± 1094.47	6375.38 ± 1199.33	<.001
Gynoid total (g)	10 789.55 ± 2886.10	10 857.39 ± 2948.64	.894
Android/Gynoid ratio	0.924 ± 0.140	0.970 ± 0.140	<.001

Abstract citation ID: lvag096.732

EP141 - ECE_3552 - Resistant hypertension and severe osteoporosis associated with mild autonomous cortisol secretion

Mariam Orjonikidze, Nino Zavrashvili and Mariam Bulashvili
Tbilisi Institute of Medicine (TIM), Tbilisi, Georgia

Background: Adrenal incidentalomas are commonly encountered in clinical practice, with prevalence increasing with age. While most lesions are benign and non-functioning, a subset exhibits subtle hormonal activity. Mild autonomous cortisol secretion (MACS) is the most frequent functional abnormality and is defined by incomplete cortisol suppression after dexamethasone administration in the absence of overt Cushingoid features. Despite its mild biochemical presentation, MACS is associated with increased cardiometabolic risk, including resistant hypertension, diabetes, and skeletal fragility.

Case Presentation: We report the case of a 61-year-old woman with a history of an adrenal incidentaloma detected in 2021 without subsequent follow-up and established osteoporosis treated with denosumab. In December 2023, she presented with resistant hypertension, with systolic blood pressure persistently around 160 mmHg despite triple antihypertensive therapy. Associated symptoms included tachycardia, dizziness, and hyperhidrosis. Initial hormonal evaluation revealed inadequate cortisol suppression following a 1 mg dexamethasone suppression test (DST), with a cortisol level of 0.9 μg/dL. Repeat DST in February 2024 confirmed MACS, demonstrating a cortisol level of 3.0 μg/dL. Investigations: Computed tomography of the abdomen identified a 30 mm left adrenal mass with radiological characteristics consistent with a benign adenoma. No clinical signs of overt hypercortisolism were present.

Management and Outcome: Given the presence of resistant hypertension and severe osteoporosis in the context of confirmed MACS, the patient underwent left adrenalectomy in May 2025. Histopathological examination confirmed an adrenocortical adenoma. The postoperative course was uncomplicated,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and the patient continues follow-up for reassessment of antihypertensive therapy and osteoporosis management.

Conclusions: This case illustrates that MACS, despite the absence of classic Cushingoid features, may have clinically significant consequences, including resistant hypertension and skeletal fragility. It highlights the importance of systematic hormonal evaluation and long-term follow-up of adrenal incidentalomas. Early recognition and timely surgical intervention in selected patients may reduce cardiometabolic and skeletal complications and improve clinical outcomes.

Abstract citation ID: lvag096.733

EP142 - ECE_1255 - Impact of maternal hypertension subtypes on offspring growth and endocrine development: a structured review

Ashraf Soliman, Fawziya Alyafei, Manal Musallam, Nada Alaaraj, Noor Hamed and Shayma Ahmed
Pediatric Endocrinology, Hamad Medical Center, Doha, Qatar

Background: Maternal hypertension—including preeclampsia, gestational hypertension, and chronic hypertension—is a major contributor to fetal growth restriction and neonatal complications. Evidence indicates these conditions also influence long-term endocrine and metabolic programming in offspring.

Objective: To compare how different forms of maternal hypertension affect offspring growth patterns and endocrine function from birth through adolescence.

Methods: A structured review of cohort and clinical studies published in the past 25 years was conducted. Outcomes were categorized by hypertension subtype and developmental stage, with a focus on birth anthropometry, growth trajectories, GH–IGF-1 and HPA axes, insulin sensitivity, and pubertal development.

Results: Preeclampsia demonstrated the greatest adverse impact. Offspring had markedly reduced birth weight and length, high rates of SGA, and low IGF-1, IGFBP-3, and leptin levels at birth. Neonates frequently exhibited elevated cortisol and ACTH, indicating heightened HPA-axis activation. These children showed slower or incomplete catch-up growth, persistently lower IGF-1 levels, and increased risk of insulin resistance, adiposity rebound, and earlier puberty, especially when rapid postnatal weight gain occurred. Bone age was often delayed initially but could accelerate during catch-up, potentially reducing adult height. **Chronic hypertension** was associated with moderate growth restriction, particularly in longstanding or poorly controlled cases. Birth weight and length were reduced but typically to a lesser degree than in preeclampsia. Endocrine alterations included mildly reduced IGF-1, slightly elevated cortisol, increased BMI in later childhood, and higher adolescent metabolic risk, especially in offspring born SGA. **Gestational hypertension** produced the mildest and most variable effects. Most infants had near-normal growth parameters, though some demonstrated mild reductions in birth size or subtle hormonal changes. Long-term endocrine outcomes were generally preserved unless gestational hypertension developed early or was accompanied by placental dysfunction. Across all subtypes, infants born SGA—regardless of maternal hypertension category—showed increased risk of reduced insulin sensitivity, central adiposity, earlier pubertal onset, and altered HPA-axis reactivity. Thyroid function remained largely intact in all groups.

Conclusions: Maternal hypertension exerts subtype-specific effects on growth and endocrine programming. Preeclampsia carries the highest risk, chronic hypertension confers moderate risk, and gestational hypertension causes limited long-term disruption. Early endocrine and growth monitoring in exposed offspring is recommended to mitigate adverse developmental outcomes.

Abstract citation ID: lvag096.734

EP143 - ECE_1333 - Audit of plasma free metanephrine and outcomes in patients with borderline elevations

Bengur Taskiran[1,2], Lakshmi Sankaran[1], Simon Whitehead[1] and Jimmy Li Voon Chong[1]
[1]*Winchester, United Kingdom;* [2]*Endocrinology, General Internal Medicine, Hampshire Hospitals Foundation Trust, Winchester, United Kingdom*

Background: There are currently no dedicated guidelines for the management of borderline or non-conclusive plasma or urinary metanephrine results. Interpretation is particularly challenging when values are less than three times the upper limit of normal. Test results may be influenced by dietary factors, medications, and pathophysiological conditions. False positive results occur in approximately 20% of cases and 20%-30% of patients with pheochromocytoma/paraganglioma may present with borderline elevations. Although follow-up is recommneded for all elevated borderline results, previous reports indicate that only 28% of patients with elevated values receive appropriate follow-up.

Aim: To identify patients with borderline elevated plasma free metanephrine levels, and to evaluate their management and testing conditions.

Methods: A retrospective review from a cohort of 137 patients aged 16 or above, who underwent plasma metanephrine testing between April 2024 and March 2025, was conducted. Plasma metanephrines were measured using high-performance liquid chromatography.

Results: The most common indications for testing were adrenal masses and/or blood pressure related disorders. Eighty-eight patients had hypertension. Seventeen had elevated normetanephrines and 3 had elevated metanephrines; all were less than 3 times upper normal limit. None had both elevated normetanephrines and metanephrines. All patients had normal levels of 3-methoxytyramine. Twelve were male. Mean age was 46.85 ± 2.21 years. Sixteen had hypertension. Six had adrenal mass on imaging. Glomerular filtration rate ranged between 59 and >90. Nine tests were done by endocrine specialist nurse following a protocol including supine position and 30 min rest, 5 were done as inpatient without following a certain protocol. The two groups (high vs normal) did not differ significantly according to gender, smoking status, protocol of testing, test setting, hypertension status, or stopping medications with interference with results. Mean age of normal group was significantly higher. Eleven patients had repeat tests and appropriately managed by endocrinology. Nine patients were lost to follow-up despite five with high repeat tests.

Conclusions: Aging and adherence to testing protocol did not significantly influence borderline elevations in plasma metanephrine levels in this cohort. However, the small size of the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

study may have limited to detect meaningful differences. Despite a substantial loss to follow-up rate (45%), this remained lower than previously reported in the literature (72%). Targeted measures are needed to reduce to improve drop-out rates and address system related factors such as delayed appointments.

Abstract citation ID: lvag096.735

EP145 - ECE_2148 - Histopathological diagnosis of surgically treated indeterminate adrenal masses

Sofia Georgiadi[1], Chrysoula Koukoula[1], Eleni Lazaridou[2], Stavroula Tzamouri[2], Georgios Kyriakopoulos[3], Sofia Avgousti[3], Kalliopi Koniari[3], Olga Papalou[1], Angeliki Angelidou[1], Sofia Chatzi[1], Stylianos Kapiris[4], Maria Sotiropoulou[4], Marinella Tzanela[1] and Dimitra Argyro Vassiliadi[1]

[1]Department of Endocrinology "D. Ikkos", Diabetes Center- EndoERN - Evangelismos General Hospital, Athens, Greece; [2]Department of CT/MR, Evangelismos General Hospital, Athens, Greece; [3]Department of Pathology, Evangelismos General Hospital, Athens, Greece; [4]Third Department of Surgery, Evangelismos General Hospital, Athens, Greece

Introduction: Adrenal incidentalomas are increasingly detected due to widespread use of advanced imaging modalities. Imaging evaluation plays a central role in assessing the risk of malignancy, with homogeneous, lipid-rich lesions (<10 Hounsfield units [HU] on unenhanced CT) considered benign. However, a substantial proportion of adrenal masses do not meet these criteria and are classified as indeterminate. Indeterminate adrenal masses are incidentally discovered lesions lacking definitive imaging or biochemical features of benignity or malignancy. While many are ultimately benign—most commonly lipid-poor adrenocortical adenomas—the differential diagnosis includes adrenocortical carcinoma and other rare malignant entities, posing a significant diagnostic challenge.

Aim: To report histopathological diagnoses of surgically treated indeterminate adrenal masses and assess their relationship with preoperative imaging characteristics, including CT in all patients and MRI and/or FDG-PET, where available.

Methods: We retrospectively identified patients who underwent adrenalectomy for indeterminate masses between 2022 and 2025. Patients with lesions showing clear features of malignancy (metastases, compatible biochemical findings, or known extra-adrenal primary malignancy) or diagnostic biochemical evidence of pheochromocytoma were excluded. Collected data included demographics, hormonal activity, imaging features and histopathological diagnosis.

Results: 32 patients were included (mean age 60.5 ± 12.4 years). Mean tumor size was 5.9 ± 3.2 cm (range 2.4-17 cm), with a mean unenhanced CT attenuation of 26.5 ± 9.7 HU. FDG-PET was available in 19 patients, with a mean SUVmax of 4.6 ± 2.0. Twenty patients (63%) had benign lesions: 16 lipid-poor adrenocortical adenomas, one black adenoma, one adrenal oncocytoma, two ganglioneuromas. Three patients had adrenocortical oncocytic neoplasms of uncertain malignant potential. Nine patients (28%) had malignant lesions: five adrenocortical carcinomas and four non-adrenocortical malignancies (metastasis, angiosarcoma, lymphoma, liposarcoma). Regarding hormonal activity, 12 patients exhibited mild autonomous cortisol secretion. Tumor size (5.4 vs 5.9 cm), unenhanced CT attenuation (26.4 vs 29.5 HU), and SUVmax (4.7 vs 6.7) did not differ significantly between benign and malignant lesions. Notably, no malignant lesion had unenhanced CT attenuation <20 HU, whereas five benign lesions and one of uncertain malignant potential did.

Conclusions: Indeterminate adrenal masses represent a diagnostic challenge, encompassing a broad spectrum of benign and malignant conditions. Although additional imaging modalities may aid risk stratification, no single technique reliably establishes a definitive diagnosis, and significant overlap exists between benign and malignant lesions, including FDG-PET uptake. Consequently, final diagnosis often remains dependent on histopathological evaluation following surgery, underscoring the need for individualized, multidisciplinary diagnostic approach.

Abstract citation ID: lvag096.736

EP146 - ECE_2248 - Primary aldosteronism and prolactinoma: an intriguing coincidence or partners in crime?

Sanja Borozan[1], Snezana Vujosevic[1], Sreten Kavaric[1], Emir Muzurovic[1], Natasa Radovic[2], Aleksandar Filipovic[1,3] and Karin Zibar Tomsic[4]

[1]Department of Endocrinology, Clinical Centre of Montenegro, Podgorica, Montenegro; [2]Intermedica Clinic, Herceg Novi, Montenegro; [3]Department of Endocrine Surgery, Clinical Centre of Montenegro, Podgorica, Montenegro; [4]Clinical Centre Zagreb, Zagreb, Croatia

Primary aldosteronism (PA) and prolactinoma are common endocrine disorders, yet their co-occurrence has occasionally been documented. However, emerging data suggest this conjunction may be more than coincidental. Recent analyses, including small case series and retrospective reviews, have reported a higher-than-expected prevalence of hyperprolactinemia among PA cohorts. Although a definitive causal link remains elusive, hypotheses suggest shared pathogenic mechanisms, such as the paracrine effects of elevated aldosterone on pituitary lactotrophs, or a higher expression of the prolactin receptor gene in aldosterone-producing adenomas. We describe a case that contributes to this evolving clinical discourse.

A 55-year-old man presented with profound fatigue, muscle weakness, palpitations, and polyuria-polydipsia syndrome. Laboratory evaluation revealed severe hypokalemia (1.67 mmol/L) with kaliuresis. A retrospective review identified persistent hypokalemia over the preceding three years, previously uninvestigated. His past medical history included hypertension diagnosed at age 42, poorly controlled on perindopril 10 mg and amlodipine 10 mg. Initial endocrine workup showed adequate suppression of cortisol on the 1 mg overnight dexamethasone test. However, his plasma aldosterone level was 785 pmol/L, with a suppressed plasma renin concentration of 1.9 mIU/L, yielding an elevated aldosterone-to-renin ratio (ARR) of 413.2 pmol/mIU. A confirmatory saline infusion test demonstrated non-suppressible aldosterone (937 pmol/L), confirming PA. Adrenal CT suggested bilateral hyperplasia, but adrenal vein sampling lateralized to the right. The patient underwent a successful right laparoscopic adrenalectomy, resulting in normokalemia without supplementation and normalization of blood pressure off all antihypertensive therapy. Concurrent hormonal evaluation revealed persistently elevated prolactin levels in profile

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(ranging from 6829 to 9755 mIU/L after dilution; macroprolactin negative), with all other pituitary axes within normal limits and no symptoms of sexual dysfunction. Subsequent pituitary MRI identified a microadenoma consistent with a prolactinoma, for which therapy with cabergoline was initiated.

This case of concurrent lateralized PA and prolactinoma adds to the growing evidence challenging the notion of a purely incidental association. It underscores the importance of a holistic endocrine evaluation, while further investigations of common genetic markers or proliferative pathways could unlock new insights into the pathogenesis of both conditions.

Abstract citation ID: lvag096.737

EP147 - ECE_1599 - Pregnancy-induced Cushing syndrome: diagnosis and management of a rare endocrine disorder

Ronit Koren[1,2,3], Efrat Markus[4,5], Yifat Wiener[1,2,3] and Yona Greenman[3,6,7]

[1]Shamir Medical Center, Zerifin, Israel; [2]Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Beer Yaakov, Israel; [3]Gray Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [4]Shamir Medical Center, Zerifin, Israel; [5]Endocrine Institute, Beer Yaakov, Israel; [6]Tel Aviv-Sourasky Medical Center, Tel Aviv 64239, Israel; [7]Institute of Endocrinology, Metabolism, Diabetes and Hypertension, Tel Aviv, Israel

Introduction: Endogenous Cushing syndrome (CS) during pregnancy is a rare condition associated with substantial maternal and fetal morbidity and mortality. Pregnancy-induced Cushing syndrome (PICS) represents an exceptionally rare subtype, resulting from aberrant expression of luteinizing hormone (LH) and/or human chorionic gonadotropin (hCG) receptors on maternal adrenal cortical cells. We report a case of PICS without detectable adrenal abnormalities on imaging, successfully managed with medical therapy until delivery.

Case Report: A 25-year-old woman presented at 26 weeks of gestation with newly diagnosed hypertension. Physical examination revealed severe acne, hirsutism, a dorsocervical fat pad, and extensive violaceous striae over the abdomen, arms, and legs. Biochemical evaluation demonstrated markedly elevated urinary free cortisol (UFC) levels (1659 μg/24 h; reference range 13-75 μg/24 h). Serum cortisol concentrations were significantly elevated in the morning (47.56 μg/dL) and remained unsuppressed at midnight (47.12 μg/dL). Midnight salivary cortisol was >3 μg/dL (reference <0.12 μg/dL), and plasma adrenocorticotropic hormone (ACTH) was suppressed (1.5 pg/mL; reference range 7.2-63 pg/mL), consistent with ACTH-independent hypercortisolism. Pituitary, adrenal, and ovarian imaging revealed no pathological findings. Medical treatment with metyrapone was initiated and gradually titrated to 2 g/day. Additional therapies included unfractionated heparin for venous thromboembolism prophylaxis, vitamin D and calcium supplementation, antihypertensive treatment with labetalol and amlodipine, insulin detemir for glycemic control, and Pneumocystis jirovecii pneumonia prophylaxis with trimethoprim-sulfamethoxazole due to severe hypercortisolism. Clinical and biochemical improvement was observed, with serum cortisol decreasing to 32 μg/dL, UFC to 530 μg/24 h, and midnight salivary cortisol to 0.59 μg/dL. A multidisciplinary team recommended on a cesarean section, that was performed at 34 + 5 weeks of gestation, resulting in the delivery of an appropriate-for-gestational-age healthy neonate, who required cortisol supplementation for several months. Following delivery, all medications were discontinued, with normalization of cortisol levels and marked clinical improvement. An hCG stimulation test confirmed the diagnosis of PICS: following administration of 13 000 units of hCG, serum cortisol increased from 15.6 μg/dL at baseline to 34 μg/dL at 48 hours, ACTH decreased from 14.4 pg/mL to undetectable levels, and UFC increased from 28 μg/24 h to 293 μg/24 h. The patient elected conservative medical management in future pregnancies.

Conclusions: PICS is a rare and diagnostically challenging cause of hypercortisolism during pregnancy. This case highlights successful medical management of severe PICS presenting in the second trimester, despite the absence of adrenal abnormalities on imaging. Early recognition, close biochemical monitoring, and comprehensive multidisciplinary care enabled favorable maternal and neonatal outcomes.

Abstract citation ID: lvag096.738

EP148 - ECE_3551 - Three newly diagnosed patients with Addison's disease presenting with adrenal crisis: illustrative case reports

Gergő Csitári

DBC-SZIEOK, Budapest, Hungary

Autoimmune primary adrenal insufficiency is an uncommon but life-threatening endocrine disorder in which diagnosis is frequently delayed, despite a recognisable yet nonspecific clinical constellation. The leading cause in high-income countries is autoimmune adrenalitis, with an incidence of only a few cases per million population per year, so the disease is rarely considered in routine internal medicine practice. The typical manifestations—weight loss, fatigue, gastrointestinal symptoms, hyponatraemia, hyperkalaemia and hypotension—overlap with many more prevalent conditions, which contributes to prolonged diagnostic odysseys and, not infrequently, presentation with adrenal crisis.

This abstract describes three instructive cases of newly diagnosed autoimmune Addison's disease, each culminating in adrenal crisis or incipient crisis during hospitalization. The objective is to highlight the protean clinical presentation and the extent of gastroenterological, nephrological, neurological and psychiatric work-up that may precede consideration of primary adrenal insufficiency. In all three patients, progressive haemodynamic instability and neurocognitive or behavioural deterioration occurred despite apparently appropriate management of the presumed alternative diagnoses.

The first case involves a 45-year-old man with abdominal pain, marked weight loss, progressive renal impairment, severe hyponatraemia and hyperkalaemia, in whom focal neurological signs led to a planned lumbar puncture before pronounced orthostatic hypotension and cutaneous hyperpigmentation prompted endocrine reassessment. The second case concerns a 51-year-old woman thoroughly investigated for suspected malignancy and subsequently labelled as having catatonic psychosis; the coexistence of vitiligo, mild hyponatraemia, hypotension, hypoglycaemia and clinical dehydration finally raised suspicion of primary adrenal insufficiency. The third case is a 35-year-old man with severe, partly iatrogenic hyponatraemia, persistent mild hyperkalaemia, significant weight loss and improved glycaemic control initially attributed to GLP-1 receptor agonist therapy, who experienced

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

recurrent syncope with low–normal blood pressure and tachycardia, necessitating transfer to intensive care.

In all three patients, biochemical evaluation confirmed primary adrenal insufficiency, prompting immediate initiation of intravenous 0.9% saline and stress-dose hydrocortisone, while cross-sectional adrenal imaging revealed no structural abnormalities. The subsequent demonstration of adrenal cortex autoantibodies was consistent with autoimmune adrenalitis as the underlying aetiology in each case. These cases underscore that Addison's disease remains a "great mimicker" in contemporary clinical practice and emphasise the need for a high index of suspicion for primary adrenal insufficiency in patients with otherwise unexplained hyponatraemia, hyperkalaemia, hypotension, hyperpigmentation or autoimmune stigmata, particularly when clinical status deteriorates despite standard therapy.

Abstract citation ID: lvag096.739

EP149 - ECE_2353 - Extrapulmonary tuberculosis—the clinical challenge and significance of adrenal insufficiency

Boban Stepanovic[1], Ljiljana Marina[2,3], Kristina Saravinovska[2,3], Sara Odalovic[2], Marina Stojanovic[1,3], Katarina Tausanovic[1,3], Dijana Jankovic[2], Vladan Zivaljevic[1,3] and Milan Jovanovic[1,3]
[1]*Clinic of Endocrine Surgery, University Clinical Centre of Serbia, Belgrade, Serbia;* [2]*Clinic of Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Belgrade, Serbia;* [3]*Faculty of Medicine, University of Belgrade, Belgrade, Serbia*

Introduction: Adrenocortical insufficiency, or Addison's disease, most commonly develops as a consequence of progressive bilateral destruction of the adrenal cortex, most often due to autoimmune adrenalitis. However, a wide range of etiologies has been described, among which adrenal tuberculosis represents a rare but important cause. Here, we present a rare case of adrenal tuberculosis manifesting as adrenal insufficiency.

Case Presentation: A 38-year-old man was diagnosed with a right adrenal mass accompanied by regional paraaortic lymphadenopathy. Multislice computed tomography (MSCT) of the abdomen revealed a poorly demarcated lesion of the right adrenal gland—60 × 37 × 36 mm, with signs of necrosis and cystic degeneration, as well as pathologically enlarged paraaortic and interaortocaval lymph nodes measuring up to 28 × 16 mm. Clinically, the patient presented with generalized skin hyperpigmentation, hypotension, loss of appetite, and abdominal pain. Hormonal evaluation confirmed primary adrenal insufficiency, with low morning serum cortisol (78 nmol/L), markedly elevated ACTH (>440 pmol/L), hyponatremia (122 mmol/L), and hyperkalemia (5.6 mmol/L), and hydrocortisone replacement therapy was initiated. The patient underwent surgery, where a right adrenalectomy with excision of the affected lymph nodes was performed via an open surgical approach. Postoperatively, the patient developed lymphorrhea and paralytic ileus, both of which were managed conservatively, alongside appropriate hydrocortisone and fludrocortisone substitution. Histopathological examination revealed granulomatous inflammation with central caseous necrosis, highly suggestive of tuberculosis. The patient tested negative for HIV.

Conclusions: The clinical course and disease presentation in our patient highlight the importance of considering adrenal tuberculosis in the differential diagnosis of adrenal masses associated with primary adrenal insufficiency, even in immunocompetent patients. Early recognition, appropriate hormonal replacement, and timely diagnosis are essential to optimize outcomes in this rare but clinically significant condition.

Abstract citation ID: lvag096.740

EP150 - ECE_2250 - Mild autonomous cortisol secretion and cardiovascular risk: a retrospective study

Zaira Benetti[1], Marianna Scordo[1], Simona Buti[1], Chiara Badiale[2], Luisa Pignata[1], Pierpaolo Falcetta[1], Elena Benelli[1], Lucia Montanelli[1], Emilio Fiore[1] and Massimo Tonacchera[1]
[1]*Department of Clinical and Experimental Medicine, Endocrine Unit, University of Pisa, Pisa, Italy;* [2]*University of Pisa, Pisa, Italy*

Mild autonomous cortisol secretion (MACS) is a condition characterized—according to the new European guidelines for adrenal incidentalomas (AIs)—by the presence of serum cortisol levels >1.8 µg/dL (50 nmol/L) after a 1 mg dexamethasone suppression test in patients with adrenal incidentalomas, in the absence of clinical signs of overt Cushing's syndrome. Several studies in the literature have demonstrated that patients with MACS show an increase in cardiovascular risk factors.

The purpose of this study was to evaluate the SCORE2, SCORE2-OP and SCORE2-Diabetes scores—developed by the European Society of Cardiology (ESC) and used to predict the 10-year risk of cardiovascular events—comparing patients with MACS to patients with non-secreting AIs. Body weight was also assessed through the calculation of body mass index (BMI).

In this retrospective study 198 consecutive patients, with no history of cardiovascular events and without clinical signs of hypercortisolism, were recruited at the Endocrinology Department of Pisa. Patients were divided into three categories: adults aged 40-69 years without diabetes mellitus (Group A—114 patients, 57.6%), adults aged 40-69 years with diabetes mellitus (Group B—14 patients, 7.1%), and elderly patients aged ≥70 years (Group C—70 patients, 35.4%).

For each patient, MACS was evaluated using the overnight 1 mg dexamethasone suppression test and data on smoking habits, systolic blood pressure (SBP), total cholesterol (TC), HDL cholesterol (HDL-C), and BMI were collected. In diabetic patients, creatinine and glycated hemoglobin (HbA1c) levels were also assessed.

No statistically significant differences were found in individual cardiovascular risk factors (SBP, TC, HDL-C, and BMI) or in the 10-year cardiovascular risk scores. In Group A, the prevalence of MACS was 23.7% (27/114 patients), and the median SCORE2 in these patients was 4.7% compared to 4.6% in patients with non-secreting AI ($P = .961$). In Group B, the prevalence of MACS was 21.4% (3/14 patients) with median SCORE2-Diabetes of 9.4% compared to 10.7%, respectively ($P = .769$). In Group C, the prevalence of MACS was 38.6% (27/70 patients), with median SCORE2-OP of 14.7% compared to 12.3% ($P = .234$).

In diabetic patients, the difference in HbA1c values between the two subgroups was not statistically significant (50 vs 50 mmol/L $P = .659$), whereas creatinine values were significantly higher in patients with MACS compared to those with non-secreting AIs (0.96 vs 0.72 mg/dL, $P = .038$).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

In conclusion, no statistically significant differences in cardiovascular risk factors were observed between patients with MACS and those with non-secreting AIs.

Abstract citation ID: lvag096.741

EP151 - ECE_3033 - Early postoperative aldosterone as a predictor of biochemical cure after adrenalectomy for primary hyperaldosteronism

Tatiana Rojas López, Jorge Escobar Gómez, Paola Parra-Ramírez, Patricia Martín Rojas-Marcos, María Luisa González Casaus, Joaquín Gómez Ramírez, Raquel Arranz and Maria Cristina Alvarez Escola
Hospital Universitario La Paz, Madrid, Spain

Introduction: The identification of early markers of cure after adrenalectomy in patients with primary hyperaldosteronism (PA) is key to optimizing follow-up and adjusting treatment more efficiently. This study aimed to evaluate the usefulness of postoperative aldosterone levels and their percentage reduction relative to preoperative values as predictors of cure.

Materials and Methods: Retrospective cohort study of patients with confirmed PA who underwent unilateral adrenalectomy between 2021 and 2025 at a tertiary hospital. Patients with plasma aldosterone measurement between 24 hours and the first postoperative week were included, and the percentage reduction relative to baseline values obtained in the confirmatory test was calculated. Associations between postoperative aldosterone concentrations and their percentage reduction with biochemical and clinical cure, according to the PASO criteria (partial or complete cure vs no cure), were analyzed. ROC curves were constructed for each parameter, the area under the curve (AUC) was estimated, and the optimal cutoff was determined using the Youden index.

Results: Sixteen patients were included, with a mean age of 57.8 ± 10.0 years, 62.5% male. Nine patients achieved biochemical cure (2 of them complete), and 13 achieved clinical cure (3 of them complete). Patients with biochemical cure had a significantly greater percentage reduction in aldosterone (mean: 55.9% ± 36.8% vs −60.1% ± 60%; $P < .01$) and lower postoperative levels (mean: 8.7 ± 6.7 ng/dL vs 30.2 ± 18.8 ng/dL; $P < .01$) compared to those without cure. No significant differences were found regarding clinical cure. In the ROC analysis, the percentage reduction in aldosterone showed an AUC of 0.94 (95% CI 0.81-1.00), with a cutoff point of 47.5%, sensitivity of 78%, and specificity of 100%. Postoperative concentration presented an AUC of 0.92 (95% CI 0.75-1.00).

Conclusions: The reduction in plasma aldosterone in the first days after adrenalectomy is significantly associated with biochemical cure of PA, supporting its value as an early prognostic marker of surgical success.

Abstract citation ID: lvag096.742

EP152 - ECE_3625 - Long-term outcome in autoimmune Addison's disease: a single-center real-world study

Ylenia Alessi[1], Carla Paola Costa[2], Elena Sofia Blanca[2], Giordana Siracusano[2], Federica Galletta[2], Damiano Siligato[2], Annalisa Giandalia[3], Angela Alibrandi[4], Salvatore Cannavò[3] and Francesco Ferraù[3]
[1]*Department of Biomedical, Dental and Morphological and Functional Imaging Sciences, University of Messina, Messina, Italy;* [2]*Endocrine Unit, University of Messina, Messina, Italy;* [3]*Department of Human Pathology of Adulthood and Childhood, University of Messina, Messina, Italy*
[4]*Department of Economics, University of Messina, Messina, Italy*

Background: Autoimmune Addison's disease (aAD) is a rare endocrine disorder characterized by primary adrenal insufficiency and frequently associated with other autoimmune conditions. Despite effective glucocorticoid (GC) replacement therapy, patients with aAD exhibit increased morbidity and reduced quality of life, suggesting that the disease should be considered a multisystem disorder. Long-term data on the evolution of cardiometabolic, skeletal and autoimmune comorbidities in aAD are still limited.

Aim: The aim of this study was to characterize the long-term clinical, metabolic and autoimmune profile of patients with aAD followed at a tertiary referral center, and to evaluate the impact of sex, disease duration and GC therapy on the development and progression of major comorbidities.

Methods: We retrospectively evaluated 53 consecutive patients with aAD (37 females; mean age at diagnosis 37 ± 14.5 years) followed between 2008 and 2025. Anthropometric, clinical, biochemical and metabolic parameters, comorbidities and associated autoimmune diseases were assessed at first evaluation and at last follow-up (mean follow-up 111 ± 89.8 months). Throughout the entire follow-up, clinical/biochemical evidence of GC overtreatment was excluded in all patients based on UFC values. Patients were also stratified according to sex and disease duration (≤10 vs >10 years).

Results: At last follow-up, body weight, BMI ($P < .001$ both) and waist circumference (P .04) were significantly increased, together with a rise in fasting glucose levels (P .031), while lipid profile and electrolytes remained stable. The prevalence of arterial hypertension increased from 7.5% to 20.7%, type 2 diabetes mellitus from 3.7% to 5.6%, and osteoporosis from 11.3% to 22.6%, although these changes did not reach statistical significance. At last follow-up, female patients showed higher HDL cholesterol and HbA1c levels, while lumbar spine bone density tended to be lower compared with males. In patients with longer disease duration (>10 years), a trend toward higher rates of hypertension, diabetes, osteoporosis and rheumatological autoimmune disorders was observed. GC dosage did not significantly impact on any of the evaluated variables. Logistic regression identified disease duration as a potential predictor of new-onset hypertension, independent of other factors.

Conclusions: Autoimmune Addison's disease is associated with a progressive burden of cardiometabolic, skeletal and autoimmune comorbidities, even despite optimal replacement treatment. The increase in the prevalence of arterial hypertension appears to be driven primarily by disease duration. These results highlight the critical need for ongoing, multidisciplinary management that goes beyond hormone dose adjustments, ensuring comprehensive care throughout the patient's lifetime.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.743

EP153 - ECE_1181 - Splenic infarction unmasking endocarditis in subclinical hyperthyroidism: a case easily confused with thyrocardiac disease

Hadami Ben Yamna, Rachel Gauvin, Sarra El Younsi, Bilariki Kalliopi and Etienne Justinien
Endocrinology Department, Compiègne Hospital Center, Compiègne, France

Introduction: Splenic infarction is an uncommon complication of infective endocarditis, usually reflecting embolic dissemination from valvular vegetations. Subclinical hyperthyroidism may obscure the clinical presentation, leading clinicians to initially attribute cardiovascular symptoms to thyroid dysfunction rather than infection. We report a case in which splenic infarction led to the diagnosis of underlying infective endocarditis in a patient with subclinical hyperthyroidism, highlighting a potential diagnostic pitfall.

Case Presentation: A 68-year-old man, previously operated four months earlier for an upper–mid rectal adenocarcinoma (pT1), presented with newly discovered subclinical hyperthyroidism. Initial laboratory tests showed persistently suppressed TSH levels (0.008 then 0.0079 mUI/L) with negative antibodies (anti-TPO, anti-Tg, and TRAb antibodies). Cervical ultrasound revealed a multinodular goiter, and scintigraphy confirmed a toxic multinodular goiter. He was started on Neomercazole 5 mg daily. He presented two weeks later to the emergency department with epigastric pain and low-grade fever (38.2 °C), and vomiting. Physical examination found isolated epigastric tenderness. An abdominopelvic CT scan demonstrated a large splenic infarction with no abnormalities of the splenic vessels. ECG showed sinus rhythm. Because of the unexplained embolic event, transthoracic echocardiography was performed and revealed a tricuspid aortic valve carrying a mobile vegetation, associated with non-severe aortic regurgitation. These findings confirmed infective endocarditis complicated by splenic embolism. The patient underwent aortic valve replacement. Postoperative evolution was favorable.

Conclusions: Despite an initial suspicion of hyperthyroidism-related paroxysmal arrhythmias, the unexpected finding of infective endocarditis underscores the importance of considering differential diagnosis in patients with subclinical hyperthyroidism who present with embolic phenomena.

Abstract citation ID: lvag096.744

EP156 - ECE_2971 - Interpreting diabetic kidney disease risk in type 2 diabetes using explainable AI

Daria Varbanets, Yanina Saienko, Yanina Rebrova, Dmytro Krasnenkov, Roman Kirilenko and Borys Mankovsky
Department for the Study of Age-Related Cardiometabolic Diseases, D. F. Chebotarev Institute of Gerontology of the National Academy of the Medical Sciences of Ukraine, Kyiv, Ukraine

Background and Aim: Chronic kidney disease (CKD) is a major complication of type 2 diabetes mellitus (T2DM), significantly impacting morbidity and mortality. The application of artificial intelligence (AI), particularly Explainable AI (XAI), offers new opportunities for predicting diabetic complications, including CKD. This study aimed to utilize XAI through H2O AutoML to identify key risk factors for CKD in T2DM patients.

Materials and Methods: Data from 133 patients with T2DM (mean age 62.7 ± 11.5 years; 36.6% female) were analyzed using H2O AutoML. Gradient Boosting Machine (GBM) models outperformed others; Stacked Ensemble and Deep Learning models were excluded. SHapley Additive exPlanations (SHAP) were used to interpret model predictions and evaluate feature importance.

Results: Peripheral neuropathy emerged as the most influential predictor of CKD, suggesting a link between microvascular damage and renal dysfunction. Age and diabetes duration were positively associated with CKD risk, reflecting physiological decline and disease progression. Chronic heart failure (CHF) and elevated low-density lipoprotein cholesterol (LDL-C) also contributed significantly, likely due to their roles in vascular impairment. Notably, historical exposure to famine, reflecting Ukraine's traumatic past, was identified as a significant risk factor, possibly due to long-term epigenetic effects on metabolic health.

Conclusions: SHAP-based analysis enabled transparent interpretation of CKD risk in T2DM patients, revealing both expected and novel predictors. These findings support the clinical utility of XAI in enhancing individualized risk assessment and informing targeted prevention strategies in diabetes care.

Abstract citation ID: lvag096.745

EP157 - ECE_2098 - Knowledge of crisis prevention strategies are highly effective, whereas vulnerability scores may elicit Addison's disease crises

Ian Ross[1], Sofia Llahana[2], Michelle Anderson[1], Belene Demeke[1], Elouise Minnie[1], John Wass[3] and Michelle Henry[4]
[1]*Division of Endocrinology, Groote Schuur Hospital, Medicine, University of Cape Town, Cape Town, South Africa;* [2]*Saint George's, School of Medical and Health Sciences, London, United Kingdom;* [3]*Department of Endocrinology, Medicine, Churchill Hospital, Oxford, United Kingdom;* [4]*Centre for Higher Education Development, University of Cape Town, Cape Town, South Africa*

Objective: The knowledge in patients with Addison's disease (AD) to prevent an adrenal crisis and the degree to which patients feel vulnerable is unknown.

Design: A telephonic interview of 47 South African patients was undertaken, determining knowledge of crisis prevention strategies and assessment of vulnerability in patients.

Methods: A score was determined in respect of knowledge of adrenal crisis (AC) and degree of vulnerability was assessed. Patients who had a crisis with those who did not. Associations with AC were evaluated and the impact of knowledge and vulnerability were determined.

Results: Two-thirds (64%) had suffered from an adrenal crisis in the previous 5 years compared with 34% who never had a crisis. Poorer knowledge prevention of an adrenal crisis was associated with an AC, especially having had a cold (31.2% vs 71%; $P = .002$), fever (44.7% vs 90.3%; $P < .001$), infection (50% vs 93.5%; $P < .001$), vomiting (50% vs 80.6%; $P = .007$) and diarrhoea (37.5% vs 71%; $P < .001$), respectively. The median proportion with vulnerability for each question was 41.5%. Disease duration was negatively correlated with vulnerability; ($r = -0.426$; $P = .003$). Number of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

comorbidities was correlated with vulnerability ($r = 0.290$; $P = .048$). A negative correlation between knowledge score and number of crises in the previous 5 years was found ($r = -0.530$; $P < .001$). Logistic regression is showed the only predictor for crisis in the past year, or past 5 years was patients' knowledge ($P < .001$). Predictors of knowledge were younger patients, more comorbidities, patients who had AC or scored higher on vulnerability questionnaire. Variables accounted for 52% of the variance ($F = 9.751$; $P < .001$).

Conclusions: Education is critical in preventing, specifically cold fever, infection, vomiting and diarrhoea. Health-care providers should provide psychological support considering the significant vulnerability burden.

Abstract citation ID: lvag096.746

EP158 - ECE_3106 - Implementation of a cohort to analyse the health status of adults with congenital adrenal hyperplasia (CaHASE2)

Cahase2 Investigators Society for Endocrinology, UK and Aled Rees
Society for Endocrinology, Bristol, United Kingdom

Congenital adrenal hyperplasia (CAH) is the most prevalent form of primary adrenal insufficiency, affecting approximately 1 in 15 000 individuals. Suboptimal health status and care provision among adults living with CAH have been described globally. Consequently, the CaHASE2 initiative was launched in 2023 to implement a robust, prospective, longitudinal cohort study aimed at analysing the health status of adults with CAH in the UK and Ireland. Centres commenced systematic collection of real-world data utilizing the international I-CAH registry. Currently, 23 centres actively contribute, having successfully recruited 488 adults with 766 clinic visits. While the cohort predominantly comprises younger to middle-aged adults, 130 participants are aged 51 years or older, providing opportunities to investigate emerging health challenges. Preliminary analyses reveal that a considerable number of patients are overweight or obese. Assessments of 17-hydroxyprogesterone concentrations suggest significant proportions may be receiving overtreatment. Although androstenedione levels remain below 8 nmol/L in most patients, a significant fraction exhibits suboptimal hormonal control. Interestingly, findings reveal no discernible correlation between current glucocorticoid dosage and patient weight or body surface area. Seven percent of patients had type-2-diabetes. Depression was commonly observed. There are clear signals of ongoing impaired health status and signs of suboptimal control in adults with CAH. Over the subsequent 12 months, the project will focus on collaborating with principal investigators to enhance longitudinal data completeness. This improved data will be crucial for comprehensively investigating variations in healthcare provision, health status, and clinical outcomes, and facilitating the provision of anonymized benchmarking data to all participating centres.

Abstract citation ID: lvag096.747

EP159 - ECE_3314 - Megestrol acetate: a hidden glucocorticoid confounding HPA axis assessment

Anca Matei[1,2], Stefana Bilha[1,2], Viviana Adam[1], Alina-Elena Șchiopu[1,2,3], Diana Martiniuc[2], Alexandru Florescu[1,2], Ana-Maria Bârcă[2], Laura Teodoriu[4] and Cristina Preda[1,2]
[1]Universitatea de Medicină și Farmacie "Grigore T. Popa" Iași, Iași, Romania; [2]Endocrinology, Spitalul Sf. Spiridon Iași, Iași, Romania; [3]Endocrinology, Hospital Saint Spiridon, Iasi, Romania; [4]Endocrinology, Regional Institute of Oncology, Iași, Romania

Introduction: Megestrol acetate (MA) is a synthetic progestin with glucocorticoid activity that may suppress the hypothalamic–pituitary–adrenal (HPA) axis. In patients with adrenal or pituitary incidentalomas, this exposure limits the interpretability of standard endocrine testing and requires a pragmatic, clinically driven approach.

Case: A 64-year-old woman was referred for endocrine evaluation due to persistently low serum cortisol levels. Medical history included endometrial carcinoma treated by total hysterectomy with bilateral adnexectomy and she had been receiving long-term megestrol acetate therapy (160 mg/day) since 2020, with stable disease and no evidence of recurrence on oncological follow-up Imaging revealed two incidental findings: a left adrenal incidentaloma measuring 8 mm, stable on serial computed tomography examinations, with benign imaging characteristics (homogeneous, attenuation <10 Hounsfield units), and a pituitary microadenoma measuring 4 mm, without mass effect or optic chiasm involvement. Basal hormonal evaluation demonstrated HPA axis suppression (low morning serum cortisol = 1.1 µg/dL, low-normal ACTH = 11 pg/mL, DHEAS = 22.6 µg/dL). No other pituitary hormone deficiencies were identified, suggesting preserved overall pituitary function; therefore, hypocortisolism could not be interpreted in a pituitary context. Mild IGF-1 elevation was attributed to newly diagnosed type 2 diabetes rather than autonomous growth hormone secretion. Given the absence of clinical features of adrenal insufficiency (stable hemodynamics, normal electrolytes, and no hypoglycemia), ACTH stimulation testing was not pursued, as it would not have changed the course of management at this stage. On the other hand, adrenal incidentaloma workup showed normal urinary metanephrines and a normal aldosterone–renin ratio. Dexamethasone suppression testing for autonomous cortisol secretion was not performed due to MA-induced HPA axis suppression. The patient also exhibited a Cushing-like phenotype, including central obesity, facial erythema, diabetes mellitus (HbA1c 7.2%), hypertension (blood pressure 155/90 mmHg), dyslipidemia, and osteopenia. It remains difficult to ascertain whether these features are directly attributable to chronic MA exposure or represent independent metabolic disease.

Conclusions: In patients receiving long-term megestrol acetate, biochemical suppression of the HPA axis should be interpreted cautiously and primarily in clinical context. When dynamic testing is limited by pharmacological suppression, management should focus on patient safety and ongoing monitoring to reassess treatment plan if needed. In the setting of stable oncological disease without recurrence, this case raises an important multidisciplinary question: should gradual tapering and discontinuation of megestrol acetate be considered to mitigate Cushing-like adverse effects, while exploring alternative strategies for oncological disease control under close surveillance?

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.748

EP160 - ECE_1107 - Successful adrenal recovery following long-term prednisolone use: a case demonstrating the value of structured steroid withdrawal and patient education

Muna Guma[1], Hassan Bukhari[1], Harry Wilson[2], Helen Addison[1] and Elliot Crowhurst[2]
[1]Endocrinology and Diabetes, County Durham and Darlington NHS Foundation Trust, Darlington, United Kingdom; [2]County Durham and Darlington NHS Foundation Trust, Darlington, United Kingdom

Background: Prolonged corticosteroid therapy is a well-known cause of secondary adrenal suppression. The process of steroid withdrawal can be challenging, and patient anxiety or premature testing may compromise successful recovery of the hypothalamic–pituitary–adrenal (HPA) axis.

Case Summary: We report a **58-year-old female** with **Crohn's disease**, managed under gastroenterology, who was referred to endocrinology for **steroid withdrawal**. She had been on **prednisolone 8 mg daily for 21 years**, which had recently been reduced by the gastroenterology team to 5 mg. The patient was subsequently managed using the **Merran Steroid Withdrawal Protocol**. Baseline cortisol and short Synacthen testing (SST) were intentionally **not performed prior to withdrawal**, as these were deemed to have limited value and could increase patient anxiety. Instead, the patient received **comprehensive education** regarding symptoms of adrenal insufficiency and adrenal crisis, and was followed up regularly with **telephone reviews every few weeks**. An **SST performed at week 4**, when the patient had been completely off prednisolone, demonstrated the following results:

- Baseline cortisol: **539 nmol/L**
- 30-minute cortisol: **901 nmol/L**
- 60-minute cortisol: **1051 nmol/L**

This excellent cortisol response confirmed **full recovery of adrenal function** and the ability of the corticotroph axis to stimulate normal adrenal physiology following gradual weaning.

Conclusions: This case highlights the **effectiveness of a structured steroid withdrawal protocol** and the **importance of patient education and reassurance** in facilitating adrenal recovery. Minimising unnecessary testing and physician interference can reduce patient anxiety and support safe, physiological restoration of HPA axis function.

Abstract citation ID: lvag096.749

EP163 - ECE_3212 - Early-onset primary aldosteronism in a 17-year-old male: identification and reclassification of a novel CACNA1H variant

Alessandro Risio[1,2], Vittoria Favero[2,3], Carmen Aresta[2], Alessandro Maloberti[4,5], Cristina Giannattasio[4,5] and Iacopo Chiodini[2,3]
[1]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [2]Unit of Endocrinology, ASST GOM Niguarda Hospital, Milan, Italy; [3]Department of Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [4]Milan, Italy [5]School of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy

Introduction: Germline mutations in *CACNA1H*, encoding the T-type voltage-gated calcium channel Cav3.2, cause familial hyperaldosteronism type 4, characterized by early-onset primary aldosteronism (PA) and hypertension. *CACNA1H* mutations can be associated with epilepsy, and additional phenotypic features such as developmental delay, autism, and immunologic and gastrointestinal involvement have been described. These patients present with normal adrenal morphology or bilateral adrenal hyperplasia rather than adenomas. These gain-of-function mutations lead to increased calcium influx, membrane depolarization, and autonomous aldosterone production in adrenal glomerulosa cells. While most reported *CACNA1H* variants are recurrent (eg, M1549V and E282K), novel variants continue to expand the genetic spectrum of this condition. Pathogenicity is established through functional studies and family segregation analyses.

Case Presentation: We describe a 17-year-old male with early-onset hypertension diagnosed at age 12 in 2019, with a family history of early-onset hypertension (maternal aunt). The patient was followed in paediatric cardiology for low-risk ventricular pre-excitation and a pericardial effusion known since 2022. Despite initiation of losartan therapy in 2023, blood pressure control remained suboptimal (mean 160/100 mmHg). Doppler ultrasound excluded renal artery stenosis. Hormonal testing revealed biochemical features of PA (aldosterone 40.1 ng/dL, renin 0.5 mIU/L, ARR 80.2, potassium 3.6 mEq/L) during treatment with alpha-1 blockers and calcium antagonists. Computed tomography showed no adrenal lesions. Adrenal vein sampling was attempted. However, right adrenal vein cannulation was unsuccessful, precluding assessment of lateralization. Hypercortisolism and glucocorticoid-remediable aldosteronism were excluded with dexamethasone tests. The most recent echocardiogram revealed early concentric left ventricular hypertrophy, which was not present in previous examinations. Low-dose spironolactone was subsequently introduced, resulting in excellent blood pressure control and increased renin (22 mIU/L) and potassium (4.5 mEq/L) levels. Given the young age at disease onset, genetic testing was performed, indentifying a c.4289T > G substitution in exon 22 of *CACNA1H*, initially classified as a variant of uncertain significance (VUS). Following family segregation studies demonstrating a de novo origin, the variant was reclassified in December 2025 as likely pathogenic (ACMG class 4: PS2, PM2, PP3).

Conclusions: This case expands the genetic spectrum of *CACNA1H*-related PA by reporting a novel de novo variant. Reclassification based on segregation analysis highlights the importance of parental testing in variant interpretation. These findings support genetic screening in patients with early-onset PA, particularly before 20 years of age, to guide clinical management and family counselling. Notably, cardiac findings in this patient have not been previously reported in association with CACNA1H mutations, unlike CACNA1D-related PASNA syndrome.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.750

EP166 - ECE_1272 - Congenital adrenal hyperplasia—a Maltese cohort

Carol Cardona Attard[1,2], Martha Spiteri[2] and Josanne Vassallo[1,3,4]

[1]Diabetes and Endocrine Centre, Mater Dei Hospital, Msida, Malta; [2]Department of Medicine, Mater Dei Hospital, Msida, Malta; [3]Faculty of Medicine and Surgery, University of Malta Medical School, Mater Dei Hospital, Msida, Malta; [4]Molecular & Cellular Endocrinology Research Lab, Centre for Molecular Medicine and Biobanking, Room 322, Msida, Malta

Background: Congenital adrenal hyperplasia (CAH), an autosomal recessive disorder, encompasses a spectrum of phenotypes secondary to impaired cortisol and variable mineralocorticoid production, and androgen excess, depending on the type and severity of enzyme deficiency in the adrenal steroidogenesis pathway. It is associated with many long-term health sequelae, usually secondary to under- or overtreatment with glucocorticoids +/− mineralocorticoids. The aim of our study was to assess the different phenotypes and quality of care provided to these patients presenting at Mater Dei hospital, Malta.

Methods: Patients with 17-hydroxyprogesterone (17-OHP) levels >10 ng/mL, measured between January 2009 and 2023, post-infancy during the follicular phase in premenopausal women or after cosyntropin stimulation, were identified. Twenty-two consented to participate out of 29 identified patients. Data collected via questionnaire included presenting symptoms, co-morbidities, fertility, management and follow-up details. Clinical assessment included blood pressure, anthropometry, biochemical testing (17-OHP, testosterone, androstenedione) and a bone mineral density (BMD).

Results: Most patients had 21-hydroxylase deficiency (20/22, 90.9%), with 2 (9.1%) having 11β-hydroxylase deficiency. Late-onset CAH accounted for 19 cases (86.4%), while 3 (13.6%) had classic CAH (2 salt-wasting, 1 simple-virilising). Eighteen participants (81.8%) were women and four (18.2%) were men (3 adults, one <16 years). Mean age was 41.7 years (SD 16.5). At study enrolment, 11 (50%) individuals were treated with steroids, predominantly prednisolone (63.6%). Weight gain was reported by 45.5% of patients, all of whom had received steroid therapy. Six patients (28.6%) were overweight and six (28.6%) had obesity. Age- and sex-standardised overweight prevalence did not differ from the Maltese population (44.1% vs 35.3%, $P = .429$), whereas obesity was less prevalent in CAH (15.4% vs 33.2%, $P = <.001$). Among those with available BMD data, osteopenia was present in 9/18 (50.0%) and osteoporosis in 1/18 (5.6%). Nine adults (42.9%; 8 women, 1 man) reported 19 spontaneous pregnancies and 13 live births; complications occurred in half of female deliveries. Genetic counselling was undertaken in 4 patients (18.2%), with partner testing in 2 (9.5%). Only 11 patients (50%) felt their symptoms were controlled, and 12 (54.5%) had endocrinology follow-up at study enrolment.

Conclusions: Late-onset CAH seems to be still underdiagnosed/confounded with other conditions such as Polycystic ovary syndrome. Inadequate screening particularly due to the lack of neonatal screening in Malta might also be a reason. This could lead to incorrect treatments, ongoing symptoms and poor quality of life. Timely screening, genetic testing and counselling would improve diagnosis and patient outcomes.

Abstract citation ID: lvag096.751

EP170 - ECE_1830 - Minor trauma, major consequences: a subacute hypertensive crisis revealing an occult pheochromocytoma

Marjeta Kermaj[1,2], Ledia Omeri[1], Dorina Ylli[1,2], Megi Lekbello[1,2], Zgjim Gola[3] and Agron Ylli[1,2]

[1]Endocrinology, University Hospital Center "Mother Tereza", Tirana, Albania; [2]University of Medecine, Tirana, Albania; [3]Cardiology, University Hospital Center "Mother Tereza", Tirana, Albania

Background: Pheochromocytoma is a rare catecholamine-secreting neuroendocrine tumor that may remain clinically silent until exposure to physiological stress precipitates excessive catecholamine release and hypertensive crisis. While major trauma is a recognized trigger, the clinical significance of minor peripheral injuries followed by cumulative inflammatory and immune stress is rarely reported.

Case Presentation: We report a young male with no significant medical history who presented with fever, severe occipital headache, palpitations, and marked blood pressure lability. Three days after sustaining a minor penetrating nail injury to the left great toe without initial medical treatment, the patient developed localized pain and presented to the emergency department. He received intramuscular human tetanus immunoglobulin (250 IU) and antibiotic therapy and was hospitalized for two weeks for wound management. No hypertensive episodes or adrenergic symptoms were documented during hospitalization. Two days after discharge, the patient developed fever followed by acute adrenergic symptoms and labile hypertension, prompting further evaluation. Contrast-enhanced abdominal CT revealed a large adrenal mass consistent with pheochromocytoma, and biochemical testing confirmed marked catecholamine excess. The patient was stabilized with alpha-adrenergic blockade followed by beta-adrenergic blockade and subsequently underwent elective adrenalectomy, with postoperative histopathology confirming pheochromocytoma and complete resolution of hypertensive episodes.

Conclusions: This case demonstrates that minor peripheral trauma, followed by cumulative physiological, inflammatory, and immune stress, may unmask an occult pheochromocytoma and precipitate a subacute, life-threatening hypertensive crisis. The delayed onset of symptoms argues against a direct pharmacologic or immunologic trigger and instead supports a threshold-dependent stress mechanism. Clinicians should consider pheochromocytoma in patients presenting with unexplained and labile hypertension following seemingly benign injuries and prolonged inflammatory stress.

Abstract citation ID: lvag096.752

EP172 - ECE_2625 - Aldosteronism: a diagnostic challenge

Bojan Markovic[1], Mirjana Stojkovic[1,2], Nata Joksimovic[1], Tamara Janic[1], Jovana Babic[1], Marija Miletic[2,3], Biljana Nedeljkovic Beleslin[1,2] and Milos Zarkovic[1,2]

[1]Thyroidology, Clinic of Endocrinology, Diabetes and Metabolic Diseases, University Clinical Center of Serbia, Belgrade, Serbia; [2]University of Belgrade Faculty of Medicine, Belgrade, Serbia; [3]Reproductive Endocrinology, Clinic of Endocrinology, Diabetes and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Metabolic Diseases, University Clinical Center of Serbia, Belgrade, Serbia

Introduction: Most patients with hypertension have essential hypertension, while secondary causes account for 5%-10% of cases, including endocrine disorders. Aldosterone plays a key role in electrolyte balance, and its excessive secretion may lead to unrecognized resistant hypertension.

Case Presentation: A female patient, a nurse without night shifts, has had arterial hypertension since the age of 30. During the last five years, antihypertensive therapy was changed approximately once per year. Usual blood pressure on therapy was 150/110 mmHg, with a maximum recorded value of 203/158 mmHg. Due to frequent headaches and hypertensive crises, she often presented to the emergency department. As part of the evaluation for secondary hypertension, imaging studies were performed. Computed tomography showed a normal right adrenal gland, while the left adrenal gland had a prominent medial limb. Initial testing was performed in a regional center on maximal doses of an angiotensin receptor blocker and a thiazide diuretic, and showed normal hypothalamic-pituitary-adrenal axis, while renin-angiotensin-aldosterone system testing showed elevated aldosterone levels (271 ng/L) with potassium at the lower normal range (K 3.7 mmol/L). For adequate aldosterone evaluation, therapy was switched to aldosterone-neutral medication (calcium channel blocker and alpha-blocker). At our center, 24-hour ambulatory blood pressure monitoring revealed a non-dipper pattern. Basal and confirmatory testing for hyperaldosteronism was performed. The aldosterone-to-renin ratio (ARR) was within the normal to borderline range. The captopril test showed appropriate suppression of aldosterone (aldosterone 0, 90, 120 min: 204.3, 109.6, 72.5 ng/L; plasma renin activity (PRA) 0, 90, 120 min: 0.79, 1.5, 2.2 ng/mL/h). The saline infusion test yielded borderline results (aldosterone 0, 30, 60, 120, 240 min: 208.6, 137.9, 123.7, 162.9, 119.6 ng/L; PRA 0, 30, 60, 120, 240 min: 1.10, 0.86, 1.10, 1.10, 0.84 ng/mL/h). A low-dose dexamethasone suppression test showed significant aldosterone suppression (aldosterone 206.2-82.1 ng/L; PRA 0.36-0.76 ng/mL/h).

Conclusions: This case describes a patient with early-onset hypertension and elevated aldosterone levels. Normal potassium levels, mostly negative confirmatory tests, and two normal ARR values (25.8; 18.9) make primary aldosteronism unlikely. However, significant aldosterone suppression during the low-dose dexamethasone test (60%), together with a family history of early-onset hypertension, suggests possible glucocorticoid-remediable aldosteronism. Genetic testing will be considered for further evaluation. If confirmed, treatment with low-dose glucocorticoids will be initiated.

Abstract citation ID: lvag096.753

EP173 - ECE_3630 - Marked biochemical severity of primary aldosteronism occurs across diverse adrenal CT phenotypes

Ia Kavtiashvili, Mariam Bulashvili and Nino Zavrashvili
Tbilisi Institute of Medicine, Tbilisi, Georgia

Background: Adrenal computed tomography (CT) is routinely incorporated into the diagnostic evaluation of primary aldosteronism (PA) and is frequently used to infer disease phenotype in clinical practice. Despite its widespread use, the extent to which adrenal CT findings reflect the biochemical severity of aldosterone excess remains uncertain, particularly outside of highly selected cohorts.

Aim: To determine whether adrenal CT phenotype is associated with biochemical severity in patients with primary aldosteronism.

Methods: We performed a retrospective case series of 11 patients with primary aldosteronism confirmed by an elevated aldosterone-to-renin ratio (ARR). All patients underwent systematic biochemical assessment including aldosterone concentration, renin measurement, and serum potassium evaluation. Adrenal CT findings were classified as unilateral adenoma or nodule, bilateral hyperplasia or adrenal thickening, normal adrenal morphology, or no focal lesion documented. Biochemical severity was assessed using aldosterone concentration, ARR, and serum potassium nadir. Analyses were descriptive and non-parametric due to the exploratory nature of the study.

Results: Adrenal CT findings were heterogeneous: unilateral adenoma ($n = 3$), hyperplasia or thickening ($n = 3$), normal adrenal morphology ($n = 3$), and no focal lesion documented ($n = 2$). Aldosterone concentrations ranged widely from 78.6 to 900 ng/L, with marked aldosterone excess observed across all CT phenotypes. ARR values were markedly elevated irrespective of imaging appearance. Hypokalemia (serum potassium <3.5 mmol/L) was present in 7 of 11 patients (64%) and occurred in every CT category. Importantly, severe hypokalemia (≤3.2 mmol/L) was identified in patients with normal or non-lateralizing CT findings.

Conclusions: In this real-world cohort, adrenal CT phenotype was not associated with biochemical severity in primary aldosteronism. Clinically significant aldosterone excess and hypokalemia occurred across all imaging categories, including normal and non-lateralizing CT findings. These findings reinforce the central role of biochemical testing in PA and caution against using CT phenotype as a surrogate marker of disease severity in routine clinical practice.

Table 1 Adrenal CT phenotype and biochemical characteristics of the study cohort.

Patient	CT phenotype	Aldosterone (ng/L)	Renin (ng/L)	ARR	K (mmol/L)
P1	Unilateral adenoma	214	<1	>214	3.9
P2	Bilateral hyperplasia	122	1.4	90	3.4
P3	Normal CT	118	2.53	46.6	4.33
P4	Unilateral adenoma	78.6	0.9	87.3	3.64
P5	Adrenal thickening	107	1.6	66	4.1
P6	Normal CT	105	<1	>105	3.78
P7	Normal CT	611	37	74	3.3
P8	Bilateral hyperplasia	114	<1	>114	3.4
P9	No focal lesion	183	<1	>183	3.1
P10	Unilateral adenoma	900	<1	>900	3.0
P11	No focal lesion	181	0.8	225	3.2

Abstract citation ID: lvag096.754

EP174 - ECE_3674 - Renal and metabolic heterogeneity in primary aldosteronism: a single-center experience

Ia Kavtiashvili[1], Mariam Orjonikidze[1] and Giorgi Vepkhishvili[2]
[1]*Tbilisi Institute of Medicine, Tbilisi, Georgia;* [2]*Tbilisi State Medical University, Tbilisi, Georgia*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Primary aldosteronism (PA) is a leading cause of secondary hypertension and is associated with increased cardiovascular and renal morbidity. While hypokalemia has traditionally been considered a hallmark of PA, a substantial proportion of patients present with normokalemia. As a result, renal involvement in PA may be overlooked, particularly in patients without overt electrolyte disturbances.

Aim: To describe renal and biochemical characteristics in patients with primary aldosteronism and to assess whether potassium phenotype reflects the degree of renal involvement in a real-world single-center cohort.

Methods: We conducted a retrospective single-center case series including 11 patients with confirmed primary aldosteronism, defined by an elevated aldosterone-to-renin ratio. Serum potassium and creatinine levels were analyzed in all patients. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI 2021 creatinine-based equation when age and sex data were available.

Results: Serum potassium levels ranged from hypokalemic to normokalemic values. Renal function demonstrated marked heterogeneity, with both preserved and mildly reduced eGFR observed across patients regardless of potassium status. Importantly, reduced eGFR was not confined to hypokalemic individuals, indicating a lack of direct correlation between potassium phenotype and renal impairment.

Conclusions: In this single-center experience, potassium phenotype alone did not adequately reflect renal involvement in patients with primary aldosteronism. Renal dysfunction was observed across both hypokalemic and normokalemic presentations, underscoring the limited utility of serum potassium as a marker of disease severity or end-organ damage. These findings are consistent with emerging evidence that aldosterone excess can exert direct deleterious effects on renal structure and function independent of potassium status. Our data support current guideline recommendations advocating comprehensive biochemical and renal assessment in all patients with suspected or confirmed primary aldosteronism. Early identification of renal impairment is particularly important, as appropriate subtype classification and targeted treatment may lead to stabilization or improvement of renal function and reduce long-term cardiovascular risk. Routine incorporation of eGFR assessment into the diagnostic evaluation of PA may therefore enhance risk stratification and inform optimal management strategies.

Table 1 Patient-level renal and biochemical characteristics.

Patient	Potassium (mmol/L)	Creatinine (μmol/L)	eGFR (mL/min/1.73 m^2)
P1	3.9	97.2	75
P2	3.4	92.0	59
P3	4.33	76	70
P4	3.64	74	104
P5	4.1	84.9	104
P6	3.78	106	83
P7	3.3	106	70
P8	3.4	59	99
P9	3.1	78.9	93
P10	3.0	128.3	75
P11	3.2	98	80

Abstract citation ID: lvag096.755

EP177 - ECE_3098 - When stress hits both sides: bilateral adrenal hemorrhage—case report and literature review

Maria Pisimisi, Maria Mathiopoulou and Mile Vidovic
Hospital of Uster, Uster, Zurich, Switzerland

Introduction: Bilateral adrenal hemorrhage (BAH) is a rare but potentially life-threatening condition that may result in acute adrenal insufficiency and adrenal crisis. Reported etiologies include severe physiological stress, sepsis, coagulopathies—particularly anticoagulant therapy and heparin-induced thrombocytopenia—antiphospholipid syndrome, and adrenal neoplasms. Mortality rates of up to 15% have been reported, with adrenal insufficiency occurring in 16%-50% of patients with bilateral involvement, underscoring the importance of early recognition and appropriate management.

Methods: An 83-year-old male was hospitalized for acute pyelonephritis and demonstrated clinical improvement under intravenous antibiotic therapy. The patient was receiving phenprocoumon and had supratherapeutic anticoagulation. Ten days into hospitalization, he developed acute-onset diffuse abdominal pain accompanied by a hypertensive crisis (204/91 mmHg). Laboratory evaluation was largely unremarkable, with no elevation of inflammatory markers and normal abdominal laboratory parameters, except for elevated lactate levels and persistent supratherapeutic anticoagulation. Initial contrast-enhanced abdominal computed tomography (CT) revealed no acute pathology. Due to persistent symptoms and rising C-reactive protein levels, repeat CT imaging performed eight days later demonstrated bilateral adrenal hemorrhage. In this case, BAH was most likely stress-induced in the context of acute infection, with concomitant anticoagulation representing an additional risk factor. The underlying pathophysiology is thought to involve adrenal vein thrombosis, vascular congestion, and subsequent hemorrhage related to increased adrenal blood flow and impaired venous drainage. Clinical presentation is frequently nonspecific, including abdominal or flank pain, hemodynamic instability, or unexplained clinical deterioration, necessitating a high index of suspicion in at-risk patients. Diagnosis relies primarily on imaging, with contrast-enhanced CT as the modality of choice, while MRI may provide further lesion characterization.

Results: Endocrine evaluation revealed serum cortisol levels in the upper normal range with normal adrenocorticotropic hormone (ACTH) concentrations, therefore, glucocorticoid replacement therapy was not initiated. BAH represents a medical emergency due to the high risk of adrenal crisis and hemodynamic instability. Prompt recognition and early management are essential, including immediate stress-dose glucocorticoid therapy in patients with suspected adrenal insufficiency, aggressive fluid resuscitation, correction of metabolic disturbances, and close

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hemodynamic monitoring. Identification and treatment of precipitating factors, such as infection or anticoagulant-related bleeding, are critical.

Conclusions: Early recognition and multidisciplinary management are key to preventing adrenal crisis and improving outcomes. Given the nonspecific clinical presentation, a high index of suspicion is required, particularly in patients exposed to physiological stress or anticoagulation. Timely imaging and endocrine evaluation enable appropriate intervention and reduce morbidity and mortality.

Abstract citation ID: lvag096.756

EP179 - ECE_2049 - Cushing disease initially presented as macronodular adrenal hyperplasia: a case report and review of literature

Ching-Hua Tseng[1] and Chia-Hung Lin[2]
[1]National Taiwan University Hospital, Zhongzheng District, New Taipei City, Taiwan; [2]New Taipei City, Taiwan

Introduction: Cushing syndrome is characterized by elevated plasma cortisol levels resulting from exogenous exposure or endogenous overproduction. Common manifestations include central obesity, proximal myopathy, striae, and impaired glucose tolerance. We report a case of recurrent Cushing syndrome, initially presenting with adrenal involvement and later diagnosed as Cushing disease. This case illustrates the diagnostic challenges of recurrent hypercortisolism and presents the importance of identifying the primary etiology to guide appropriate treatment and long-term management.

Case: A 61-year-old male presented in 2020 with moon face, weight gain, easy bruising, and muscle weakness for six months. Physical examination revealed a buffalo hump, central obesity, and purple striae. Initial laboratory testing showed loss of the diurnal cortisol rhythm with ACTH within the normal range. Imaging demonstrated bilateral adrenal nodules, more prominent on the left. Pituitary MRI revealed no lesion. Cushing syndrome due to a primary adrenal adenoma was diagnosed, and left adrenalectomy was performed in February 2021. In May 2023, the patient developed recurrent symptoms, including progressive facial acne, oily scalp, easy bruising, and lower limb weakness. Laboratory testing showed loss of the diurnal cortisol rhythm, now with elevated ACTH. Repeat pituitary MRI identified a 4 mm microadenoma. Inferior petrosal sinus sampling (IPSS) in January 2024 confirmed Cushing disease. Transsphenoidal adenomectomy was performed in February 2024, with subsequent resolution of symptoms. Follow-up MRI in May 2024 showed postoperative changes without residual tumor.

Discussion: The patient initially presented with bilateral adrenal nodules, Cushing syndrome, and borderline ACTH levels. Imaging suggested adrenal involvement, leading to left adrenalectomy. Two years later, recurrent Cushing syndrome with elevated ACTH was diagnosed as Cushing disease. Literature review suggests the presentation is compatible with ACTH-dependent macronodular adrenal hyperplasia (MAH). This autonomous secretion suppresses pituitary ACTH, resulting in relatively low ACTH levels. We postulate that an undetectable pituitary microadenoma initially stimulated adrenal growth and cortisol secretion. Adrenalectomy removed the source of auto-suppression, possibly permitting pituitary tumor progression and subsequent recurrence. As up to 23% of Cushing disease patients have normal pituitary MRI findings, IPSS remains an important diagnostic tool. However, due to its cost and procedural risks, shared decision-making is essential.

Conclusions: Cushing disease may present as an adrenal tumor, such as MAH, making identification of the primary cause essential. When clinical findings and test results are inconsistency, the diagnosis should be reconsidered. A negative sellar MRI does not exclude Cushing disease, and IPSS remains a valuable diagnostic tool in challenging cases.

Abstract citation ID: lvag096.757

EP180 - ECE_2358 - Pheochromocytoma during pregnancy: a case report

Ghofran Shahat[1], Hatim Aljohani[2] and Ali Alenazi[3]
[1]King Faisal Specialist Hospital & Research Centre, Madinah, Saudi Arabia; [2]Prince Mohammed bin Abdulaziz Hospital, Riyadh, Saudi Arabia; [3]Royal College of Physicians of Ireland, Dublin, Ireland

Introduction: Pheochromocytoma is a rare catecholamine-secreting tumor originating from adrenal chromaffin cells. Although uncommon, its occurrence during pregnancy is associated with significant maternal and fetal morbidity and mortality. Diagnosis is often delayed due to symptom overlap with hypertensive disorders of pregnancy, emphasizing the need for heightened clinical suspicion.

Case Presentation: We present the case of a 44-year-old gravida 14 para 10 woman with chronic hypertension who presented at 24 weeks of gestation with recurrent episodes of palpitations, dyspnea, diaphoresis, and markedly labile blood pressure reaching 180/130 mmHg despite methyldopa therapy. Abdominal ultrasound revealed a right adrenal mass measuring 31 × 28 mm. Magnetic resonance imaging without contrast confirmed a well-defined right adrenal lesion (27 × 31 mm) with high T2 signal intensity. Biochemical investigations demonstrated markedly elevated plasma and 24-hour urinary catecholamines and metanephrines, confirming the diagnosis of pheochromocytoma.

Management and Outcome: Methyldopa was discontinued and alpha-adrenergic blockade with prazosin was initiated with gradual dose titration, resulting in improved hemodynamic stability. Due to the advanced gestational age at diagnosis, surgical resection was postponed. The patient underwent an elective cesarean section at 34 weeks of gestation, delivering a healthy female infant who required brief neonatal observation only. Two weeks postpartum, she underwent a successful laparoscopic right adrenalectomy without complications. Postoperatively, her symptoms resolved completely, blood pressure normalized, and follow-up biochemical testing returned to normal.

Conclusions: This case illustrates the diagnostic challenge of pheochromocytoma in pregnancy and emphasizes that refractory or labile hypertension associated with adrenergic symptoms should prompt evaluation for secondary causes. MRI without contrast combined with biochemical testing remains the diagnostic cornerstone. Individualized multidisciplinary management with appropriate alpha-blockade, planned delivery, and delayed adrenalectomy can result in excellent maternal and fetal outcomes even when diagnosis is made late in pregnancy.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Keywords pheochromocytoma, adrenal mass, pregnancy, hypertension

Abstract citation ID: lvag096.758

EP182 - ECE_2355 - Endocrine hypertensions: from Conn's syndrome to the gut microbiome

Sanja Borozan[1,2] and Joseph Pappachan[3,4,5]
[1]*Department of Endocrinology, Clinical Centre of Montenegro, Podgorica, Montenegro;* [2]*Faculty of Medicine, Podgorica, Montenegro;* [3]*Faculty of Science, Manchester Metropolitan University, Manchester, United Kingdom;* [4]*Department of Endocrinology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, KA, India;* [5]*Department of Endocrinology, Countess of Chester Hospital NHS Trust, Cheshire West and Chester, United Kingdom*

Hypertension remains one of the most significant global health challenges even in the 21st century, affecting approximately 40% of the adult population. While most individuals with high blood pressure have essential hypertension, recent estimates indicate that secondary hypertension, mostly of endocrine origin, accounts for up to 30% in those aged <40 years. Among those with refractory hypertension, nearly 50% have an identifiable underlying cause. Although endocrine hypertension (EH) is fairly common, it is often overlooked or diagnosed late, with an average delay of 3-5 years. This delay can lead to serious complications, including irreversible damage to target organs and, ultimately, premature mortality.

From the initial descriptions of Conn's and Cushing's syndromes to modern molecular and genetic classifications, diagnostic algorithms for EH have undergone a significant transformation, enabling active case-finding, early detection, and a personalized approach to treatment. Today, EH is no longer viewed solely through the lens of classical hormonal dysfunctions but as a diverse group of disorders that include genetic predisposition, autoimmune mechanisms, and interactions with other systems. Recent advances in genetics have enabled further subclassification of the disease and the use of targeted therapies, thereby increasing the level of individualization in treatment. Alongside well-established pathophysiological mechanisms, there is growing interest in the role of the gut microbiome in EH, particularly its influence on blood pressure through the production of metabolites such as short-chain fatty acids and trimethylamine-N-oxide, and its effects on systemic inflammation and endothelial dysfunction. These mechanisms open new perspectives for the development of diagnostic biomarkers and innovative therapeutic strategies.

A multidisciplinary approach, together with new molecular and biochemical markers and advanced imaging techniques, is essential in today's clinical management of EH. Early diagnosis of the underlying condition is essential for a potential cure or optimal control of hypertension.

Abstract citation ID: lvag096.759

EP183 - ECE_3184 - Artificial intelligence in adrenal imaging: detection and segmentation of adrenal glands

Zuzanna Roszkowska[1], Malgorzata Bobrowicz[1], Radoslaw Roszczyk[2] and Urszula Ambroziak[1]
[1]*Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland;* [2]*Faculty of Electrical Engineering, Warsaw University of Technology, Warsaw, Poland*

Background: Accurate visualization of the adrenal glands is crucial for the evaluation of adrenal pathology. However, their small size, variable shape, and proximity to other retroperitoneal structures make automated analysis challenging. Artificial intelligence (AI) tools capable of detecting and segmenting adrenal glands could significantly improve workflow efficiency and lay the groundwork for future tumor characterization.

Objective: At the current stage of the project, we aim to develop and validate an AI-based algorithm for automated detection and 3D segmentation of adrenal glands in non-contrast CT scans. This constitutes a foundational step for subsequent modules that will analyze adrenal lesions.

Methods: A multidisciplinary team from the Medical University of Warsaw and Warsaw University of Technology is collaborating to build a comprehensive dataset of anonymized abdominal CT scans. Using state-of-the-art deep learning architectures, we are training models to precisely identify and segment both adrenal glands, generating accurate three-dimensional reconstructions. The performance of the model is evaluated based on segmentation accuracy and anatomical consistency.

Conclusions: The AI algorithm successfully detects and segments adrenal glands in three dimensions, offering a robust and scalable tool for future applications in adrenal imaging. This stage represents a critical foundation for further development of AI systems aimed at lesion detection and classification in adrenal pathology.

Keywords artificial intelligence, adrenal glands, 3D segmentation, CT imaging, deep learning, radiology, endocrine diagnostics

Abstract citation ID: lvag096.760

EP187 - ECE_1434 - Cardiovascular events and target organ demaged in primary aldosteronism

Natasa Vujacic[1,2] and Goran Zoric[1]
[1]*Clinic of Endocrinology, Diabetes and Metabolic Disease, Kliničkі Centar Srbije, Beograd, Serbia;* [2]*Clinical Center of Serbia, Belgrade, Serbia*

Introduction: Primary aldosteronism (PA) is the most frequent secondary hypertension wich can lead to increased occurrence of cardiovascular, renal and central nervous system complications. Subjects with PA due to aldosterone-producing adenoma (APA) are diagnosed mostly due to clinical picture of hypokalaemia and hypertension.

Materials and Methods: The study group of PA included 40 patients (25 females, 15 males). The study groups (CS $n = 20$; A+HT $n = 40$) did not differ by age and sex. Standardized endocrinological testing for the diagnosis confirmation was done. The aim of this study was analyze clinical characteristics of the PA due to adenoma (PA) and to compare the frequency of many cardiovascular, renal and cerebrovascular events with those found in adrenal Cushing syndrome (CS) and adrenal tumour associated with essential hypertension (A+HT).

Results: There was no significant difference between groups related to the age, nor sex distribution, although a higher number of women in all groups was recorded ($P = .099$). Systolic and diastolic blood pressures were significantly higher in PA group ($P = .005$ and $P = .002$ respectivaly), with the lowest levels in NFA+HT group. The significanteley higher mean arterial pressure (MAP)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

was also found in PA group ($P = .001$). The longest hypertension duration was recorded in the PA group, and was significantly longer ($P = .001$) than in CS+SCS group. PA patients had also the longest hypertension history ($P = .01$) and all had hypokalaemia. The smallest mean tumour diameter was found in PA group ($P < .001$). Atrial fibrillation is found to be twelve times more frequent in PA than in essential hypertension (EHT), but only patients older than 50 years have myocardial infarction 6.5 times and cerebrovascular infarction (CVI) 4.2 times independent of blood pressure and PA subtypes. Chronic renal failure was found in 20% of patients. Chronic renal failure was quite common in all three groups of hypertensive patients

Conclusions: It revealed that patients with aldosterone-producing adenoma have significantly higher systolic, diastolic and mean blood pressures compared to patients with nonfunctioning adrenal adenoma with hypertension. All patients with PA also had hypokalaemia, which aggravated organ damage or hypertensive emergencies.

Abstract citation ID: lvag096.761

EP189 - ECE_2854 - Adrenal function in clinically stable liver transplant candidates: an exploratory pre-transplant assessment

Daniela Cuboni[1], Elena Musso[2], Mattia Rossi[3], Letizia Meomartino[1], Valentina Gasco[1], Ezio Ghigo[1], Roberta Giordano[1,4], Gianluca Aimaretti[1] and Loredana Pagano[1]

[1]Division of Endocrinology, Diabetes and Metabolism, Department of Medical Science, University of Turin, Turin, Italy; [2]University of Turin, Turin, Italy; [3]Turin, Italy; [4]Department of Biological and Clinical Sciences, University of Turin, Turin, Italy

Background: Adrenal dysfunction has been described in advanced liver disease, particularly in critically ill patients, where it has been associated with adverse outcomes. In clinically stable liver transplant candidates, however, adrenal function is more difficult to interpret, and both the prevalence and clinical significance of hypothalamic–pituitary–adrenal (HPA) axis alterations remain uncertain. This analysis is part of a broader project investigating endocrine comorbidities in patients with liver cirrhosis.

Objective: To explore adrenal function in clinically stable liver transplant candidates undergoing pre-transplant evaluation and to assess the contribution and limitations of basal cortisol measurement and ACTH stimulation testing in this setting.

Methods: We retrospectively analyzed adult patients referred for endocrine consultation within the liver transplant pathway at a tertiary center between January 2021 and September 2024. Patients with available 08:00 AM. serum cortisol measurements, in the absence of ongoing systemic glucocorticoid therapy, were included. Basal cortisol <50 µg/L was considered suggestive of adrenal insufficiency, values >150 µg/L normal, and values between 50-150 µg/L defined a grey zone, prompting a standard 250 µg ACTH stimulation test. An adequate response was defined as a peak cortisol >180 µg/L.

Results: Twenty-five patients were included; median age was 58 years (IQR 54-66), 68% were male, median MELD score was 11.5 (IQR 8-16), and 68.2% were Child–Pugh class A. Hepatocellular carcinoma was present in 68%. Median morning cortisol was 83 µg/L (IQR 72-101). Based on basal cortisol alone, only 3/25 patients (12%) were within the normal range, whereas 21/25 (84%) fell within the grey zone and 1/25 (4%) had cortisol <50 µg/L. Of the grey-zone patients, 12/21 (57.1%) underwent ACTH stimulation testing; 7/12 (58.3%) achieved an adequate cortisol response, while 5/12 (41.7%) did not, indicating heterogeneous adrenal responsiveness despite clinical stability.

Conclusions: In clinically stable liver transplant candidates, basal total cortisol measurement was frequently inconclusive, with most patients falling into an indeterminate range. ACTH stimulation testing revealed substantial interindividual variability in adrenal responsiveness, highlighting the diagnostic challenges of adrenal assessment in this population. Alterations in cortisol-binding proteins may further confound interpretation of total cortisol measurements, supporting the need for more refined approaches to HPA axis evaluation in the pre-transplant setting. In this context, ongoing analysis of morning salivary cortisol within this cohort, although not formally validated at peak morning levels, may help to refine future approaches to HPA axis evaluation.

Abstract citation ID: lvag096.762

EP190 - ECE_2960 - Prevalence and predictors of testicular adrenal rest tumors in adults with congenital adrenal hyperplasia

Giulia Bovo, Irene Tizianel, Pierluigi Mazzeo, Giacomo Voltan, Chiara Sabbadin, Filippo Ceccato and Mattia Barbot

Ponte San Nicolò, PD, Italy

Background: Testicular adrenal rest tumors (TARTs) represent a significant complication in males with congenital adrenal hyperplasia (CAH), potentially impairing fertility and quality of life. Although TARTs are well-documented in pediatric populations, evidence regarding their prevalence and clinical significance in adult CAH patients remains limited, particularly regarding biochemical features and implications for disease management.

Aim of the Study: This study aimed to assess the prevalence of TARTs in adult males with CAH and to investigate potential associations with clinical features, biochemical parameters and indicators of disease control.

Methods: We conducted a retrospective analysis of 28 adult males with CAH (26 with 21-hydroxylase deficiency, 25 classic and 1 non-classic form, 2 with 11β-hydroxylase deficiency, median age 34 years) followed at our adult endocrinology unit. Clinical data included age at diagnosis, morphometric and biochemical parameters, and treatment regimens. TARTs were assessed via testicular ultrasonography.

Results: TARTs were identified in 12/28 patients (42.9%) with a mean age of 42 years. Patients with TARTs were significantly older at first adult endocrinology evaluation compared to those without TARTs (27.5 vs 19 years, $P = .026$) and had higher body weight (70 vs 66 kg, $P = .041$). All patients with 11β-hydroxylase deficiency developed TARTs. No significant differences were observed between patients with and without TARTs in biochemical parameters, for example 17 OHP (418 vs 398, $P = .237$) or androstenedione/testosterone ratio (1.3 vs 1.5, $P = .305$), hydrocortisone equivalent doses (median 20 mg in both groups, $P = .508$),

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

or phenotype distribution. Longitudinal evaluation between the first adult endocrinology visit and last follow-up showed that six patients experienced an increase in TART size or new TART development over time, one patient underwent surgical removal, and one showed a reduction in TART size, possibly related to improved disease control.

Conclusions: TARTs affect approximately half of adult males with CAH in our cohort, with a particularly high prevalence in those with 11β-hydroxylase deficiency. Older age and higher body weight emerge as risk factors for TART development. These factors may reflect, respectively, loss of follow-up during the transition to adult care and the effects of glucocorticoid overtreatment aimed at achieving stricter disease control in patients with TARTs. These findings pinpoint the importance of a structured transition of care from pediatric to adult endocrinology and underscore the need for long-term follow-up. Larger studies are needed to confirm these observations and define optimal screening protocols.

Abstract citation ID: lvag096.763

EP191 - ECE_3063 - Primary hyperaldosteronism

Ana Chokhonelidze
IBSU, Caucasus Medical Center, Nutrition and Metabolism Centre, Tbilisi, Georgia

Patient: 40-year-old female

Anthropometrics: Weight 89.5 kg, Height 164 cm, BMI 33, Waist circumference 120 cm

Complaints at Presentation: Recurrent hypertension (up to 200/100 mmHg), generalized weakness, dizziness, palpitations, emotional lability, imbalance.

History of Present Illness: For one year, persistent hypertension with disturbed sleep and diet, emotional stress. Diagnosed with nodular euthyroid goiter and carbohydrate metabolism disorder. One month earlier hospitalized for hypertensive crisis.

Hospital Investigations:

- **Brain CT:** No acute pathology; moderate frontal cortical atrophy.
- **Echocardiography:** Mild LV hypertrophy, diastolic dysfunction, EF 60%, mild ascending aortic dilation.
- **Vascular Duplex:** Significant stenosis of right internal carotid artery (>65%), bilateral vertebral artery deformities.
- **Laboratory:** Hypokalemia (K = 3.2 mmol/L), hyperglycemia (glucose 6.0 mmol/L).
- **Consultations:** Neurology and cardiology.

Medications at Presentation: Metformin XR 500 mg, Verapamil 80 mg, Magne-B6, Betahistine 24 mg.

Outpatient Findings:

- CBC/urinalysis: Normal.
- **Electrolytes:** Na 142, K 4.0, Ca++ 1.2 mmol/L.
- **Lipids:** Total cholesterol 192, HDL 41, LDL 109, VLDL 40, TG 206 mg/dL.
- **Creatinine:** 45 μmol/L.
- **Glucose/Insulin:** Glucose 99 mg/dL; Insulin 8.74; HOMA-IR 2.1; HbA1c 5.9%.
- **Liver function:** Tbil 0.6; Dbil 0.3; ALT 42; AST 28; GGT 41; ALP 95.
- Magnesium: 1.03.
- **Hormonal tests:** TSH 1.12; Anti-TG 16; Anti-TPO 12.6; Aldosterone 183; Renin 2.9; ARR 64; 24 h urine metanephrine 261; normetanephrine 320; cortisol 26.
- **Ultrasound:** Borderline hepatomegaly, fatty liver; right adrenal lesion 18 × 13 mm hypoechoic. Thyroid volume 20 cm^3; right lobe nodule 23 × 13 × 19 mm (FNA: colloid, BSRTC-II).
- **CT Imaging:** Bilateral adrenal nodules with fatty components, consistent with adenomas.

Main Diagnosis: Primary hyperaldosteronism (E26.0)

Comorbidities: D44.1; E74.8; E04.1; I15.2; E78.2; E66.8; K76.0; E55.9

Treatment: Spironolactone 50 mg initially controlled BP but caused menstrual irregularities. Therapy switched to eplerenone 25 mg, stabilizing BP and restoring cycle. Patient declined surgery; AVS recommended for functional assessment of bilateral adenomas.

Additional Therapy: Metformin XR 500 mg, Rosuvastatin/Ezetimibe 10/10 mg, Vitamin D3 2000 IU. Lifestyle modifications: balanced diet, physical activity, sleep hygiene.

Summary: 40-year-old female with hypertensive crisis. Imaging revealed bilateral adrenal adenomas. Outpatient labs confirmed dyslipidemia, impaired carbohydrate metabolism, and fatty liver. Hormonal studies established primary hyperaldosteronism. Medical therapy with mineralocorticoid receptor antagonists stabilized blood pressure and improved symptoms. Patient currently refuses surgical intervention and remains under endocrinology follow-up.

Abstract citation ID: lvag096.764

EP192 - ECE_3382 - Clinical, imaging and pathological features of adrenal ganglioneuromas: a series of 3 cases in a tertiary center

Danai Barlampa[1], Eirini Kaliakatsou[1], Athanasios Fountas[1], Kostis Karachalios[1], Charikleia Paschalidi[1], Chrysoula Samara[2], Dimitrios Bouklas[3], Marina Sassi[3], Giorgos Zografos[4], Chrysanthi Aggeli[4], Athina Markou[1] and Labrini Papanastasiou[1]
[1]Unit of Endocrinology, and Diabetes, Endocrinology, "G. Gennimatas" General Hospital of Athens, Athens 11527, Greece; [2]Radiology Department, "G. Gennimatas" General Hospital of Athens, Athens, Greece; [3]Surgical Pathologist Department, "G. Gennimatas" General Hospital of Athens, Athens, Greece; [4]Third Department of Surgery, "G. Gennimatas" General Hospital of Athens, Athens, Greece

Background: Adrenal ganglioneuromas are rare, benign tumors originating from neural crest cells and an uncommon cause of adrenal incidentalomas. They are typically non-functioning and often display non-specific imaging features, limiting reliable differentiation from other benign or malignant adrenal lesions. Due to non-specific radiological characteristics, definitive diagnosis is established postoperatively.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Aim: To present three cases of adrenal ganglioneuroma with heterogeneous imaging features, highlighting the diagnostic challenges and favorable outcomes after surgery.

Case Presentations: The first case is a 47-year-old woman who presented with persistent low back pain. A CT scan revealed a 4.2 cm retroperitoneal mass localized to the left adrenal bed, in contact with the adrenal gland with a non-contrast density of 20 HU. Subsequent MRI identified a 4.5 cm heterogeneous lesion characterized by high T2 signal intensity and absence of signal loss on out-of-phase T1 sequence. 123I-MIBG scintigraphy was unremarkable. Hormonal work-up excluded catecholamine, cortisol and aldosterone hypersecretion. The patient underwent left adrenalectomy and histopathological examination showed a maturing ganglioneuroma composed predominantly of Schwannian stroma (Ki-67 0.5%, S100, SOX10, synaptophysin positive). Postoperatively, the patient remains disease-free with no evidence of recurrence. The second case concerns a 34-year-old woman with a 2.8 cm left adrenal incidentaloma on CT, with a baseline attenuation of 35 HU. MRI revealed a 3 cm lesion with intermediate-to-low signal intensity on T2-weighted sequences and absence of signal loss on out-of-phase T1 images. The lesion was hormonally inactive. Due to indeterminate imaging characteristics surgical excision was performed. Histopathology confirmed an adrenal ganglioneuroma with predominant Schwannian stroma maturing subtype. The post-operative course was uneventful, and no relapse has been observed during follow-up. The third case involves a 61-year-old woman with bilateral adrenal adenomas (2.1 and 2.8 cm on the right and the left side, respectively) with evidence of cortisol autonomy. Contiguous with the right adrenal adenoma a 3.3 cm additional lesion was detected showing high T2 signal and marked contrast enhancement on MRI, raising suspicion for pheochromocytoma. While MIBG scintigraphy showed mildly increased uptake, urinary fractioned metanephrine and normetanephrine levels were within normal limits. The patient underwent right adrenalectomy and histopathological analysis revealed an adrenal adenoma adjacent to an adrenal ganglioneuroma (Ki-67:1.5%. SOX10, synaptophysin, S100 positive).

Conclusions: Adrenal ganglioneuromas may present with diverse and misleading imaging features. Despite thorough biochemical and radiological evaluation, pre-operative diagnosis remains challenging. Surgical resection allows definitive diagnosis and is associated with excellent prognosis.

Abstract citation ID: lvag096.765

EP193 - ECE_1036 - Adrenal tumors: a retrospective single-center overview of functional and histological characteristics

Tamara Dojcinovic[1,2], Jelena Malinovic Pancic[1,2] and Boris Dojcinovic[2,3]

[1]*University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina;* [2]*Faculty of Medicine, University of Banja Luka, Banja Luka, Bosnia and Herzegovina;* [3]*Primary Health Care Center of Banja Luka, Banja Luka, Bosnia and Herzegovina*

Introduction: Adrenal tumors are increasingly diagnosed due to the widespread use of imaging techniques, and they are often classified as incidentalomas when discovered during imaging conducted for reasons unrelated to suspected adrenal pathology. While most incidentalomas are nonfunctional, some require therapeutic intervention due to their size or functional activity.

Objective: The aim of the research is to present the most common indications for surgical treatment of adrenal tumors in one center.

Methods: This retrospective study included 74 patients with a mean age 58 years, who underwent surgical resection of adrenal tumors at the University Clinical Center of the Republic of Srpska between 2014 and 2024. Data were collected from electronic medical records.

Results: Among the 74 analyzed patients, 73% were female. The mean age at diagnosis was 57.74 ± 13.16 years (range 26-83), and the mean tumor size was 56.26 ± 22.52 mm (range 22-115 mm) Regarding hormonal activity, 51.4% of the tumors were nonfunctional. Among functional tumors, 27% ($n = 20$) of patients had Cushing syndrome, 15% ($n = 11$) had pheochromocytoma, 1.4% ($n = 1$) had paraganglioma, 2.7% ($n = 2$) had primary hyperaldosteronism, and 4.1% ($n = 3$) had adrenal cortical carcinoma. Histopathological subtypes included adenoma (48.6%), pheochromocytoma (13.5%), hyperplasia (9.5%), adrenocortical carcinoma (4.1%), and various benign lesions (ganglioneuroma, myelolipoma, cyst, paraganglioma, etc.) in smaller numbers. No statistically significant association was found between tumor size and hormonal activity ($P = .79$). Additionally, no significant difference in tumor size was observed between genders.

Conclusions: The majority of adrenal tumors surgically treated in our center were nonfunctional, consistent with data reported in the literature. Surgical intervention was mainly indicated due to tumor size.

Abstract citation ID: lvag096.766

EP194 - ECE_1654 - Primary aldosteronism with concomitant mild autonomous cortisol secretion and bilateral adrenal nodules: a management challenge

Stefania-Alexandra Bunceanu[1], Bena Andreea[2], Roxana Pui[1] and Stoian Dana[2]

[1]*Department of Doctoral Studies, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania;* [2]*Timisoara, Romania*

Background: Primary aldosteronism (PA) with concurrent mild autonomous cortisol secretion (MACS) represents a form of hormonal co-secretion that is far more common than previously appreciated, with major consequences for cardiovascular and renal morbidity, as well as substantial metabolic impact. When this co-secretion is present and imaging identifies bilateral adrenal adenomas, management becomes particularly challenging, as selecting the optimal therapeutic strategy often requires careful balancing of diagnostic uncertainty, clinical benefits, and long-term risks.

Case: A 61-year-old patient was referred for endocrine evaluation after an emergency presentation with precordial pain and palpitations, later diagnosed with paroxysmal atrial fibrillation and resistant hypertension. Severe hypokalaemia with borderline hypernatraemia prompted investigation for secondary hypertension. During the endocrine work-up, aldosterone was elevated with borderline renin, raising strong suspicion for PA. To allow accurate confirmatory testing, spironolactone was discontinued for four weeks. On reassessment, plasma renin activity was suppressed, aldosterone remained elevated, and the aldosterone-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

to-renin ratio was markedly increased (580), confirming the diagnosis of PA. Additional hormonal evaluation showed borderline ACTH, and cortisol failed to suppress adequately after the 1 mg overnight dexamethasone test, supporting concomitant MACS. For adrenal morphology, an unenhanced CT scan was performed because of chronic kidney disease (eGFR ~32 mL/min/1.73 m^2). Non-contrast CT demonstrated bilateral, homogeneous adrenal nodules (10 mm left, 12 mm right), with an initial attenuation of 20 HU. Given the contraindication to iodinated contrast, contrast-enhanced ultrasound (CEUS) was used for further characterisation: the left lesion showed no enhancement, whereas the right showed mild enhancement with heterogeneous washout, raising concern for that nodular lesion. Although CEUS is not yet standardised in adrenal imaging guidelines, it provided clinically useful information when conventional contrast-based pathways were not feasible. The patient initially declined surgery. However, as renal function deteriorated and the right adrenal nodule showed a substantial increase in attenuation to 37 HU on follow-up CT, the patient agreed to right laparoscopic adrenalectomy eight months after the initial evaluation. Histology confirmed a 1 cm adrenal adenoma with spironolactone bodies and low proliferative activity (Ki-67 2%). Histological confirmation of cortisol secretion was not available.

Outcome: After surgery, blood pressure normalised and renin recovered from suppression, consistent with biochemical remission of aldosterone excess. Renal function improved, with a higher eGFR at three months. Reassessment of cortisol autonomy showed adequate suppression on the postoperative 1 mg overnight dexamethasone test (cortisol 1.2 µg/dL), arguing against persistent MACS. The left adrenal nodule remained radiologically stable on follow-up imaging.

Abstract citation ID: lvag096.767

EP196 - ECE_3031 - A rare case of adrenal pheochromocytoma with normal plasma and urinary metanephrine levels

Elena-Maria Pavel[1], Teodora Puscas[1], Claudiu Zaharia[1], Miruna Prie[1], Diana Stanciu[2], Mihaela Stanciu[1,2] and Codruta Lebada[1,2]

[1]Department of Endocrinology, County Clinical Emergency Hospital of Sibiu, Sibiu, Romania; [2]Department of Endocrinology, Lucian Blaga University of Sibiu, Sibiu, Romania

Introduction: Pheochromocytoma is a rare tumor originating from chromaffin cells of the adrenal medulla and is characterized by excessive catecholamine secretion. The clinical presentation varies from the classic triad of hypertension, headache, and diaphoresis to entirely asymptomatic cases. Diagnosis is based on biochemical evidence of catecholamine excess and radiological localization of the tumor. Surgical resection is the treatment of choice; however, long-term postoperative surveillance is recommended.

Case Report: We report the case of a 27-year-old male with no known comorbidities who presented with right upper abdominal pain. He denied symptoms suggestive of catecholamine excess: headaches, palpitations, diaphoresis, or hypertension. Abdominal ultrasonography demonstrated a right adrenal mass. Further abdominal computed tomography (CT) and magnetic resonance imaging (MRI) confirmed the presence of a 3 × 3 cm lesion arising from the right adrenal gland. Biochemical evaluation revealed normal 24-hour urinary metanephrine levels (135 µg/24 h; reference range <400 µg/24 h), while urinary normetanephrine levels were markedly elevated (4040 µg/24 h; reference range <500 µg/24 h). Plasma metanephrine concentrations were within the normal range; however, plasma normetanephrine levels were increased approximately eightfold above the upper limit of normal. This biochemical profile was suggestive of an extra-adrenal pheochromocytoma. Despite these findings, imaging studies localized the tumor to the adrenal gland, raising suspicion of a clinically silent adrenal pheochromocytoma. The patient underwent successful laparoscopic right adrenalectomy. Histopathological examination confirmed the diagnosis of pheochromocytoma. Postoperatively, the patient had an uneventful recovery, with complete resolution of symptoms and normalization of plasma metanephrine (25 µg/24 h; reference range <100 µg/24 h) and normetanephrine levels (32 µg/24 h; reference range <216 µg/24 h).

Conclusions: This case highlights the importance of integrating clinical presentation, biochemical evaluation, and imaging findings in the diagnosis of pheochromocytoma. Two unusual features were observed: the absence of classical clinical symptoms and the presence of normal plasma and urinary metanephrine levels in the context of markedly elevated normetanephrine concentrations. Although this biochemical pattern is typically associated with extra-adrenal pheochromocytoma, imaging confirmed an adrenal origin of the tumor.

Abstract citation ID: lvag096.768

EP197 - ECE_1768 - Effective cortisol synthesis control with markedly low-dose osilodrostat in ACTH-independent Cushing syndrome: a case report

Gabriela Handzlik[1], Anna Chudek[1], Maria Świerkot[2], Ewa Płoskonka[2], Joanna Staniszewska-Mróz[2] and Jerzy Chudek[1]

[1]Department of Internal Medicine and Oncological Chemotherapy, Medical University of Silesia, Katowice, Poland; [2]Independent Public Clinical Hospital named after Andrzej Mielęcki, Medical University of Silesia in Katowice, Katowice, Poland

Introduction: Surgical adrenalectomy is the treatment of choice in ACTH-independent Cushing syndrome (CS). However, it may be contraindicated in patients with advanced age or severe comorbidities. Pharmacological treatment options include osilodrostat, an oral 11β-hydroxylase inhibitor approved for ACTH-dependent CS, which has been used sporadically in ACTH-independent CS. We present a case of ACTH-independent CS successfully controlled with extremely low doses of osilodrostat.

Case Presentation: A 64-year-old female was admitted to the endocrinology unit for evaluation of resistant hypertension with persistent hypokalemia. The initial evaluation suggested primary aldosteronism, but subsequent hormonal work-up established ACTH-independent CS, with elevated 24-hour urinary free cortisol, loss of the diurnal cortisol rhythm, unresponsiveness to 1 mg overnight dexamethasone suppression test, and decreased plasma ACTH level. Abdominal CT imaging revealed a 17-mm adrenal tumour of the right gland with benign radiological features. The patient presented with multiple, potentially CS-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

related comorbidities, including obesity (BMI 35.7 kg/m^2), type 2 diabetes mellitus, severe hypertension with kidney disease, osteoporosis (with low-trauma vertebral fractures), and severe obstructive sleep apnea. Her medical history was complicated by life-threatening infections, including severe COVID-19 pneumonia requiring ICU admission (2020) and septic shock in the course of necrotizing soft tissue infection of the lower extremity (2024). Due to the very high perioperative risk, adrenalectomy was contraindicated and pharmacological treatment with osilodrostat was initiated in March 2025 at a standard starting dose of 2 mg bid. This regimen resulted in a rapid decrease of cortisol secretion with serum cortisol levels below 3 µg/dL and concomitant symptoms of adrenal insufficiency, including nausea and hypotension, requiring temporary hydrocortisone substitution. After a gradual reduction of osilodrostat dose to 1 mg every 5 days, serum cortisol and free cortisol concentrations in daily urine collections remained within the reference. Treatment resulted in normalization of serum potassium levels, improved blood pressure control, and overall clinical status.

Conclusions: In clinical trials and in real-world settings, osilodrostat is typically administered in Cushing disease at daily doses of two to sixty milligrams. Published evidence on the use of osilodrostat in ACTH-independent CS is limited, and reports specifically addressing low-dose efficacy are lacking. This case demonstrates the effectiveness and tolerance of very low-dose osilodrostat as a treatment option for ACTH-independent Cushing syndrome in patients ineligible for surgery. It raises awareness of a wide range of osilodrostat dosing in Cushing syndrome.

Abstract citation ID: lvag096.769

EP198 - ECE_3472 - Pseudohyperkalaemia in thrombocytosis—a reminder

Bara Taufik and Asjid Qureshi
Department of Diabetes & Endocrinology, Northwick Park Hospital, London, United Kingdom

Introduction: Pseudohyperkalaemia is defined as a raised serum potassium with concurrent plasma potassium levels within the normal range. There is usually a slight difference between serum and plasma potassium levels, owing to release of potassium from activated platelets during clotting; pseudohyperkalaemia occurs where there is a difference greater than 0.4 mmol/L between the two values, in the absence of symptoms or ECG changes. While pseudohyperkalaemia occurs relatively frequently in primary care, owing to difficulties in storage and transportation of samples, it is far less common in the hospital setting.

Case: A gentleman with a background of ulcerative colitis, pancreatic cancer and diabetes mellitus was seen during a routine consultation while an inpatient for management of his diabetes. Routine blood tests showed a serum potassium of 6.0 mmol/L. There were no concerning ECG features; the hyperkalaemia was refractory to standard treatment. He did not take any medications that would predispose him to hyperkalaemia, and was adherent to a low-potassium diet as advised by a dietitian. Random cortisol was checked and was found to be 464 nmol/L, excluding Addison's disease. It was noted that he had significant thrombocytosis, with an apparent positive correlation between his platelet count and serum potassium levels. Repeat blood tests showed serum potassium of 5.6 mmol/L; the same sample was simultaneously run through a blood gas analyser, with a potassium of 4.8 mmol/L. Given all other causes of hyperkalaemia had been excluded, it would appear that this was a case of pseudohyperkalaemia secondary to thrombocytosis. He has since been referred onto a Haematologist for further investigation.

Conclusions: Pseudohyperkalaemia should always be considered in patients with unexplained, hyperkalaemia where the clinical context or progress is unusual. Identifying pseudohyperkalaemia may avoid subjecting patients to unnecessary investigations and potentially harmful treatments.

Abstract citation ID: lvag096.770

EP199 - ECE_1862 - Demographic and clinical characteristics of pheochromocytomas and paragangliomas at the University Hospital of the Canary Islands

Selena Rodriguez Fernandez, Kevin David Díaz Gorrín, Javier Panizo Fra, Paula Pérez, Óliver Quintero Rodríguez, Ana Paola Leon Ocando, MacArena Sánchez-Gallego Alonso, Itziar Aznar Ondoño and Juan Ignacio Márquez De La Rosa
Endocrinology and Nutrition, Hospital Universitario de Canarias, San Cristóbal de La Laguna, Spain

Introduction: Pheochromocytoma is a rare neuroendocrine tumor arising from chromaffin cells of the adrenal medulla, responsible for catecholamine production. Approximately 80%-85% of cases are adrenal, while the remainder occur at extra-adrenal sites (paragangliomas). The estimated annual incidence is 1-2 cases per 100 000 habitants, affecting men and women equally, with peak incidence between the third and fifth decades of life. In Spain, 83% of cases are sporadic and 17% hereditary, mainly associated with multiple endocrine neoplasia type 2A. The treatment of choice is surgical resection, preceded by alpha-adrenergic blockade. Recurrence occurs in approximately 10%-16% of patients and is more common in those with a family history or extra-adrenal tumors.

Objective: To study the clinical characteristics of patients with pheochromocytomas or paragangliomas at the University Hospital of the Canary Islands.

Materials and Methods: A retrospective observational study including patients diagnosed with pheochromocytoma and followed in the Endocrinology outpatient clinic between 2024 and 2025. A total of 14 patients were included, with a mean age of 63.78 years, of whom 71.43% were female.

Results:

- Median age at diagnosis was 57.5 years.
- Presentation as incidentaloma occurred in 47.05%, with hypertension present in 65% (17.6% paroxysmal). Other symptoms were reported in 52.9%.
- Catecholamines were elevated at diagnosis in 76.92%.
- Most frequent location was adrenal (76.47%), followed by carotid (17.64%) and auricular (5.88%). Laterality was left unilateral in 52.92%, right unilateral in 23.53%, and bilateral in 23.52%. Unifocal disease was present in 82.35%.
- Mean tumor size was 5.44 cm.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

- The most commonly used imaging modality for diagnostic confirmation was MRI (40.04%), followed by CT (33.3%) and MIBI scintigraphy (26.66%).
- Genetic testing was performed in 5 patients, with positive results in 3. Only one patient had disease associated with a syndrome (Neurofibromatosis type 1).
- The treatment of choice was laparoscopic surgery (82.35%), followed by medical therapy (11.7%) and radiotherapy (5.88%).
- Postoperative complications occurred in 5.88%.
- Additional treatment was required in 17.64% (mostly radiotherapy). Recurrence occurred in 23.53% (2 local recurrences and 2 paragangliomas at other sites).
- Mean follow-up duration was 10.07 years. Persistent hypertension was present in 23.53%, and 100% of patients currently have stable disease.

Conclusions: Given the severity of the disease, early diagnosis and surgical intervention are fundamental in the management of pheochromocytoma. Although rare, recurrence is not negligible, supporting the need for long-term follow-up.

Abstract citation ID: lvag096.771

EP200 - ECE_1398 - A calm before the catecholamine storm: case of normotensive pheochromocytoma

Radmila Milosheska[1,2], Risto Pejkov[3], Ivana Mickovski[4] and Daniela Buklioska Ilievska[5]

[1]*Endocrinology and Diabetes, General City Hospital "8th September", Skopje, North Macedonia;* [2]*Endocrinology, Diabetes and Metabolic Diseases, General City Hospital "8th September", Skopje, North Macedonia;* [3]*Urology, University Surgery Clinic "St. Naum Ohridski", Skopje, North Macedonia;* [4]*PZU Vasileva Kardio, Skopje, North Macedonia;* [5]*Pulmonology and Alergology, General City Hospital "8th September", Skopje, North Macedonia*

Background: Pheochromocytomas are functional tumors that originate from the adrenal medulla and extramedullary sympathetic ganglia, arising from chromaffin cells that secrete catecholamines. It is estimated that 5%-6.5% of all adrenal incidentalomas are pheochromocytomas, which are associated with a diverse array of clinical symptoms. Notably, around 8% of these cases may involve patients who are asymptomatic, with their diagnosis occurring incidentally or prompted by discomfort due to tumor mass growth.

Case Presentation: An 18-year-old female patient presented at the endocrinology outpatient clinic with a complaint of recurrent pain in the left lumbar region, accompanied by episodes of vomiting over the past two months. Prior imaging at another institution, specifically an abdominal ultrasound, indicated a notable displacement of the left adrenal gland, measuring 76 mm × 50 mm × 56 mm. A subsequent CT scan of the abdomen and pelvis confirmed this finding, confirming the presence of a heterogeneous ill-defined tumor mass in the area of the right adrenal gland, which also led to a comprehensive hormonal evaluation with the same measurements. The hormonal assessment revealed significant results: VMA levels were measured at 112.7 umol/dU (7.0-68.0 umol/dU), Metanephrines at 26.2 umol/dU (<5 umol/dU), Cortisol at 897 nmol/L (55-690 nmol/L), and ACTH at 28.7 pg/mL (7.2-63.3 pg/mL). These findings suggested a diagnosis of pheochromocytoma.

Management: She opted to commence treatment with a minimal dose of prazosin and planned to titrate to the optimal dosage while maintaining careful monitoring to prevent hypotensive episodes. During the laparoscopic surgical procedure, several hypertensive crises were encountered and subsequently managed by the anesthesiology team. Following this, the tumor was successfully excised using a traditional surgical approach, resulting in the removal of the tumor-altered adrenal gland, which weighed 99 grams and measured 9 cm × 6 cm × 2.7 cm. Pathological and immunohistochemical analyses indicated that the tumor was positive for Chromogranin and Synaptophysin, and S100 was positive in the sustentacular cells. Post-operative evaluations of VMA and metanephrine levels were conducted to verify normalization of both cortisol and ACTH levels.

Conclusions: Pheochromocytoma is a rare condition that presents significant challenges regarding timely diagnosis, particularly in cases involving normotensive patients, who may remain asymptomatic for extended periods until a compressive effect manifests. Therefore, it is essential to conduct hormonal evaluations for all adrenal incidentalomas, irrespective of clinical symptoms. This approach facilitates timely diagnosis and ensures appropriate preoperative preparation for patients, thereby minimizing potential complications during surgical intervention.

Abstract citation ID: lvag096.772

EP201 - ECE_1362 - Gender differences in adrenal disorders: a 16-year retrospective analysis of clinical and biochemical findings from Oman

Muzna AlHinai[1,2], Isa Alsalmi[1] and Ehab Abdelrazek[1]

[1]*The Royal Hospital, Bawshar, Oman;* [2]*Oman Medical Speciality Board, Muscat, Oman*

Background: Adrenal disorders are individually uncommon but clinically important. The incidence and prevalence of adrenal disorders in the active component of the Omani population have not been previously described.

Aim: To characterize the clinical, biochemical, and imaging profiles of all patients with confirmed primary adrenal disorders managed at the Royal Hospital Oman.

Methods: Retrospective cross-sectional situational analysis. Data retrieved from Alshifa system (Jan 2006-Dec 2022). Inclusion criteria were confirmed diagnoses of primary adrenal disorders. Patients with unconfirmed diagnoses or secondary adrenal disorders were excluded. Incidental adrenal findings not investigated were not included.

Results: A total of 129 patients met inclusion criteria. Mean age was 34.9 ± 22.4 years, with male predominance (63.8%). Statistical disparities included the prevalence of chronic hypokalaemia in males (14.5% of men vs 2.2% of females ($P = .026$). Another disparity noted is 17-hydroxyprogesterone levels were higher in women, with a mean ~201 ng/mL in females vs 51.8 ng/mL in males ($P = .021$). Imaging patterns showed no sex effect: computed tomography and Magnetic resonance imaging showed similar rates of adrenal mass detection. No gender disparity appeared in diagnostic imaging or tumour size. Most adrenal diagnoses were distributed similarly in males and females. Adrenal lipomas tended to be more frequent in women,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

but this didn't reach significance ($P = .102$). Among all studied adrenal disorders, most prevalent in our cohort was congenital adrenal hyperplasia (25%) followed by adrenal adenoma (17%). The mortality was higher in adrenocortical carcinoma compared to other included adrenal disorders, regardless of gender.

Conclusions: This 16-year analysis highlights gender differences in adrenal disorders in Oman, with CAH and adrenal adenomas being predominant. While overall disease distribution was similar between both genders, important sex-specific differences emerged: chronic hypokalaemia was more common in men, women had higher 17 hydroxyprogesterone. These results support sex-sensitive diagnostic approaches and provide baseline data to guide future research. High prevalence of CAH is likely due geographical variation, sub-analysis to investigate underlying consanguinity as contributing factor is recommended.

Abstract citation ID: lvag096.773

EP202 - ECE_3249 - Connshing syndrome: a case report

Chayma Besrour[1], Hiba Bettaieb[2], Wiem Helali[3], Manel Boudokhane[4], Rim Bourguiba[5] and Syrine Bellakhel[5]
[1]*Endocrinology, Internal Security Forces Hospital Marsa, Tunis, Tunisia;* [2]*Rhumatology, Hopital de Force de Sécurité Interieure de la Marsa, Tunis, Tunisia;* [3]*Internal Medecine, Hopital de Force de Sécurité Interieure de la Marsa, Tunis, Tunisia;* [4]*Tunis, Tunisia;* [5]*Internal Security Forces Hospital Marsa, Internal Medecine, Tunis, Tunisia*

Introduction: Primary hyperaldosteronism (Conn's syndrome) is a common cause of secondary hypertension, characterized by autonomous aldosterone secretion and suppressed renin levels. Mild autonomous cortisol secretion (MACS), often detected incidentally, is associated with subtle cortisol excess without overt Cushingoid features. The coexistence of both conditions termed «Connshing syndrome»is rare but clinically significant due to its potential impact on cardiovascular and metabolic risk.

Case report: A 60-year-old male patient with a history of type 2 diabetes mellitus, hypertension, and coronary artery disease was evaluated following incidental hypokalemia discovered during hospitalization for an acute coronary syndrome. Clinical examination did not show any abnormalities.

Endocrine Findings first exluded pheochromocytoma, Then the exploration of mineralocorticoid secretion showed an elevated plasma aldosterone level at 1346 pmol/L with renin level at 6.7 mU/L and an aldosterone-to-renin ratio of 201.9 (>64), confirming primary Hyperaldosteronism (Conn's Syndrome). As for the glucocorticoid secretion an initial 1 mg overnight dexamethasone suppression test (DST)yielded to a cortisol level of 92 nmol/L > 50 nmol/l (no suppression); repeat Standard DSTs confirmed elevated cortisol level at 111.7 nmol/L and 153.8 nmol/L, with unsuppressed levels compared to a reference threshold of 50 nmol/L. ACTH was measured at 14.4 pg/ml in favour of a mild autonomous cortisol secretion (MACS).

Contrast-enhanced adrenal CT revealed bilateral adrenal nodules: two left-sided (10 mm external limb, 8 mm internal) and one right-sided (9 mm internal). A follow-up scan after one year confirmed persistence of similar bilateral nodules.

The patient exhibits primary hyperaldosteronism with concurrent mild autonomous cortisol secretion, consistent with a Connshing syndrome.

Discussion: Connshing syndrome affects approximately 20%-30% of patients with primary hyperaldosteronism and is associated with a higher cardiovascular risk profile due to the synergistic effects of aldosterone and cortisol excess on blood pressure, glucose metabolism, and vascular remodeling.

Early recognition of dual hormone secretion is crucial for optimal management and risk stratification, particularly in patients with pre-existing cardiovascular disease.

Abstract citation ID: lvag096.774

EP203 - ECE_3824 - Significance of primary aldosteronism forms not meeting syndrome's conventional criteria

Piotr Kmieć
Department of Endocrinology and Internal Medicine, Medical University of Gdańsk, Gdańsk, Poland

Significance of Primary Aldosteronism Forms Not Meeting Syndrome's Conventional Criteria

The established diagnostic work-up of primary aldosteronism (PA) has consisted of three consecutive steps: screening of at-risk populations using the aldosterone-to-renin ratio (ARR), confirmatory testing in those with a positive screen, and subtyping (between a familial form, adrenocortical carcinoma, bilateral or unilateral disease). PA has been effectively excluded if: 1) the patient did not belong to one of the risk groups, 2) screening, or 3) confirmatory test were negative.

A plethora of evidence in the last two decades has proven the inadequacy of this dichotomous approach. Like other endocrinopathies, PA encompasses a wide spectrum of clinical and hormonal presentations. It can be present in individuals with normotension and normokalemia as well as lead to life-threatening hypertensive crises and/or hypokalemia.

The 2025 Endocrine Society guideline has reframed the PA diagnostic work-up radically. It mirrored the European Society of Cardiology 2024 guideline in suggesting PA screening among all adult patients with HT (McEvoy et al., European Heart Journal, 2024(45); Adler et al., JCEM, 2025(110)). Conversely, the application of confirmatory tests is to be limited, owing to lack of/poor evidence that using them improves the management. The document repeatedly emphasizes the difficulty of defining diagnostic thresholds due to the continuous nature of hormonal parameters, which necessitates a probabilistic approach (diagnosis more or less likely). The progressive hormonal severity of mild/subclinical PA has been evidenced (Buffolo et al., Hypertension, 2024(81)).

Mild PA forms have become more relevant in light of to-date studies associating dysregulated aldosterone secretion with the development of HT, vascular, renal, and metabolic complications. Just as overt PA can be successfully managed with targeted treatment, it is necessary to consider the same therapies in its less severe forms.

Clear renin suppression justifies mineralocorticoid-receptor antagonist (MRA) therapy and warrants consideration of surgically treatable PA. However, intermediate (PRA 0.5-1.0 ng/mL/h or direct renin 6-15 mIU/L) levels that yield an ARR below overt PA criteria (2.0-2.5 ng/mIU) constitute a diagnostic gray zone. The PATHWAY-2 trial, its substudies, and a recent meta-analysis indicate MRAs are superior in low-renin HT but optimal thresholds

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

remain undefined (Shah et al., J Hum Hypertens 2024(38), Williams et al., Lancet 2015(386), Williams et al. Lancet Diabetes Endocrinol 2018(6)). The ongoing REMASTER trial may help clarify whether patients in this intermediate zone benefit more from MRA or conventional HT therapy (Shah et al., J Hum Hypertens 2024(38)).

Abstract citation ID: lvag096.775

EP205 - ECE_2162 - Clinical profile of primary aldosteronism patients attending a tertiary endocrine center in Nepal

Ansumali Joshi[1,2], Srijana Karmacharya[1], Puspa Dahal[1], Smriti Khadka[1], Radhika Tuladhar[1] and Sapana Yadav[1]
[1]*Kathmandu Diabetes and Thyroid Center, Lalitpur, Nepal;* [2]*Kathmandu Diabetes and Thyroid Centre, Kathmandu, Nepal*

Primary aldosteronism patients' data is scarce in Nepal. We retrospectively reviewed all 18 patients with Primary aldosteronism from 2010 to 2024. 10(55.56%) patients were males and 8(44.44%) were females with M: F ratio 1.25:1. Mean age was 53.66 ± 12.86 years and mean BMI was 25.26 ± 3.71 Kg/m^2. Presenting clinical features were uncontrolled hypertension in 7(38.89%), hypertension with hypokalemia in 6(33.33), incidental adrenal adenoma in 1(5.56%) and asymptomatic in 6(33.33%). Resistant hypertension was seen in 3(16.67%) patients. Mean SBP at presentation was 155.55 ± 17.2 mmHg and DBP was 98.88 ± 10.22 mmHg. Mean Potassium level was 3.67 ± 0.62 mEq/L, sodium level was 139.16 ± 2.72 mEq/L and eGFR was 83.58 ± 28.02 ml/min/1.723 m^2. Plasma aldosterone level was 103.83 ± 145.04 ng/dl and plasma renin activity was 0.59 ± 0.74 ng/ml/hr. In some patients, direct renin measurement was done and mean was 1.31 ± 1.13 mlU/l. Mean aldosterone: plasma renin activity ratio was 371.65:1 and mean aldosterone: direct renin ratio was 207.56:1. Bilateral adrenal hyperplasia was seen in 7 (38.89%) and unilateral in 1(5.56%). Adenoma was seen in 9 (50%). Right sided adrenal adenoma was seen in 3(16.67%) and left sided in 6(33.33%). Surgery for unilateral adenomas was done in 7 (38.89%) patients. Rest was put on Spironolactone. Surgery was curative with no anti-hypertensives required in 1 patient only and 1-2 anti-hypertensive in 6 (33.33%) patients at 6 months follow up. With spironolactone use, hypertension was well controlled in all patients.

Abstract citation ID: lvag096.776

EP206 - ECE_3638 - Adrenal hemorrhage: a rare diagnostic challenge

Bárbara Jesus[1], Ana Margarida Sobral[1], Adriana Duarte[1], Mariana Coelho[1], Leonor Rodrigues[2], Alice Monsanto[1], Tânia Carvalho[1], Gustavo Rodrigues[1], Mariana Lavrador[1], Dírcea Rodrigues[1] and Leonor Gomes[1]
[1]*Local Health Unit of Coimbra, Coimbra, Portugal;* [2]*Local Health Unit of Aveiro, Aveiro, Portugal*

Introduction/Background: Adrenal incidentalomas are frequently detected on cross-sectional imaging and require systematic evaluation to exclude hormonal hypersecretion and malignancy. Adrenal hemorrhage is rare, occurring in approximately 0.11% of imaging studies, and can closely mimic adrenal neoplasms, often presenting as a suspicious mass. Clinical manifestations range from incidental findings to nonspecific abdominal pain, acute adrenal insufficiency, or cardiovascular compromise. Predisposing factors include anticoagulation, trauma, neoplastic disease, infections, acute stress, coagulopathy and systemic disorders. We present a case of a left adrenal mass initially suspected to be neoplastic, ultimately diagnosed as an adrenal hemorrhage.

Clinical case: A 63-year-old male was referred to Endocrinology after incidental detection of an adrenal mass on chest CT, performed for chronic cough. A subsequent abdominal CT was requested to further characterize the lesion, revealing a 5.3 cm left adrenal nodule, slightly heterogeneous with focal calcification, with 33HU and markedly low absolute (33%) and relative (5%) washout values. Small abdominal lymph nodes were noted, the largest measuring 1 cm.

Due to the size and highly suspicious imaging features, the patient was admitted directly in the Endocrinology ward for expedited evaluation. He was asymptomatic, denying abdominal pain or symptoms suggestive of hormonal hypersecretion. Medical history included hypertension diagnosed approximately 10 years earlier, well controlled with perindopril/amlodipine; type 2 diabetes, dyslipidemia, anemia, alcohol-related chronic liver disease, peripheral arterial disease, and active smoking. Medications also included carvedilol, metformin/dapagliflozin, sitagliptin, rivaroxaban and atorvastatin/ezetimibe.

During hospitalization, a comprehensive hormonal evaluation was performed, including plasma metanephrines and 3-methoxytyramine, 24-hour urinary free cortisol, ACTH/cortisol circadian rhythm, 1mg dexamethasone suppression test, and androgens, all within the reference ranges, effectively excluding pheocromocytoma, hypercortisolism and androgen excess.

The patient subsequently underwent laparoscopic left adrenalectomy, without complications. Histopathology revealed an organized, thrombosed adrenal hematoma and no evidence of malignancy. The postoperative course was uneventful, and he was discharged from both Urology and Endocrinology follow-up.

Discussion/Conclusions: This case illustrates that adrenal hemorrhage can mimic neoplastic adrenal lesions, posing a diagnostic challenge. The combination of low washout, focal calcification and size >5 cm raised substantial concern for malignancy, justifying surgical intervention despite an asymptomatic presentation. In this patient, anticoagulation and advanced chronic liver disease likely contributed to hemorrhage risk. While most adrenal hemorrhages resolve spontaneously, surgical resection should be considered when imaging cannot reliably exclude neoplasia, particularly given that 48% of hemorrhages with associated masses harbor pheochromocytoma. Comprehensive hormonal assessment, careful imaging interpretation, and multidisciplinary management are essential for appropriate treatment decisions.

Abstract citation ID: lvag096.777

EP207 - ECE_1395 - Adrenal crisis in a 36-year-old male with pneumonia: a case report of complications leading to adrenal coma, rhabdomyolysis, and acute kidney failure

Ivana Mickovski[1,2], Radmila Milosheska[3] and Daniela Buklioska Ilievska[1,3]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Faculty of Medical Sciences, Goce Delcev University, Stip, North Macedonia; [2]PZU Vasileva Kardio, Skopje, North Macedonia; [3]General City Hospital 8th September, Skopje, North Macedonia

Background: Adrenal crisis is a rare but life-threatening emergency caused by acute adrenal insufficiency, often triggered by infections or physiological stress. Rapid diagnosis and treatment are essential to prevent multi-organ failure.

Case presentation: We present a 36-year-old previously healthy male admitted with pneumonia who developed adrenal crisis complicated by adrenal coma, rhabdomyolysis, and acute kidney failure. The patient presented with hypotension, fever, and altered consciousness. Laboratory findings revealed hyponatremia (Na 122 mmol/L), hyperkalemia (K 6.1 mmol/L), hypoglycemia, elevated creatine kinase (12 000 U/L), and acute renal impairment (creatinine 3.8 mg/dL). Serum cortisol was critically low (2.1 µg/dL), confirming adrenal insufficiency.

Management and Outcome: Immediate treatment with intravenous hydrocortisone (100 mg bolus followed by infusion), aggressive fluid resuscitation, and broad-spectrum antibiotics resulted in rapid hemodynamic stabilization. Supportive measures for rhabdomyolysis and renal failure were implemented, leading to full recovery within one week. The patient was discharged on maintenance oral corticosteroid therapy and scheduled for endocrinology follow-up.

Conclusions: This case highlights the importance of early recognition and prompt corticosteroid replacement in adrenal crisis, particularly in patients with infection-related triggers. Rapid intervention with hydrocortisone, antibiotics, and intensive fluid therapy remains the cornerstone of successful management.

Keywords adrenal crisis, adrenal insufficiency, pneumonia, rhabdomyolysis, acute kidney failure

Abstract citation ID: lvag096.778

EP208 - ECE_1597 - Dual ectopic thyroid tissue with a eutopic thyroid gland: an unusual presentation of struma ovarii

Arshiya Dutta[1], Amal Shaharyar[2] and Pinaki Dutta[2]
[1]Medicine, Maharishi Markandeshwar University, MBBS, Solan Tehsil, India; [2]Endocrinology, Postgraduate Institute of Medical Education and Research Chandigarh, Chandigarh, India

Context: Struma ovarii is an exceptionally rare monodermal ovarian teratoma characterized by the predominance of thyroid tissue and is frequently misdiagnosed due to its nonspecific clinical and radiological features. Preoperative differentiation from other ovarian neoplasms is challenging, and definitive diagnosis is usually established only on histopathological examination.

Case description: We report a case of unilateral benign struma ovarii in a 19-year-old unmarried female, in which the tumor closely mimicked ovarian malignancy on imaging owing to its large size and complex morphology, despite normal tumor markers and thyroid function tests. The patient was successfully managed with fertility-preserving surgical excision. Postoperative endocrine evaluation confirmed a normally functioning eutopic thyroid gland and a coexisting thyroglossal duct cyst, representing a rare occurrence of dual ectopic thyroid tissue in the presence of a eutopic thyroid gland.

Conclusions: This case highlights the diagnostic challenges of struma ovarii, particularly in young patients, and underscores the importance of histopathology in establishing the diagnosis. Surgical resection remains the cornerstone of treatment and is associated with an excellent prognosis in benign cases.

Keywords struma ovarii, ovarian goitre, ovarian thyroid, euthyroid

Abstract citation ID: lvag096.779

EP1675 - ECE_1980 - CT-based radiomics for differentiation of adrenal lesions

Almaz Manaev[1,2], Natalya Tarbaeva[1], Kseniya Vysotskaya[1], Anastasia Chevais[1], Anna Roslyakova[1], Ekaterina Troshina[1], Nadezhda Platonova[1], Galina Melnichenko[1] and Natalia Mokrysheva[1]
[1]Endocrinology Research Centre, Moscow, Russia; [2]National Research Nuclear University MEPhI, Moscow, Russia

Introduction: Adrenal lesions present a significant diagnostic challenge, as their etiologies range widely from benign adenomas to aggressive malignancies. Accurate differential diagnosis is therefore critical for determining appropriate treatment and prognosis. Recent advances in quantitative image analysis, particularly radiomics, offer a promising solution by identifying subtle patterns invisible to the human eye. Integration of quantitative imaging data with machine learning algorithms provides a powerful framework for building objective diagnostic models

Objective: Development and validation of a machine learning model utilizing CT texture analysis for the differential diagnosis of adrenal lesions.

Methods: This retrospective single-center study included 570 patients with histologically confirmed adrenal tumors: 40 cases of adrenocortical carcinoma, 180 lipid-poor adenomas, 50 lipid-rich adenomas, 15 cysts, 35 myelolipomas, 15 lesions of neurogenic origin, and 235 pheochromocytomas. Radiomic features were extracted from four-phase contrast-enhanced CT images using the PyRadiomics 3.1.0 module after manual 3D segmentation.

Feature reproducibility was assessed using the intraclass correlation coefficient (ICC), and feature variability was evaluated via the coefficient of variation (CV). To mitigate technical variability, CT attenuation data were standardized using the mean aortic attenuation as an internal reference. A LightGBM gradient boosting model was implemented in Python (version 3.9.21) for classification tasks.

The study protocol was approved by the Institutional Review Board of the Endocrinology Research Centre (Protocol No. 20, dated November 13, 2024).

Results: The extracted radiomic features demonstrated high reproducibility, with 70.3%-82.3% exhibiting an ICC > 0.9 across the different CT phases. Standardization using aortic attenuation significantly reduced feature variability, increasing the proportion of stable features (CV < 0.15) from 12.9%-27.7%.

The binary classification model (malignant vs benign) achieved high diagnostic performance on the test set, with a sensitivity of 0.945, specificity of 0.932, and an area under the receiver operating characteristic curve (AUC) of 0.944. However, the multiclass model for differentiating specific tumor subtypes showed limited accuracy. Performance was particularly low for

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

lipid-rich adenomas, cysts, and lesions of neurogenic origin, with F1-scores ranging from 0 to 0.333.

The main limitations of this study include its retrospective design, the lack of a standardized CT acquisition protocol, and an imbalanced dataset.

Conclusions: The proposed CT radiomics-based model demonstrated high efficacy for the binary classification of adrenal lesions as benign or malignant, highlighting its potential utility for initial screening. However, its diagnostic value for the precise subtyping of adrenal tumors remains limited.

Abstract citation ID: lvag096.780

EP1677 - ECE_1420 - Regional and gender disparities in lipid-lowering therapy among diabetic patients: a comprehensive Spanish nationwide study 2020-2024

Jessica Ares Blanco[1,2,3], Miguel García[1,2], Alicia Martín-Nieto[3], Elías Delgado[1,2,3] and Edelmiro Luis Menéndez-Torre[1,2,3]

[1]University of Oviedo, Oviedo, Spain; [2]Instituto de Investigación Sanitaria del Principado de Asturias, Oviedo, Spain; [3]Hospital Universitario Central De Asturias, Oviedo, Spain

Introduction: Cardiovascular disease remains the leading cause of morbidity and mortality in patients with diabetes. Lipid-lowering therapy is a cornerstone of cardiovascular prevention in this population, yet treatment patterns and equity of access across different demographic groups remain incompletely characterized. With Spain's diabetes prevalence reaching 14.8% and over 5.1 million affected adults, understanding treatment distribution patterns is essential for optimizing preventive strategies.

Objectives: To analyze geographic, gender, and age-related patterns in lipid-lowering treatment among Spanish diabetic patients over a five-year period, and to identify potential disparities in treatment access and utilization.

Methods: Comprehensive descriptive analysis of lipid-lowering therapy data from 2020 to 2024 across all 19 Spanish administrative regions. Data were stratified by sex, four age groups (0-14, 15-34, 35-64, ≥65 years), and year. Regional treatment distributions were contextualized within known diabetes prevalence patterns. Temporal trends were analyzed to assess treatment expansion and consistency across demographic subgroups.

Results: Overall treatment coverage expanded from 3 440254 cases (2020) to 3 962 928 (2024), representing 15.2% growth. Based on national diabetes prevalence estimates, approximately 77%-78% of Spanish diabetic patients receive lipid-lowering therapy.

A persistent gender gap was observed throughout the study period, with men representing 54.1% of treated patients vs 45.9% women, remaining stable across all years. This disparity was most pronounced in the 35-64 age group (60.1% men vs 39.9% women) but attenuated in elderly c 46.6% women).

Age distribution revealed that elderly patients (≥65 years) comprised 64% of all treatments, with particularly high representation among women (68.4% of treated women vs 60.6% of treated-men belonged to this age group).

Geographic analysis showed substantial variation in absolute treatment numbers, with Andalusia leading (759 164 cases in 2024), followed by Catalonia (586 075) and Valencia (505 628). These patterns align with regional diabetes prevalence variations, ranging from 4.51% in Castilla-León to 9.72% in Canary Islands. However, the male-to-female treatment ratio remained consistent across all regions, suggesting systemic rather than regional gender disparities.

Conclusions: Spain demonstrates high overall lipid-lowering therapy coverage in diabetic patients with consistent expansion across regions. However, significant gender disparities persist, particularly in middle-aged populations, with women accessing treatment predominantly at older ages. These findings suggest potential undertreatment or delayed treatment initiation in women, representing a critical gap in cardiovascular prevention. Future research should investigate whether these patterns reflect differences in diabetes phenotypes, prescribing practices, patient preferences, or healthcare access barriers to inform targeted public health strategies.

Abstract citation ID: lvag096.781

EP1683 - ECE_2487 - Cardiometabolic burden and predictors of functional status in adrenal incidentalomas

Mădălina Elena Iftimie[1,2], Iulia Florentina Burcea[1,2], Ramona Dobre[1,2] and Cătălina Poiană[1,2]

[1]Endocrinology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [2]Endocrinology I, "C.I.Parhon" National Institute of Endocrinology, Bucharest, Romania

Introduction: Adrenal incidentalomas (AIs) are a frequent discovery nowadays because of routine cross-sectional imaging. While functioning AIs, including mild autonomous cortisol secretion (MACS) are linked to cardiometabolic morbidity, emerging data show that non-functioning incidentalomas also carry significant metabolic risks and higher mortality than controls. We aim to characterize the clinical and epidemiological features of AIs evaluated in a tertiary endocrinology clinic.

Methods: We conducted a retrospective observational study of all patients investigated for incidentally discovered adrenal tumors at "C.I. Parhon" National Institute of Endocrinology between October 2023-October 2025. We excluded patients with tumors <1 cm and incomplete records. Demographic, imaging, hormonal and comorbidity data were collected and compared between functioning and non-functioning AI.

Results: 194 patients were included in the final analysis (83.5% female, mean age 59.68 ± 9.48 years). The majority of adrenal masses were discovered by computed tomography scans (75.3%), performed for abdominal pain or digestive complaints. Mean tumor diameter was 26.5 ± 12.4 mm. Most lesions had benign imaging characteristics (91.8%) and were unilateral (62.4%). Functional classification: non-functioning AI 51.0%, MACS 40.7%, overt Cushing's 4.1%, primary hyperaldosteronism 2.1%, pheochromocytoma 1.0% and mixed cortisol-aldosterone hypersecretion 1.0%. Cardiometabolic comorbidities were common overall (dyslipidemia 87.6%, hypertension 78.9%, diabetes mellitus (DM)/impaired glucose tolerance 51.0%, obesity 47.9%) and were similarly prevalent in functioning and non-functioning AI subgroups, irrespective of hypersecretory phenotype. Functioning AIs had larger maximum tumor diameters than non-functioning lesions (29.6 vs 23.5 mm; $P < .001$), but no significant differences were found between the two subgroups for

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

major cardiovascular events ($P = .193$) or mortality ($P = .703$). Multivariate logistic regression identified maximum tumor diameter (OR 1.049 per mm, $P < .001$), presence of DM (OR 1.598, $P = .031$) and female sex (OR 2.606, $P = .033$) as independent predictors of functioning status. Receiver Operating Characteristic (ROC) analysis of a combined prediction model showed moderate discrimination between functioning and non-functioning adrenal tumors (area under the curve 0.666).

Conclusions: In this tertiary cohort, adrenal incidentalomas carried a high burden of cardiometabolic comorbidity, regardless of their functional status, suggesting that the line between functioning and non-functioning AIs may be a false dichotomy. Maximum tumor diameter, female sex and presence of DM could predict the functional status of AI, but these findings warrant prospective validation.

Abstract citation ID: lvag096.782

EP209 - ECE_1985 - Parathyroidectomy reduces systemic inflammatory indices in patients with primary hyperparathyroidism

Jake Schembri, Simon Mifsud and Mark Gruppetta
Department of Diabetes and Endocrinology, Mater Dei Hospital, Msida, Malta

Introduction: The classical manifestations of primary hyperparathyroidism (PHPT) mainly involve skeletal and renal end-organ complications. However, a spectrum of non-classical manifestations associated with PHPT has also been described, including cardiovascular (CV) and neurocognitive sequalae.[1] Recent literature reports elevated inflammatory markers such as high-sensitive C-reactive protein and tumour necrosis factor-alpha in patients with PHPT. Since chronic low-grade inflammation is central to the pathogenesis of atherosclerosis, this may represent a mechanism underlying the increased risk of CV disease observed in PHPT patients.[2] In this study, we investigated whether systemic inflammatory indices (derived from readily available haematological parameters) change following curative parathyroidectomy in patients with PHPT.

Method: We retrospectively reviewed patients with PHPT who underwent parathyroidectomy between 2017 and 2019. Parathyroid hormone (PTH), corrected calcium, white cell count (WCC), neutrophil count, lymphocyte count, platelet count, neutrophil-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII) were evaluated at baseline (pre-parathyroidectomy) and 6 months post-parathyroidectomy.

Results: 56 patients with PHPT underwent parathyroidectomy during the study period. The mean age was 60.4 years (SD 12.3), with a female predominance of 71.4% ($n = 40$). Significant pre-operative to post-operative decreases were observed in corrected calcium (median 2.80 mmol/L (IQR:2.73-2.9) to 2.30 mmol/L (IQR:2.23-2.35), $P < .001$) and PTH (median 160 ng/L (IQR:121.1-235.7) to 35.4 ng/L (IQR:27.7-54), $P < .001$).

WCC and neutrophil counts also declined significantly post-parathyroidectomy. Median WCC decreased from 7.21×10^9/L (IQR:5.97-7.96) to 6.59×10^9/L (IQR:5.36-7.82) ($P = .004$) and median neutrophil count decreased from 4.61×10^9/L (IQR:3.46-5.3) to 3.7×10^9/L (IQR:2.97-5.13) ($P = .002$). There was no significant difference between pre- and post-operative lymphocyte or platelet counts ($P = .159$ and $P = .92$, respectively).

Post-parathyroidectomy, median SII improved from 557.8 (IQR:440.8-789.4) to 540.8 (IQR:331.7-734.4) ($P = .011$), and median NLR decreased from 2.41 (IQR:1.81-2.99) to 2.13 (IQR:1.51-2.84) ($P = .037$).

Conclusions: In this retrospective cohort, curative parathyroidectomy for patients with PHPT was associated with significant improvement in systemic inflammatory indices (SII and NLR) and reductions in WCC and neutrophil counts at 6 months. Overall, the observed reduction in SII and NLR following parathyroidectomy is consistent with previous studies, suggesting that this low-grade inflammation observed in PHPT may be reduced following surgical intervention.

References

1. El-Hajj Fuleihan G, Chakhtoura M, Cipriani C, et al. Classical and nonclassical manifestations of primary hyperparathyroidism. *J Bone Miner Res*. 2022;37(11):2330-2350. https://doi.org/10.1002/jbmr.4679
2. Christensen MHE, Dankel SN, Nordbø Y, et al. Primary hyperparathyroidism influences the expression of inflammatory and metabolic genes in adipose tissue. *PLoS One*. 2011;6(6):e20481. https://doi.org/10.1371/journal.pone.0020481

Abstract citation ID: lvag096.783

EP210 - ECE_1576 - Divergent roles of the vitamin D receptor in the osteoclast lineage and cathepsin K-expressing cells in bone homeostasis

Dong-Kyo Lee[1], Kyung-Hwa Kim[1], Na-Rae Park[1], Xian Jin[1], Ying Cui[1], Xiangguo Che[1], Sihoon Lee[2], Shigeaki Kato[3], Hyun-Ju Kim[1] and Je-Yong Choi[1]
[1]Department of Biochemistry and Cell Biology, Cell and Matrix Research Institute, School of Medicine, Kyungpook National University, Daegu, South Korea; [2]Department of Internal Medicine and Laboratory of Genomics and Translational Medicine, Gachon University College of Medicine, Incheon, South Korea; [3]Graduate School of Life Science and Engineering, Iryo Sosei University, Iwaki, Fukushima, Japan

Vitamin D receptor (VDR) signaling is a central regulator of bone homeostasis, yet its cell-specific function within the bone microenvironment remains controversial. Here, we show that VDR is highly expressed in early-stage osteoclastogenic cells but is barely detectable in fully mature osteoclasts. To dissect lineage-specific roles of VDR, we utilized two conditional knockout models: *LysM;Vdr$^{f/f}$*, lacking VDR in osteoclast precursors, and *Ctsk;Vdr$^{f/f}$*, lacking VDR in cathepsin K–expressing cells. In vitro, $1,25(OH)_2D_3$ suppressed osteoclastogenesis in WT cells, an effect abolished in *LysM;Vdr$^{f/f}$* cells but retained in *Ctsk;Vdr$^{f/f}$* cultures, indicating that the inhibitory action of vitamin D-VDR signaling occurs primarily at the precursor stage. Mechanistically, $1,25(OH)_2D_3$ promoted proteasome-dependent degradation of c-Fos in WT cells, a process absent in *LysM;Vdr$^{f/f}$* cells. VDR interacted with c-Fos in pre-osteoclasts, and this association was reduced following $1,25(OH)_2D_3$ treatment, consistent with ligand-induced c-Fos degradation. Despite these in vitro findings, *LysM;Vdr$^{f/f}$* mice exhibited normal bone homeostasis under

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

physiological conditions. In contrast, *Ctsk;Vdr*$^{f/f}$ mice displayed increased bone mass driven by enhanced osteoblast activity rather than altered osteoclast function. Collectively, these findings suggest that while VDR in the osteoclast lineage is not a major regulator of physiological bone homeostasis, VDR in non-osteoclastic Ctsk-expressing cells, potentially including periosteal stem cells, may act as a negative regulator of bone formation, providing a novel perspective on vitamin D action in the skeleton.

Abstract citation ID: lvag096.784

EP211 - ECE_1721 - Familial hypocalciuric hypercalcaemia with CaSR missense variant, two case reports

Alhasan Al-Saadi[1,2], Emmon Kiyani[1], Sucheeth Gowda[1], Abdullatif Farhat[1] and Ravikumar Ravindran[1]
[1]*Aneurin Bevan Health Board, Newport, United Kingdom;* [2]*The Aneurin Bevan—JD Wetherspoon, Newport, United Kingdom*

Background: Familial hypocalciuric hypercalcaemia (FHH) is a rare benign genetic condition, with an estimated prevalence of approximately 1 in 78 000 people in the general population. It displays an autosomal dominant pattern of inheritance with high penetrance, and it affects both men and women equally. FHH is caused by loss of function mutation in the CaSR gene leading to decreased receptor activity in response to serum calcium levels. CaSR in the parathyroids, senses minute changes in blood calcium and controls parathyroid hormone release and hence regulates serum calcium levels. Loss of function mutation in CaSR reduces the receptors' ability to detect high calcium levels, leading to inappropriately high calcium levels in the blood and normal to slightly elevate PTH levels in the blood. The inactivating mutation also affects the CaSR in the kidneys. In normal conditions, the CaSR in the kidneys normally sense high serum calcium levels and reduces calcium reabsorption. This defect leads to a relative over-reabsorption of calcium in the renal tubules, resulting in hypocalciuria.

Methods: 2 case studies are reported involving patients with hypercalcemia with a normal Parathyroid hormone (PTH) The clinical presentation, the investigations and the genetic test results are reviewed alongside a literature review was conducted to understand the importance of CaSR gene testing.

Case presentation: We report two cases,

The first case is one of a 60-year-old female. She was referred with High Calcium 2.86 mmol/L since November 2022. Her main symptom was fatigue with a family history of hypercalcemia. PTH was normal and Vitamin D level was corrected with no improvement in her biochemistry. Other blood tests were unremarkable.

The second case is one of a 41-year-old male who presented with nausea & fatigue. His Calcium Levels were 2.71 mmol/L with a normal PTH and corrected Vitamin D level. His mother had asymptomatic longstanding hypercalcaemia

Their Calcium Creatinine clearance ratio was calculated to be 0.00662, 0.00888 respectively.

Subsequently both cases underwent Genetic testing which confirmed the Diagnosis of FHH (Consistent with a genetic diagnosis of CaSR-related hypocalciuric hypercalcaemia)

Conclusions: We recommend a two-step diagnostic process as follows: the calcium/creatinine clearance ratio (CCCR) is measured from a 24-hour urine sample and then all patients with CCCR of 0.020 or less are tested for mutations in the CASR gene. Patients who have a family history of Hypercalcemia with Higher CCCR are also recommended for testing. The diagnostic sensitivity of this setup is 98%.

Abstract citation ID: lvag096.785

EP212 - ECE_2899 - Laser thermal ablation of the parathyroid glands in a patient with MEN1 syndrome—a case report

Dominika Kaszewska-Perka[1], Łukasz Krotowski[1], Małgorzata Wichlińska[1], Ewelina Witkowska[1], Agnieszka Domańska-Czajka[1], Monika Pacocha[1], Janusz Łuczak[1], Anna Fedorczak[1], Renata Stawerska[1,2] and Arkadiusz Zygmunt[1,2]
[1]*Department of Endocrinology and Metabolic Diseases, Polish Mother's Memorial Hospital—Research Institute, Lodz, Poland;* [2]*Department of Developmental Age and Adult Endocrinology, Medical University of Lodz, Lodz, Poland*

Introduction: Multiple endocrine neoplasia type 1 (MEN1) is a hereditary disorder caused by germline mutations in the *MEN1* gene, most commonly manifesting as multiglandular and recurrent primary hyperparathyroidism. Surgical treatment is associated with a risk of disease recurrence or the development of permanent hypoparathyroidism. Minimally invasive techniques, such as percutaneous laser thermal ablation, may represent an alternative therapeutic option in selected patients.

Case description: A case of a 38-year-old man with genetically confirmed MEN1 syndrome (c.781C > T mutation in the *MEN1* gene, detected in September 2021) and a positive family history of MEN1 was presented. The patient was diagnosed with primary hyperparathyroidism complicated by nephrolithiasis, osteopenia, and arterial hypertension. Imaging studies revealed three focal lesions corresponding to the parathyroid glands, including a dominant enlarged parathyroid gland located posterior to the middle portion of the left thyroid lobe ($15 \times 10 \times 18$ mm). Biochemical evaluation showed an elevated parathyroid hormone level (PTH 145.4 pg/mL), hypercalcemia (total calcium 2.85 mmol/L, ionized calcium 1.55 mmol/L), hypophosphatemia (0.69 mmol/L), and concomitant hypercalciuria.

Methods: Under ultrasound guidance, the patient underwent two sessions of percutaneous laser thermal ablation of the parathyroid glands using the EchoLaser system. The first procedure, performed in May 2025, was carried out with an energy of 1204 J, resulting in a partial improvement in biochemical parameters. Due to the persistence of primary hyperparathyroidism, a second procedure targeting the same lesion was performed in November 2025, using a higher energy setting (4013 J).

Results: Twenty-four hours after the second procedure, a significant reduction in PTH levels was observed (from 116 pg/mL to 69 pg/mL), accompanied by normalization of serum calcium (from 2.87 mmol/L to 2.54 mmol/L) and phosphate levels (from 0.76 mmol/L to 1.00 mmol/L). No adverse events related to the thermal ablation procedures were observed, and no hypoparathyroidism developed.

Conclusions: Percutaneous laser thermal ablation enabled effective biochemical control of hyperparathyroidism in the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

presented patient with MEN1 syndrome, without the occurrence of complications. Given the multifocal and recurrent nature of hyperparathyroidism in MEN1, laser thermal ablation may represent a safe, repeatable, and minimally invasive therapeutic option in carefully selected patients, particularly in those at high surgical risk or who do not consent to surgical treatment.

Abstract citation ID: lvag096.786

EP214 - ECE_1803 - Type 2 diabetes control—managing bone strength and microarchitectural damage

Iustina Cosmina Mogos[1,2], Dan Alexandru Niculescu[2,3], Roxana Dusceac[3] and Catalina Poiana[2,3]
[1]*Endocrinology, Spitalul Clinic de Urgență Prof. Dr. Agrippa Ionescu, București, Romania;* [2]*Carol Davila University of Medicine and Pharmacy, București, Romania;* [3]*Institutul Național de Endocrinologie CI Parhon, București, Romania*

Introduction: The bone paradox of type 2 diabetes patients consists of the higher incidence of fracture numbers encountered despite high bone mineral density measured by X-ray osteodensitometry. One of the potential explanations is the intricated microarchitecture deterioration.

Methods: We conducted an observational, prospective, single-center study including 604 postmenopausal women and men with type 2 diabetes (281), prediabetes (197) or normal glycemic profile (126). X-ray densitometry with trabecular bone score measurement were performed measuring the lumbar spine, femur neck and distal radius. We collected data on participants' glycemic balance and vitamin D levels.

Results: Bone mineral density was higher at all sites in the prediabetes and type 2 diabetes groups. We did not find a relationship between glycemic control—glycosylated hemoglobin and bone damage reflected by bone mineral density or T-score, at any of the three investigated sites. Adjusted absolute bone mineral density after analysis of covariance showed in the control group a BMD in lumbar spine 1.056 ± 0.018, femur neck 0.832 ± 0.12 , distal radius 0.764 ± 0.009. The prediabetes cohort had a BMD in lumbar spine 1.076 ± 0.013, femur neck 0.840 ± 0.009, distal radius 0.775 ± 0.007. The type 2 diabetes patients had a BMD in lumbar spine 1.132 ± 0.011, femur neck 0.892 ± 0.007, distal radius 0.792 ± 0.006. The BMI difference between groups was not statistically significant. The trabecular bone score did not differ significantly between the three groups. The majority of patients had normal TBS 283 (55.49%), 216 patients (42.35%) had partly degraded microarchitecture, and only 11(2.6%) had degraded bone microarchitecture. The densitometry results showed that 193 (31.9%) patients had osteoporosis, 284 had osteopenia (46.94%) and 128 (21.16%) patients had normal BMD. Osteoporosis was found in 22.7% of T2DM patients and 34.8% of prediabetes patients. The diabetes cohort had a good glycemic balance, with a mean glycated hemoglobin 6.3% (5.8-6.6) and 25 OH vitamin D was in target for 64.9% of the participants-37 ng/mL (29,43) in the control group, 35 ng/mL (28,42) for prediabetes group and 33 ng/mL (25,39) in diabetics.

Conclusions: Our study emphasises that a good glycemic balance and vitamin D status can delay the bone deterioration and maybe the literature published cut-offs of 7.5% HbA1c begin to shift the balance toward bone deterioration.

Abstract citation ID: lvag096.787

EP215 - ECE_3036 - From symptoms to sequencing: a case of hypophosphatemic osteomalacia with a novel genetic variant

Smritimayee Panda[1], Pragya Kafley[1], Vaibhav Singhal[2], Kausik Mandal[1] and Preeti Dabadghao[1]
[1]*Medical Genetics, Sanjay Gandhi Postgraduate Institute of Medical Science, Lucknow, India;* [2]*Max Super Speciality Hospital Vaishali, Ghaziabad, India*

Background: Fanconi renotubular syndrome is an uncommon group of disorders characterized by proximal tubulopathies. There are five recognized subtypes of Fanconi syndrome, designated FRTS1-5.

Case presentation: A 40-year-old woman presented with bilateral hip pain ongoing for three years. She had sustained fractures in both legs from minor trauma three years earlier. Laboratory investigations revealed hypophosphatemia and a decreased TMP-GFR. Urinalysis showed proteinuria, calcinuria, and glucosuria. Whole-exome sequencing identified a novel heterozygous missense mutation in GATM, which was a VUS. Sanger sequencing of family members confirmed the same variant in affected relatives.

She was treated with phosphorus supplements and alkali therapy. After one year of follow-up, her pain improved, and she experienced no further fractures.

Conclusions: This case describes a novel GATM variant in a patient with hypophosphatemic osteomalacia. It underscores the importance of thorough evaluation for early diagnosis and targeted management to achieve better outcomes.

Abstract citation ID: lvag096.788

EP216 - ECE_1837 - Role of MEN1 genetic status on clinical phenotype of MEN1 disease: a single center cohort

Laura Pierotti[1], Elena Pardi[1], Chiara Sardella[2], Anna Dal Lago[1], Giacomo De Leo[1], Paolo Piaggi[3,4], Fausto Bogazzi[1], Liborio Torregrossa[5], Angela Michelucci[6], Maria Adelaide Caligo[6], Claudio Marcocci[1] and Filomena Cetani[1]
[1]*Department of Clinical and Experimental Medicine, Endocrine Unit, University of Pisa, Pisa, Italy;* [2]*Endocrine Unit, University Hospital of Pisa, Pisa, Italy;* [3]*NIDDK, National Institutes of Health, Phoenix, AZ, United States;* [4]*Department of Information Engineering, University of Pisa, Pisa, Italy;* [5]*Department of Surgical, Medical and Molecular Pathology and Critical Area, University of Pisa, Pisa, Italy;* [6]*Laboratory of Molecular Genetics, University Hospital of Pisa, Pisa, Italy*

Multiple Endocrine Neoplasia type 1 (MEN1) is a rare hereditary syndrome characterized by the neoplastic transformation of multiple endocrine tissues. The disease is caused by inactivating mutations of the *MEN1* gene. However, MEN1 diagnosis may also be based on clinical criteria, even in the absence of genetic confirmation. Consequently, some patients meet clinical diagnostic criteria for MEN1 despite lacking an identifiable MEN1 mutation. These MEN1-negative individuals may represent phenocopies and could display a distinct clinical behavior.

The aim of this retrospective observational study was to compare the clinical phenotype, disease progression, and outcomes of *MEN1*-positive and *MEN1*-negative patients in a large single-center cohort.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

We included 205 patients with a clinical diagnosis of MEN1 (116 index cases, 89 relatives) followed at a tertiary referral center between 1993 and 2023. Based on genetic testing, patients were classified as *MEN1*-positive ($n = 157$) or *MEN1*-negative ($n = 48$). Age at disease onset and diagnosis, number and type of MEN1-related manifestations, skeletal and renal complications, overall survival, and time to development of a third MEN1-related manifestation were evaluated in the entire cohort and in index cases.

MEN1-positive patients developed MEN1-related manifestations at a significantly younger age compared with *MEN1*-negative patients. In the overall cohort, the mean age at first manifestation was 35.8 ± 14.4 years in *MEN1*-positive vs 45.7 ± 14.4 years in *MEN1*-negative patients ($P < .001$). Comparable differences were observed for the second (39.7 ± 14 vs 50.6 ± 12, $P < .001$) and third manifestations (42.5 ± 13.7 vs 54.6 ± 11.1, $P < .001$) and for age at MEN1 diagnosis (36.9 ± 12.5 vs 45.7 ± 14.4, $P = .002$). *MEN1*-positive patients exhibited a higher disease burden, with a greater prevalence of three or more manifestations compared with *MEN1*-negative patients (40.8% vs 25.0%; $P = .048$). This difference was more pronounced in the index cases group (52.9% vs 25.0%; $P = .003$). Time to development of a third MEN1-related manifestation was significantly shorter in *MEN1*-positive patients, who showed an increased age-adjusted risk both in the overall cohort (HR 2.46, $P = .009$) and among index cases (HR 3.02, $P = .003$). In addition, *MEN1*-positive patients had a higher prevalence of nephrolithiasis and significantly lower age-adjusted Z-scores at the femoral neck and lumbar spine. Overall survival did not differ significantly between groups.

In conclusion, MEN1-positive patients exhibit earlier onset and a more aggressive and penetrant disease course than MEN1-negative patients, who appear to follow a milder clinical course. These findings support the concept of MEN1 phenocopies and highlight the clinical relevance of genetic status for risk stratification and individualized surveillance strategies.

Abstract citation ID: lvag096.789

EP217 - ECE_1222 - A systematic review and network meta-analysis of pharmacological strategies to improve bone mineral density in functional hypothalamic amenorrhoea

Agathoklis Efthymiadis[1], Konstantinos Tsikopoulos[2], Edouard G. Mills[1], Andrew Milne[3], Waljit Dhillo[1], Ali Abbara[1] and Alexander Comninos[1]

[1]Section of Endocrinology and Investigative Medicine, Imperial College London, London, United Kingdom; [2]Department of Orthopaedics, University Hospitals Bristol, Bristol, United Kingdom; [3]Hammersmith Campus Library, Imperial College London, London, United Kingdom

Background: Functional hypothalamic amenorrhoea (FHA) underlies up to 30% of secondary amenorrhoea. One of the most detrimental consequences of FHA is its impact on bone health, due to hypoestrogenaemia and nutritional deficiencies. Indeed, up to 44% of affected women have low bone mineral density (BMD) resulting in sevenfold higher risk of fractures compared with healthy women. Although first-line management of FHA typically involves a combination of psychological/dietetic interventions, over two-thirds of women remain amenorrhoeic despite one year of intensive treatment. When lifestyle measures fail to restore menses within 6-12 months, pharmacological treatments are usually required to protect bone health, but the comparative efficacy of these interventions remains uncertain.

Aim: To compare the efficacy of available pharmacological treatments for BMD in women with FHA using network meta-analysis (NMA) for the first time.

Methods: Medline/Embase/Emcare/Cochrane/CENTRAL/ISRCTN/ClinicalTrials.gov were searched until September 20, 2025. Eligible randomised-controlled trials evaluating pharmacological treatments for lumbar spine (LS), femoral neck (FN), or total hip (TH) BMD were included. PRISMA-NMA guidance was followed. Outcomes were expressed as standardised mean differences (SMDs) with 95% confidence intervals (CIs). The CINeMA (Confidence in Network Meta-Analysis) framework was employed to assess certainty.

Results: Thirteen RCTs, comprising 897 women in total, were included (LS BMD: $n = 897$; FN BMD: $n = 370$; TH BMD: $n = 750$). *Transdermal* hormone replacement therapy (HRT) (LS BMD: 77, FN BMD: 22) was more effective than control (placebo or no intervention) in increasing LS BMD with SMD 0.34 (95% CI 0.03, 0.64) and FN BMD with SMD 0.57 (0.04, 1.10) over 12-18 months. By contrast, *oral* HRT and the combined oral contraceptive pill (COCP) (LS BMD: $n = 166$, FN BMD: $n = 30$, TH BMD: $n = 54$) did not increase BMD in any of the assessed skeletal sites over 12-24 months. Furthermore, teriparatide administered for 6 months was superior to *transdermal* HRT and COCP for LS BMD with SMDs 1.48 (0.38, 2.59) and 1.75 (0.66, 2.83), but not FN or TH BMD.

Conclusions: *Transdermal* HRT and teriparatide both increase LS BMD in women with FHA, with *transdermal* HRT also improving FN BMD. By contrast, *oral* HRT and COCP do not exert benefits at any skeletal site. These differences may be partly explained by the differential effect of transdermal vs oral oestrogens on osteoanabolic insulin-like growth factor-1 (IGF-1). This is the first NMA of all available pharmacological strategies for BMD in FHA and has important clinical implications for the bone management of women with FHA.

Study registration: PROSPERO (CRD42024576872).

Abstract citation ID: lvag096.790

EP218 - ECE_1474 - Prevalence of vertebral fractures and incidental discovery of vertebral fractures using Vertebral Fracture Assessment (VFA)—a retrospective population-based study in Brasov, Romania

Oana-Maria Capraru[1], Paula Bucur[1] and Daniela Chetan[2]

[1]Endocrinology, Săcele County Hospital, Brasov, Romania; [2]Nuclear Medicine, Regional Oncology Institute, Iasi, Romania

Introduction: Vertebral fractures (VF) are a major complication of osteoporosis and are associated with an elevated risk for subsequent vertebral and nonvertebral fractures. Despite the increased morbidity, many VF are clinically silent and frequently do not come to medical attention. In this analysis we observed the prevalence of VF and the clinically silent VF discovered during VFA.

Material and Method: Data were included from 364 consecutive subjects who had measurement of BMD of posterior-anterior lumbar spine (LS), total hip (TH) and femoral neck (FN) with Hologic Horizon W® densitometer and VFA using lateral spine

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

imaging IVA™ mode in the supine position. Vertebral fractures were quantified using the Genant Semi-Quantitative Grading System for Vertebral Deformity as mild = 1, moderate = 2 and severe = 3. Standardized self-reported questionnaires were used to collect data regarding lifestyle factors influencing the risk of osteoporosis and fractures. Questionnaires included medical history, medication, and prior fracture.

Results: From the total study population, 352 were females, mean age 65.9 years and 12 males, mean age 65.3 years, mean LS BMD was 0.830 g/cm^2 and mean TH BMD was 0.798 g/cm^2. Vertebral fractures were observed in 89 patients (24%) among whom 59 patients (16%) were incidentally discovered by VFA and 30 patients had a self-reported VF. Low TH BMD and T score, advanced age, use of corticosteroids, parental hip fracture, previous fracture and years postmenopausal were observed to increase the risk of VF in our cohort. Among all patients with VF, 52.8% had osteoporosis at the LS or FN by BMD criteria and 41% (37 patients) had more than one VF. The most frequent VF were at T12, T11 and L1 and 24.7% had grade 3 VF. From the 59 patients with clinically silent VF, 40% had T scores suggestive of osteopenia, and 7% had normal BMD. 30% of patients had more than one VF and the most frequent silent VF were grade 1 and 2. Only 11% had grade 3 VF and 30% had previous pharmacological treatment for osteoporosis with or without other non-vertebral fractures. We did not find any differences in LS, TH or FN BMD between the group of patients with self-reported and silent VF but patients with clinically silent VF had a better TH T score.

Conclusions: Accurate radiographic detection of VF through VFA in addition to BMD has a substantial impact on the strategy of treatment and possible prevention of future osteoporotic fractures.

Abstract citation ID: lvag096.791

EP219 - ECE_1655 - The impact of the updated 24-hour urinary calcium excretion threshold on aPHPT management

Elena Castellano, Chiara Bona, Micaela Pellegrino, Irene Comune, Federico Arecco, Andrea Craparo, Claudia Baffoni and Anna Rosa Pia
Department of Endocrinology, Diabetes and Metabolism, Santa Croce and Carle Hospital, Cuneo, Italy

Introduction: The Fifth International Workshop on the management of asymptomatic primary hyperparathyroidism (PHPT) updated criteria for surgical indication. Specifically, the 24-hour urinary calcium excretion threshold was lowered and differentiated by sex, potentially expanding surgical eligibility. The impact of this modification, has not been yet assessed in real clinical practice.

Methods: We analyzed a consecutive series of 540 patients diagnosed with PHPT.

Among the, 70 patients did not meet any surgical criteria according to the IV International Workshop.

This subgroup included 54 women and 16 men (mean age 65 ± 9.5, being 13.2% e 12.9% of total M and F respectively).

We evaluated how many of these patients would newly fulfill surgical criteria when applying the updated, sex-specific urinary calcium thresholds (>250 mg/day for women and >300 mg/day for men).

Results: Among women without prior surgical indication, 5/54, corresponding to 9.3% of this subgroup, met the criteria for surgery. On the other hand, none of the 16 men without surgical indication met the updated hypercalciuria criterion.

Conclusions: In our consecutive PHPT series, lowering the urinary calcium threshold increased surgical eligibility among women, while no effect was observed in men. Several factors may contribute to this sex-specific finding, including the lower urinary calcium cutoff established for women and the relatively small number of men without surgical indication. Overall, these data suggest that the revised hypercalciuria criterion has an impact on surgical indication predominantly in women.

Abstract citation ID: lvag096.792

EP220 - ECE_1767 - "Determinants of osteoporosis in patients with primary hyperparathyroidism: the role of calcium–phosphate metabolism"

Sebastian Szewczyk and Michal Popow
Department of Internal Medicine and Endocrinology, University Clinical Centre of the Medical University of Warsaw, Warsaw, Poland

Background: Primary hyperparathyroidism (PHPT) is characterized by chronic parathyroid hormone (PTH) excess, leading to hypercalcemia, increased bone turnover, and an elevated risk of skeletal complications. Osteoporosis is a frequent manifestation of PHPT; however, the biochemical determinants of bone loss remain incompletely understood. In particular, the roles of active vitamin D (1,25-dihydroxyvitamin D, calcitriol) and renal phosphate handling in the pathogenesis of osteoporosis in PHPT require further clarification.

Objective: To identify biochemical determinants of osteoporosis in patients with PHPT, with a particular focus on calcitriol levels and renal phosphate handling, and to evaluate their predictive performance in discriminating osteoporotic from non-osteoporotic individuals.

Methods: We retrospectively analyzed 74 adult patients with biochemically confirmed primary hyperparathyroidism eligible for parathyroid surgery. All patients underwent comprehensive biochemical assessment, including serum total calcium, phosphate, parathormone (PTH), 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D (calcitriol), and 24-hour urinary calcium excretion. Renal phosphate handling was estimated using the tubular maximum for phosphate reabsorption per glomerular filtration rate (TMP/GFR). Osteoporosis was defined according to WHO criteria based on dual-energy X-ray absorptiometry. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of osteoporosis. Receiver-operating characteristic (ROC) curve analysis was used to assess diagnostic performance and determine optimal cutoff values.

Results: Osteoporosis was present in 33.8% of the study population. Patients with osteoporosis exhibited significantly higher calcitriol levels and significantly lower TMP/GFR values, indicating impaired renal phosphate reabsorption, compared with non-osteoporotic individuals. These associations remained significant in multivariate analysis. In contrast, serum total calcium, phosphate, PTH, and 25-hydroxyvitamin D levels did not differ significantly between groups. ROC analysis demonstrated clinically meaningful discriminatory performance for both calcitriol

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and TMP/GFR, with identifiable cutoff values for osteoporosis risk stratification.

Conclusions: Elevated levels of the active form of vitamin D and impaired renal conservation of phosphate are independently associated with osteoporosis in patients with primary hyperparathyroidism, outperforming traditional biochemical markers. These findings suggest that excessive calcitriol activity and renal phosphate wasting may play a key pathophysiological role in PHPT-related bone loss. Incorporating calcitriol measurement and assessment of renal phosphate handling into routine clinical evaluation may improve identification of patients at high skeletal risk and support more individualized management strategies in primary hyperparathyroidism.

Abstract citation ID: lvag096.793

EP221 - ECE_2094 - Impact of fat and muscle mass on low bone mass in young adults: a health screening center-based study

Han Na Jang
Seoul, South Korea

Background: Compared to osteoporosis in older adults and postmenopausal women, the epidemiology and risk factors of low bone mass in young adults remain under-investigated. This study aimed to investigate the prevalence and risk factors of low bone mass in young adults using data from the Kangbuk Samsung Hospital Health Screening Center.

Methods: In this retrospective cohort study, adults <50 years who underwent bone mineral density (BMD) test between January 2012 and December 2024 were included. Low bone mass was defined as a lowest Z-score ≤ −2.0 among the lumbar spine, femoral neck, and total hip. Vitamin D deficiency was defined as total 25-hydroxyvitamin D ≤20 ng/mL.

Results: A total of 107 612 individuals underwent BMD test (37.5% men; median age 42.0 [37.0, 45.0] years; median body mass index (BMI) 22.6 [20.5, 25.1] kg/m^2). The median total vitamin D level was 19.0 [13.7, 25.7] ng/mL, and 54.5% had vitamin D deficiency. The median lowest Z-score was −0.5 [−1.1, 0.2]. Low bone mass was observed in 6 779 subjects (6.3%), affecting 11.1% of men and 3.4% of women. Prevalence in men increased in the 20s, peaked in the 30s (8.4%, 12.4%, 10.7% for 20s, 30s, 40s), whereas women showed lower but stable prevalence (1.8%, 3.4%, 3.6%). In men, subjects with low bone mass had a higher BMI (26.0 [23.8, 28.8] vs 24.5 [22.8, 26.5] kg/m^2, $P < .001$), lower skeletal muscle mass (41.7 [39.0, 44.2] vs 43.4 [41.2, 45.5]%, $P < .001$), and higher fat mass (26.1 [21.8, 31.0] vs 23.1 [19.6, 26.8]%, $P < .001$), with higher proportion of current smoker, hypertension, diabetes, and dyslipidemia. In women, subjects with low bone mass had a lower BMI (21.0 [19.1, 23.4] vs 21.3 [19.7, 23.4] kg/m^2, $P < .001$), lower skeletal muscle mass (37.0 [34.6, 39.6] vs 37.6 [35.3, 40.0]%, $P < .001$), and higher fat mass (30.9 [26.1, 35.5] vs 30.2 [25.9, 34.5]%, $P < .001$), with higher prevalence of diabetes and dyslipidemia. Skeletal muscle mass was inversely associated with low bone mass in women (OR [95% CI] 0.907 [0.885, 0.930]), while increased fat mass was associated with higher risk of low bone mass in both men (1.106 [1.087, 1.126]) and women (1.220 [1.194, 1.247]).

Conclusions: Low bone mass is not uncommon among young adults, particularly in men. Altered body composition—characterized by reduced skeletal muscle mass and increased fat mass—was associated with low bone mass. Early screening and body composition-focused interventions may help prevent low bone mass in young adults

Abstract citation ID: lvag096.794

EP222 - ECE_2766 - Ethnicity is associated with fragility fracture incidence independent of age, sex and socio-economic disadvantage: a single centre Australian study

Michael Fogarty[1,2], Tung Pham[3], Jacqueline Seiffert[1], Anna Kwok[1], Dhiraj Samarasinghe[1], Ritoo Chowdhury[1], Christopher Preston[1], Tanita Botha[4], Vivian Grill[1,5] and Hanh Nguyen[1,5,6]
[1]Endocrinology and Diabetes, Western Health, Melbourne, Australia; [2]Endocrinology and Diabetes, Northern Health, Melbourne, Australia; [3]Western Health, Performance Unit, Health Information Services, Melbourne, Australia; [4]Statistics, Deakin University, Melbourne, Australia; [5]Medicine, The University of Melbourne, Melbourne, Australia; [6]Medicine, School of Clinical Sciences, Monash University, Melbourne, Australia

Background: Western Health(WH) provides care to an ethnically diverse community. We examined the burden of minimal trauma fractures in adults aged ≥50 years presenting to WH over a five-year period and analysed the differences in incidence across the major ethnic groups.

Methods: Fracture presentations at WH in adults aged ≥50 years between 2018-2022 were identified by ICD-10AM codes from the hospital electronic database. Fractures of the skull, hands, feet, and presentations with trauma codes were excluded. Admission and demographic data were extracted. Ethnicity was defined by birth country, grouped according to Australian Bureau of Statistics(ABS) Standard Australian Classification of Countries. Cumulative fracture incidence was estimated for total fractures, hip fractures, and major osteoporotic fractures(MOF), stratified across each major ethnic group. ABS 2021 Census data for postcodes was used to calculate fracture incidence in the WH catchment. Index of Relative Socioeconomic Disadvantage(IRSAD) scores was derived from Census data, applied at the area-code level and presented in quintiles.[1] Analysis included logistic regression to assess association with ethnicity, sex age, and IRSAD.

Results: Of 251 750 adults aged ≥50 years residing in the WH catchment, majority are born in Australia-Oceania(47%), Europe(25%), and Asia(21%). Between 2018-2022, 7 943 fractures occurred in7 315 persons residing in the WH catchment. The WH fracture cohort had a median age(min-max) of 62(50-105) years, 52.3% were female, IRSAD was 4(2-5). Fracture incidence per 1000 persons for Asian-born, Australia-Oceania-born, and European-born groups was: Total Fractures—14.9, 26.1, and 43.8, respectively; MOF—7.7, 13.8, and 26.6, respectively; Hip fracture—2.3, 5.2 and 11.0, respectively.

After adjusting for differences in age, sex and IRSAD, Australia-Oceania-born and European-born cases had a significantly higher total fracture incidence than Asian-born, [OR(95%CI): 1.76(1.60-1.94) and 1.94(1.75-2.14), respectively, all $P < .001$]. This finding was also demonstrated for hip fractures [Australia-Oceania-born cf. Asian-born: 1.86(1.47-2.4), $P < .0001$; European born cf. Asian-born: 1.97(1.56-2.50), $P < .0001$] and MOF [Australia-Oceania-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

born cf. Asian-born: 1.65(1.45-2.89), $P < .0001$; European-born cf. Asian-born: 1.96(1.71-2.24), $P < .0001$] subgroups. European-born persons had lower fracture incidence than Australia-Oceania-born when accounting for the same variables [OR 0.85(0.78-0.99), $P < .001$].

Conclusions: Asian-born cases consistently demonstrated lower fracture incidence than Australian-Oceanic and European peers at our Australian tertiary service, independent of age, sex and social disadvantage. This finding highlights ethnicity as an independent determinant of fracture risk, and supports the need to consider ethnicity when evaluating the risk-benefit of osteoporosis therapies.

Reference

1. Australian Bureau of Statistics. *Socio-Economic Indexes for Areas (SEIFA): Technical Paper*. ABS. 2021. https://www.abs.gov.au/statistics/detailed-methodology-information/concepts-sources-methods/socio-economic-indexes-areas-seifa-technical-paper/2021.

Abstract citation ID: lvag096.795

EP224 - ECE_2871 - Developing a standard dataset for adult Chronic Non-bacterial Osteitis (CNO) in the European Registries for Rare Endocrine and Bone Conditions (EuRREB)

Gitanjali Jaywant Sukhtankar[1], Mariya Cherenko[1], Anne Leerling[2], Simone Appenzellers[3], Gunter Assmann[4], Judith Bubbear[5], Roland Chapurlat[6], Gavin Clunie[7], Martine Cohen-Solal[8], Salvatore D'angelo[9], Dmitirios Daoussis[10], Olaf Dekkers[2], Olivier Fogel[11,12], Natalia Fontana[13], Victoria Furer[14,15], Roba Ghossan[16], Tiara Gill[17], Hermann Girschick[18], Neveen A.T. Hamdy[1], Barbara Hauser[19], Gilles Hayem[20], Philip Helliwell[21], Antonella Insalaco[22], Aruni Jayatilleke[23], Kishimoto Mitsumasa[24], Mikhail Kostik[25], Willem Lems[26], Paivi Miettunen[27], Murugan Sudhakar[28], Ahimalaipet V Ramanan[29], Marion Roderick[29], James Teh[30], Charlotte Verroken[31,32], Yongdong Zhao[33], Hans-Georg Zmierczak[31,32,34], Natasha Appelman-Dijkstra[1] and Elizabeth M. Winter[1]

[1]Leiden University Medical Center, Center for Bone Quality, Department of Internal Medicine, Div. Endocrinology, Leiden, The Netherlands; [2]Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands; [3]Department of Orthopedics, Rheumatology and Traumatology (DORT), University of Campinas (UNICAMP), School of Medical Science, Sao Paulo, Brazil; [4]Department of Rheumatology, Ruhr-university medical faculty, Minden, Germany; [5]Centre for Metabolic Bone Disease, Royal National Orthopaedic Hospital, London, United Kingdom; [6]Université Claude Bernard-Lyon 1, INSERM UMR 1033, Hospices Civils de Lyon, Lyon, France; [7]Department of Rheumatology, Cambridge University Hospitals, Cambridge, United Kingdom; [8]Rheumatology Department, Lariboisiere hospital, Paris, France; [9]Department of Health Science, University of Basilicata, Potenza, Italy; [10]Department of Internal Medicine, Division of Rheumatology, Patras University Hospital, Patras, Greece; [11]Department of Rheumatology, Cochin Hospital, Paris, France; [12]Centre for Research in Epidemiology and Statistics (CRESS), Université Paris Cité and Université Sorbonne Paris Nord, Inserm, INRAE, Paris, France; [13]Department of Rheumatology and Pediatric Rheumatology, Immunology Group, Hospital Universitario Marques de Valdecilla, Santander, Cantrabria, Spain; [14]Tel Aviv Sourasky Medical Center, Rheumatology Department, School of Medicine, Tel Aviv, Israel; [15]Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel; [16]Department of Rheumatology, Hospital Cochin, Paris, France; [17]Metabolic Bone Disease Unit, Royal National Orthopaedic Hospital, Stanmore, United Kingdom; [18]Department of Pediatrics, Vivantes Klinikum im Friedrichshain, Berlin, Germany; [19]Rheumatic Diseases Unit, Western General Hospital, Edinburgh, United Kingdom; [20]Department of Rheumatology, Paris-Saint Joseph Hospital Group, Paris, France; [21]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; [22]ERN- RITA Center, Department of Rheumatology, IRCCS Bambino Gesù Children's Hospital, Rome, Italy; [23]Rheumatology, Department of Medicine, Lewis Katz School of Medicine at Temple University, Philadelphia, United States; [24]Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, Japan; [25]Saint-Petersburg State Pediatric Medical University, Saint-Petersburg, Russia; [26]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, The Netherlands; [27]Department of Paediatrics, Calgary, University of Calgary McCaig Institute for Bone and Joint Health, Alberta, Canada; [28]Department of Pediatrics, Christian Medical College, Vellore, India; [29]Paediatric Immunology, Bristol Royal Hospital for Children (BRHC), Bristol, United Kingdom; [30]Department of Radiology, Nuffield Orthopaedic Centre Girdlestone Memorial Library, Oxford, United Kingdom; [31]Department of Internal Medicine and Pediatrics, Ghent University, Ghent, Belgium; [32]Department of Endocrinology, Ghent University Hospital, Ghent, Belgium; [33]Department of Rheumatology, Seattle Children's Hospital, Washington, United States; [34]Endocrinology, Ghent University Hospital, Ghent, Belgium

Background: Chronic non-bacterial osteitis (CNO) is a heterogenous, rare, sterile inflammatory bone disorder characterized by painful, sclerotic lesions most often involving the anterior chest wall, but may affect any bone in adults. Owing to the absence of population-based studies in adults, the global prevalence of CNO is estimated to range from 1/160 000-1/200 000. CNO is likely underdiagnosed due to limited clinical awareness. Furthermore, its pathophysiology remains incompletely understood, and there is a lack of validated diagnostic criteria and standardized therapeutic approaches.

Purpose and Methods: The Core Registry within the European Registries for Rare Endocrine and Bone Conditions (EuRREB) collects mandatory Core Data Elements for ERN registries and allows for the collection a specific dataset within a condition-specific module (CSM), including clinical data (i.e., clinical manifestations, patient history, imaging results and treatment modalities) and Patient Reported Outcome Measures (PROMS).

The CNO condition-specific module was created following a consensus meeting, during which the initial initiative was launched and a proposal for the set-up was suggested. This module was then further developed over 1.5 years through the multi-stakeholder (European Calcified Tissue Society, ERN-BOND, European Society of Endocrinology) collaboration of clinicians, researchers, and a patient advocacy group (Chronic non-bacterial osteitis-sterno costoclavicular hyperostosis (CNO-SCCH) NL).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

The aim was to create a framework supporting observational studies leading to future interventional projects elucidating the CNO phenotype, disease-course, pathophysiology, diagnosis, and treatment.This module was derived from the 2024 consensus guidelines for CNO diagnosis and treatment and refined through a 9-point Likert scale survey ($n = 29$) providing iterative feedback during testing. Variables were included if 80% of participants scored > 7 on the Likert scale.

Results: All 52 proposed variables (i.e., patient history, past/current medication, diagnostic tools, ASAS/CASPAR criteria, bone-pain, imaging, clinical follow-up, among others) were included. PROMS included EQ-5D-5L, BPI-SF, and BFI-SF questionnaires. A beta version was launched in August 2025 featuring CNO-unique variables. After incorporating revisions from the final feedback round, the completed module was officially launched on 01-12-2025.

Conclusions: This module is the first multicenter initiative to prospectively monitor and longitudinally characterize CNO patients. Addressing rare-disease research challenges via international data collection, this registry provides a powerful platform to meet patient needs and improve clinical care. As participation expands, the data will enable studies of clinical practices, disease course, treatment effects, and geographical variability. Researchers and clinicians worldwide may add patient data to the registry, and request access to the module to support collaborative CNO research.

Abstract citation ID: lvag096.796

EP225 - ECE_2995 - Bone mineral density trajectories following parathyroidectomy in patients with primary hyperparathyroidism

Simon Mifsud[1], Jake Schembri[1], Christian Camenzuli[2], Matthew Cassar[2] and Mark Gruppetta[1]
[1]*Department of Diabetes and Endocrinology, Mater Dei Hospital, Msida, Malta;* [2]*Safi, Malta*

Introduction: Parathyroidectomy is indicated in patients with primary hyperparathyroidism (PHPT) and osteoporosis. This study evaluates pre- and post-operative dual-energy X-ray absorptiometry (DEXA) findings to assess the timeframe and pattern of bone mineral density (BMD) improvement after surgery.

Method: We retrospectively reviewed DEXA scans and biochemical profiles of PHPT patients who underwent parathyroidectomy between 2017 and 2024. Femoral neck and lumbar spine BMD were evaluated at baseline (pre-parathyroidectomy) and at 1-, 2-, and 5-years post-parathyroidectomy using a linear mixed-effects model adjusting for age and gender.

Results: A total of 104 patients with PHPT underwent parathyroidectomy during the study period. The mean age was 61.6 years (SD: 12.54), with a female predominance of 76% ($n = 79$). The median serum calcium at diagnosis was 2.76 mmol/L (IQR:2.68-2.87), with a median PTH of 120 ng/L (IQR:96.5-160.5).

Following parathyroidectomy, both femoral neck and lumbar spine BMD demonstrated significant improvement over time. Femoral neck log-transformed BMD estimated marginal means (EMM) rose from −0.187 preoperatively to −0.159 at 1 year, −0.140 at 2 years, and −0.111 at 5 years. Pairwise comparisons (Bonferroni-adjusted) revealed significant improvement corresponding to approximately 4.8% at 2 years (ΔEMM 0.047, $P = .006$) and 7.8% at 5 years (ΔEMM 0.075, $P < .001$) compared with baseline. The increase observed at 1 year (2.7%) did not reach statistical significance ($P = .388$).

Lumbar spine log-transformed BMD EMM similarly increased from −0.113 preoperatively to −0.064 at 1 year and −0.025 at 2 years, with a slight decline to −0.041 at 5 years. Pairwise comparisons (Bonferroni-adjusted) demonstrated significant gains from baseline at all post-operative timepoints: +5% at 1 year (ΔEMM 0.049, $P < .001$), +9.2% at 2 years (ΔEMM 0.088, $P < 0.001$), +7.5% at 5 years (ΔEMM 0.072, $P < 0.001$). Although lumbar spine BMD remained significantly higher than baseline at 5 years, a modest non-significant decline occurred between 2- and 5-years post-parathyroidectomy ($P = 1.0$).

Age negatively impacted femoral neck log-transformed BMD ($P = .03$) but had no significant effect on lumbar spine log-transformed BMD ($P = .90$). Males exhibited higher log-transformed BMD EMM than females at both sites (both $P < 0.001$).

Conclusions: Our study revealed that both femoral neck and lumbar spine BMD increase significantly post-parathyroidectomy. Lumbar spine BMD improved more rapidly, reaching statistical significance at 1-year post-parathyroidectomy, whereas femoral neck BMD improvement became significant at 2- and 5-years post-operatively. Appreciating the trajectory of BMD improvement following parathyroidectomy in PHPT patients may guide physicians in managing persistent osteoporosis, allowing for appropriately timed intervention without premature or delayed therapy.

Abstract citation ID: lvag096.797

EP226 - ECE_1550 - Integrated clinical, genetic and histopathological analysis with long-term follow-up of nine Italian families harboring germline variants in the CDC73 gene

Anna Dal Lago[1], Laura Pierotti[1], Simone Della Valentina[1], Chiara Sardella[2], Giacomo De Leo[1], Elena Pardi[1], Angela Michelucci[3], Maria Adelaide Caligo[3], Gianluca Frustaci[4], Luigi De Napoli[4], Gabriele Materazzi[4], Liborio Torregrossa[5] and Filomena Cetani[1,2]
[1]*Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy;* [2]*Endocrine Unit 2, University of Pisa, Pisa, Italy;* [3]*Laboratory of Molecular Genetics, University of Pisa, Pisa, Italy;* [4]*Pisa, Italy;* [5]*Department of Surgical, Medical and Molecular Pathology and Critical Area, University of Pisa, Pisa, Italy*

Germline mutations of cell division cycle 73 (*CDC73*) gene are associated with Hyperparathyroidism-Jaw Tumor Syndrome (HPT-JT) and some cases of familial isolated hyperparathyroidism (FIHP). HPT-JT is a rare autosomal dominant syndrome with incomplete penetrance, characterized by the variable association of primary hyperparathyroidism (PHPT), renal lesions, jaw tumors, and uterine lesions. Atypical parathyroid tumors and carcinomas are more prevalent in HPT-JT compared to sporadic or other familial forms of PHPT. FIHP is a familial form of PHPT, it is a heterogeneous disease, which has also been related to other mutations.

We evaluated the clinical, histopathological, and genetic features of nine families carrying *CDC73*-related PHPT followed at our outpatient clinic.

The total group included 29 patients. 22 members (females: 12; males:10) were affected by PHPT, two had renal cysts, one presented with jaw tumor and one female had a uterine polyp. The

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

remaining 7 members (females: 4, males: 3) were asymptomatic carriers of the disease, with no clinical manifestations. PHPT was the first disease manifestation in all affected subjects, with a median age of 29 years (IQR: 20-39) at diagnosis. Nephrolithiasis/nephrocalcinosis affected 7 patients (63%) and osteoporosis at any site was present in 2 subjects (19%). The median value of calcium was 13,9 mg/dl (IQR: 11,9-16,6), The median parathyroid hormone (PTH) level, assessed as a fold increase, was 2,27. Genetic analysis revealed a large heterozygous deletion of all exons of the *CDC73* gene in two families, whereas the other seven families had different heterozygous frameshift mutation of the *CDC73* gene. The surgery consisted of selective parathyroidectomy in 11 patients (78%) whereas bilateral neck exploration was performed in 3 subjects (22%). Histological examination revealed chief cell adenoma in 6 cases (43%), oncocytic adenoma in 1 (7%), atypical tumor in 6 patients (43%) and carcinoma in 1 (7%). Nine patients (69%) were disease free at a median follow-up of 3,5 years (IQR: 2,75-7). Recurrent PHPT was present in 4 patients (31%) after a disease-free interval of 7 years (IQR: 3-11,25).

As regards the 7 asymptomatic carriers of the disease, none of them developed any manifestation of the syndrome during follow up.

In conclusion, family history assessment and genetic testing are essential for accurate diagnosis and proper follow-up in young PHPT patients.

Abstract citation ID: lvag096.798

EP227 - ECE_1928 - Primary hyperparathyroidism associated with multiple endocrine neoplasia type 1 in patients aged ≤21 years: results from a single-center study

Simone Della Valentina[1], Laura Pierotti[1], Chiara Sardella[2], Elena Pardi[1], Anna Dal Lago[1], Gianluca Frustaci[3], Gabriele Materazzi[3,4] and Filomena Cetani[1,2]

[1]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [2]Endocrine Unit, University Hospital of Pisa, Pisa, Italy; [3]Endocrine Surgery, University Hospital of Pisa, Pisa, Italy; [4]Department of Surgical, Medical, Molecular and Critical Care Pathology, University of Pisa, Pisa, Italy

Background: In multiple endocrine neoplasia type 1 (MEN1), primary hyperparathyroidism (PHPT) is typically the earliest and most prevalent manifestation. When PHPT occurs during adolescence or early adulthood, clinically relevant renal and skeletal complications may already be present, yet data in this age group remain limited.

Methods: We conducted a single-center retrospective study including MEN1 patients aged ≤21 years, followed at the University Hospital of Pisa between 2001 and 2024 with genetically confirmed MEN1. We assessed age at PHPT diagnosis, baseline PHPT-related renal and skeletal complications (including DXA Z-scores), and longitudinal outcomes under surgery, medical therapy, or active surveillance.

Results: Among 21 MEN1 patients aged ≤21 years, 15 (71%) developed PHPT; 14/21 (67%) were diagnosed at age ≤21. Median age at PHPT diagnosis was 18 years (IQR 15-19; range 12-21), with no significant sex-related difference. At baseline, 10/15 patients (67%) exhibited at least one PHPT-related complication: hypercalciuria (>4 mg/kg/24 h) in 8/14 (57%), silent nephrolithiasis in 4/14 (29%), and reduced bone mass (DXA Z-score <−2.0) in 6/14 (43%). Reduced bone mass predominantly involved the one-third distal radius (5 patients; median Z-score −2.7), followed by femoral neck/total hip (3 patients; median Z-scores −2.4 and −2.1, respectively) and lumbar spine (2 patients; median Z-score −2.4). No morphometric fragility fractures were observed. Bone turnover markers showed osteocalcin above the age-adjusted upper limit (median 36.2 µg/L; IQR 26.9-50.8), while bone-specific alkaline phosphatase and CTX were variably elevated (median fold increase 0.72 and 0.54, respectively). Follow-up data were available for 14/15 patients over a median of 8 years (IQR 6-12). Five patients (33%) underwent parathyroidectomy at a median age of 22 years (IQR 19-25; two before age 21); histology showed multiglandular hyperplasia in 4 and an atypical parathyroid tumor in one. Postoperatively, 3/5 had persistent PHPT, 1 developed hypoparathyroidism, and 1 experienced recurrence ~10 years after surgery. During follow-up, 7/14 (50%) received cinacalcet, with overall acceptable tolerability.

Conclusions: In MEN1 patients diagnosed at ≤21 years, PHPT is common and frequently complicated by early renal involvement and reduced bone mass—particularly at cortical sites. Long-term management should be individualized, integrating careful surveillance, timely surgery when indicated, and adjunctive medical therapy to mitigate complications and recurrence.

Abstract citation ID: lvag096.799

EP228 - ECE_2697 - Analytical performance of the automated ionify vitamin D LC-MS/MS assay for the quantification of 25-hydroxyvitamin D and 24,25-dihydroxyvitamin D

Katie Weaver[1], Tom de Waal[2], Michael Vogeser[3], Sven Groesgen[4], Christina Fan[4], Elie Fux[4], Anton Hilger[4], Raymond T. Suhandynata[5], Russell P. Grant[6], Barry J. Toole[5], Pieter Vermeersch[2], William A. Clarke[1] and Dusanka Kasapic

[1]Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, United States; [2]Clinical Department of Laboratory Medicine, UZ Leuven, Leuven, Belgium; [3]Institute of Laboratory Medicine, LMU University Hospital, Munich, Germany; [4]Roche Diagnostics GmbH, Mannheim, Germany; [5]Department of Pathology, University of California San Diego, San Diego, United States; [6]Center for Esoteric Testing, Labcorp, Burlington, United States

Introduction: Measurement of 25-hydroxyvitamin D [25(OH)D] is clinically important because both elevated and deficient levels are associated with disturbances in calcium and phosphorus homeostasis. The metabolite 25-hydroxyvitamin D [25(OH)D] serves as the primary clinical biomarker for establishing vitamin D sufficiency. Beyond total 25(OH)D, the measurement of 24,25-dihydroxyvitamin D [24,25(OH)2D] has gained clinical relevance for identifying patients with CYP24A1 gene mutations and overcoming limitations associated with fixed 25(OH)D cutoffs. Consensus statements highlight the important role of vitamin D metabolites, in particular of the 24,25 to 25(OH)D ratio.

Although LC-MS/MS offers superior specificity, its routine use is often limited by the need for specialized staff and complex manual workflows. This study evaluated the analytical performance of the Ionify® Vitamin D iPack on the Cobas® i 601 analyzer, a fully automated LC-MS/MS system.

Methods: Repeatability and reproducibility (CLSI EP05-A3) were assessed across three laboratories using three reagent lots over five days. Inter-laboratory accuracy was evaluated at six sites

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

using External Quality Assessment (EQA) samples (DEQAS, CAP) compared to Reference Measurement Procedures (RMPs). Additionally, a method comparison (CLSI EP09c) was performed against a validated in-house LC-MS/MS Laboratory Developed Test (LDT) using patient serum samples.

Results: The assay demonstrated robust precision across all sites and reagent lots. Coefficients of variation (%CV) for repeatability and reproducibility (lot-to-lot and site-to-site) ranged from 2.7%-4.8% for 25(OH)D and 2.3%-3.5% for 24,25(OH)2D, with nearly all %CVs remaining below 6%. Accuracy assessment revealed median recoveries ranging from 89% to 110% of expected values and 92%-109% of the reference method values. Method comparison showed high correlation with the validated LDT for both metabolites (Pearson r: 0.984-0.995; slopes: 0.913-1.027). The test duration for one sample on the system for the tested analytes was 34 minutes, respectively.

Conclusions: The Ionify Vitamin D assay on the Cobas i 601 analyzer provides precise, accurate, and reproducible measurements of 25(OH)D and 24,25(OH)2D. By combining the analytical superiority of LC-MS/MS with full automation, this system supports timely and accurate measurements of vitamin D metabolites in routine laboratory settings.

Abstract citation ID: lvag096.800

EP231 - ECE_2233 - Autoimmune polyendocrine syndrome type 1 caused by a momozygous aire mutation: report of two siblings

Maria-Eleni Chondrogianni[1,2,3], Anna Papadopoulou[4,5], Katerina Ioannidou[1], Maria Yavropoulou[1,3], Eirini Dikaiakou[6], Elpis Vlachopapadopoulou[6] and Eva Kassi[1,2,3]

[1]Endocrine Unit, 1st Department of Propaepeudic Internal Medicine, Laiko Hospital, National and Kapodistrian University of Athens, Athens, Greece; [2]Department of Biological Chemistry, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [3]Center of Excellence for Rare Endocrine Diseases (C.E.R.E.D.), General Hospital of Athens, LAIKO, National and Kapodistrian University of Athens, European Reference Network on Rare Endocrine Conditions (ENDO-ERN), Athens, Greece; [4]Division of Endocrinology, Metabolism & Diabetes, First Department of Pediatrics, Medical School, National and Kapodistrian University of Athens, 'Aghia Sophia' Children's Hospital, Athens, Greece; [5]Department of Clinical Biochemistry, National and Kapodistrian University of Athens Medical School, University General Hospital "Attikon", Athens, Greece; [6]Department of Endocrinology-Growth and Development, Children's Hospital P. & A. Kyriakou, Athens, Greece

Introduction: APS-1 (Autoimmune Polyendocrine Syndrome type 1) or APECED (Autoimmune Polyendocrinopathy–Candidiasis–Ectodermal Dystrophy) is a rare disease caused by biallelic genetic changes in the AIRE gene. The three most common clinical manifestations are chronic mucocutaneous candidiasis, hypoparathyroidism, and primary adrenal insufficiency (Addison's disease). More than 126 different mutations in the AIRE gene have been described. There is no clear genotype–phenotype correlation. A wide variability in the spectrum and severity of clinical manifestations has been described even among carriers with the same AIRE genetic change, even among siblings. We present the cases of two siblings (an older sister, 20 years old, and a younger brother, 17 years old) with a homozygous loss-of-function mutation in the AIRE gene.

Case presentation: The older sister was initially diagnosed at 6.5 years old with hypoparathyroidism and at 8 years with primary adrenal insufficiency. At 11 years, she remained at Tanner stage I, and biochemical evaluation revealed primary hypogonadism. She developed onychomycosis at 12 years and was also diagnosed with hypothyroidism at 16 years.

The younger brother developed onychomycosis before the age of 9. At 9 years old, he was diagnosed with hypoparathyroidism and Addison's disease. He was also diagnosed with hypothyroidism at 10 years old. At the latest biochemical evaluation, at 17 years old, his gonadotropin levels showed an increasing trend indicative of primary gonadal insufficiency.

Genetic testing revealed a homozygous AIRE variant, c.892G > A (p.Glu298Lys) in both siblings, while their parents were found to be heterozygous carriers.

Conclusions: Despite the well-known poor genotype–phenotype correlation in patients carrying the same pathogenic *AIRE* variants, herein, we describe two siblings with the same homozygous *AIRE* mutation who exhibited similar clinical manifestations, albeit with disease onset at different ages. Moreover, in the older sister, a switch from conventional therapy to palopegteriparatide was initiated upon reaching adulthood because of poorly controlled hypoparathyroidism.

Abstract citation ID: lvag096.801

EP233 - ECE_3128 - Impact of romosozumab on quality of life in women with osteoporosis: a prospective pilot study

Giacomo Voltan[1,2], Carlo Mogno[1,2], Giacomo Contini[1,2], Michela Ferrarese[1,2] and Valentina Camozzi[1,2]

[1]Endocrinology Unit, University Hospital of Padova, Padova, Italy; [2]Department of medicine—DIMED, University of Padova, Padova, Italy

Background: Romosozumab is a monoclonal anti-sclerostin antibody with a dual anabolic and antiresorptive mechanism of action and currently represents the most effective therapy in terms of bone mineral density (BMD) increase and fracture risk reduction in patients with osteoporosis. While its skeletal efficacy is well established, data on its impact on patient-reported outcomes, particularly quality of life (QoL), are currently lacking. The aim of this study was to evaluate the effect of romosozumab on QoL in women treated for osteoporosis.

Methods: This was a prospective, single-center study including 59 postmenopausal women with osteoporosis treated with romosozumab according to national reimbursement criteria (Nota 79). Quality of life was assessed using the validated ECOS-16 questionnaire at baseline, 6 months and 12 months. Biochemical parameters were collected at baseline, 6 and 12 months, while BMD at the lumbar spine and femoral sites was evaluated by DXA at baseline and after 12 months of treatment.

Results: At the time of analysis, 14 patients had completed the full 12-month course of romosozumab. After 12 months of therapy, a significant increase in BMD was observed at both the lumbar spine (0.744 vs 0.619 g/cm^2, $P = .029$) and the femoral site (0.623 vs 0.585 g/cm^2, $P = .001$). Quality of life significantly improved as early as 6 months of treatment, with a reduction in ECOS-16 score (50.0 vs 54.33, $P = .013$), which was maintained

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

at 12 months (47.17 vs 54.33, $P = .041$). Notably, the percentage increase in BMD was inversely correlated with ECOS-16 score at 12 months (Spearman's rho = −0.709, $P = .022$), indicating that greater skeletal gains were associated with better patient-reported quality of life.

Conclusions: Romosozumab confirms its efficacy as a highly effective treatment for osteoporosis and is associated with a clinically meaningful improvement in quality of life. Given that lower ECOS-16 scores reflect better QoL, the observed inverse correlation between BMD gain and QoL score suggests that skeletal improvement translates into tangible clinical benefits for patients. This pilot study provides the first prospective evidence that romosozumab therapy positively impacts quality of life in addition to its well-established effects on bone mass, supporting the inclusion of patient-reported outcomes in future osteoporosis trials.

Abstract citation ID: lvag096.802

EP234 - ECE_1656 - Cinacalcet for preoperative primary hyperparathyroidism: insights into clinical-phenotypes and surgical outcomes from real-word observational data

Cosmina Schiteanu[1,2], George Varughese[1] and Laks Varadhan[1]
[1]Stoke-On-Trent, United Kingdom; [2]Stoke-on-Trent, Diabetes and Endocrinology, Endocrinology, Stoke-on-Trent, United Kingdom

Introduction: Primary hyperparathyroidism (PHPT) can present with severe hypercalcemia. Parathyroidectomy remains the definitive treatment but medical optimization before surgery with cinacalcet may be required. Beyond its role in biochemical stabilization, the need for cinacalcet may reflect a more severe disease phenotype, potentially correlating with identifiable parathyroid pathology and higher likelihood of surgical cure.

The aim of the study was to assess the preoperative use of cinacalcet and evaluate the phenotype of patient group it represents in real-world clinical practice.

Methods: All patients with primary hyperparathyroidism (PHPT) who were given cinacalcet over last 3 years was accessed. Patients who were specifically initiated for pre-operative control of calcium and underwent surgery were identified. Demographic and clinical parameters and radiological investigations (ultrasound [US] and technetium-99m sestamibi single-photon emission computed tomography with CT[MIBI-SPECT/CT] were collated.

Results: $N = 46$ (20.5% of all cases operated for PHPT over 3 years).

Females: 69.6% ($n = 32$).

Mean age: 61.2 ± 15.5 years (median 62; 22-82).

Mean starting calcium was 3.02 mmol/L (2.74-3.71)[normal:2.2-2.6] and PTH 22.3 pmol/L (6.83-88.96) [normal:2.0-8.5]. Indication for starting cinacalcet was symptomatic hypercalcemia in 76% ($n = 35$) or severe hypercalcemia (Ca > 3.0 mmol/L) in 52.2% ($n = 24$). Evidence of end-organ damage (osteoporosis ± fractures, renal stones) was present in 30.4%. ($n = 14$).

Mean duration of usage of cinacalcet was 66 weeks (4-178). Mean cinacalcet dose required used immediately before surgery was 63 mg/day (15-240). Immediate pre-op calcium was 2.79 mmol/L (2.29-3.38). 52.2% ($n = 24$) achieved adequate control of calcium with cinacalcet alone; others required additional treatment such as hospital visit for pamidronate infusion and/or intravenous fluids when clinically indicated.

US was done in all patients and positive in 84.8% ($n = 39$); MIBI-SPECT/CT in 44 and positive in 72.7% ($n = 32/44$). 61.4% ($n = 27/44$) had positively concordant scan results; 15.9% ($n = 7$) had both scans being negative, and while the rest had one scan positive and other reported as normal.

89.1% ($n = 41/46$) were successfully operated and cured. Of these, 25/41 had concordant positive scans and 10 at least one scan positive. Histology was parathyroid adenoma ($n = 40$) or carcinoma.

In 5 patients, cure was not achieved: 2/5 had concordant scans being positive and histology was adenoma/hyperplasia. In other 3/5 no intraoperative lesion found.

Conclusions: A significant proportion of patients may need cinacalcet to optimize calcium awaiting surgery, Use of a cinacalcet, a surrogate marker of severe and symptomatic hypercalcemia, may help to identify a phenotype of patients with operable, localized disease and to predict better localisation and cure rates.

Abstract citation ID: lvag096.803

EP237 - ECE_3124 - 18F-Fluorocholine positron emission tomography/computed tomography (18F-Choline PET/CT) in localization of parathyroid adenomas: a case series

Aggeliki Kyriakou[1], Angeliki Angelidou[1], Vasiliki Antonopoulou[1], Sofia Georgiadi[1], Kalliopi Pantelia[1], Anna Louisa Chaliasou[1], Stavros Karakozis[2], Lampros Karakozis[2], Stylianos Gavriilidis[3], Nikoletta Pianou[3], Phivi Rontogianni[3], Marinella Tzanela[1] and Theodora Stratigou[1]
[1]Department of Endocrinology "D. Ikkos"- Diabetes Center- EndoERN-Evangelismos General Hospital, Athens, Greece; [2]Thyroid Surgery Clinic, Athens, Greece; [3]Department of Nuclear Medicine and PET-CT, General Hospital «Evangelismos- Polyclinic», Athens, Greece

Background: Primary hyperparathyroidism (PHPT) is a common endocrine disease, most frequently caused by solitary parathyroid adenoma. Diagnosis is established biochemically, and surgical removal of hyperfunctioning parathyroid gland is the only curative treatment. Accurate localization is therefore essential for the success of minimally invasive parathyroidectomy (MIP). Although conventional imaging modalities are effective in most cases, they yield negative or discordant results in approximately 10%-15% of cases. ^{18}F-Fluorocholine positron emission tomography/computed tomography (^{18}F-Choline PET/CT) is a promising advanced imaging technique demonstrating high sensitivity and positive predictive value in the detection of parathyroid adenomas. Herein, we report the results of ^{18}F-Choline PET/CT in a case series of nine patients ($N = 9$) with PHPT following negative or inconclusive preoperative imaging.

Case-series: ^{18}F-Choline PET/CT was performed at our hospital from 2023 to 2025. The mean age of the nine patients was 58 years old, and the female-to-male ratio was 7:2. All patients had previously undergone neck ultrasound, 6/ 9 had Sestamibi scintigraphy (99mTc-Sestamibi), 3/9 had 99mTc-Sestamibi SPECT/CT, 6/9 had 4D/CT and 1/9 had MRI.

^{18}F-Choline PET/CT was positive in six out of nine patients (6/9), revealing parathyroid adenoma. All six patients had mild hypercalcemia (mean serum calcium: 11 mg/dl) and an average parathyroid hormone (PTH) of 147 pg/ml. In 2/6 patients all conventional imaging modalities were negative, while in 4/6 the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

findings were discordant. All six patients underwent minimally invasive parathyroidectomy, and histopathology confirmed parathyroid adenomas in all cases. Calcium and PTH levels normalized. All three patients with negative ^{18}F-Choline PET/CT (3/9) had normocalcemic PHPT and mean PTH:130 pg/ml. In 2/3, neck ultrasound was negative, while in one patient a small lesion was detected representing either atypical adenoma or hyperplasia. Although all three patients had positive 99Tcm Sestamibi scans (2/3 with SPECT/CT), the findings were not definitive for adenomas.

Discussion: 18F-Choline PET/CT is highly effective preoperative localization imaging technique for patients with PHPT, providing crucial guidance for MIP. Currently, it is available in a limited number of specialized centers and is performed when conventional imaging is negative or inconclusive. In our case-series, 18F-Choline PET/CT detected parathyroid adenomas in the majority of patients, leading to successful surgery. However, it was negative in three patients. This finding should be interpreted with caution, as these patients did not undergo surgery. Our results, in line with current literature, highlight the significance of this method as a valuable tool in the effective management of PHPT.

Abstract citation ID: lvag096.804

EP238 - ECE_3443 - Cosmetic procedure-induced granulomatous disease presenting with hypercalcemia: a case report

Tânia Fernandes[1], Filipa Barros Alves[1], Marta Castro Tomé[1], Alexandra Novais Araújo[1,2] and Rosa Maria Príncipe[1,2]
[1]*Endocrinology, Local Health Unit of Matosinhos, Matosinhos, Portugal;* [2]*Faculty of Medicine of University of Porto, Porto, Portugal*

Hypercalcemia is a disorder of calcium metabolism, often classified as parathyroid hormone (PTH)-dependent or PTH-independent. However, less common causes may explain this frequent metabolic disturbance. Polymethylmetacylate (PMMA), used as a permanent cosmetic filler, has been linked to delayed foreign-body reactions and metabolic complications.

We report a clinical case of a 55-year-old woman with hypercalcemia, admitted for acute obstructive pyelonephritis due to E. coli infection, with impaired kidney function and ureterohydronephrosis.

Initial laboratory results revealed severe hypercalcemia, with serum corrected calcium levels for albumin of 14.56 mg/dL. She presented with no symptoms typically associated with this ionic disturbance. Further workup revealed PTH 14.1 pg/mL (normal range: 15.0-68.3 pg/mL), alkaline phosphatase enzyme of 81 U/L (40-180 U/L) and phosphorus levels 4.9 mg/dL (2.3-4.7 mg/dL) and markedly elevated 1,25-dihydroxycalciferol levels (242.8 pg/mL). She presented with decreased kidney function (creatinine of 4.6 mg/dL). Previous analytic studies showed that hypercalcemia was already present three years before her hospital admission (calcium 11.8 mg/dL), as well as chronic kidney disease (creatinine 1.76 mg/dL). We actively excluded malignant and autoimmune etiologies. Our patient revealed she had done an aesthetic procedure in her glutes eight years ago with injections of PMMA, a cosmetic filler used for soft-tissue augmentation. Imaging findings revealed multiple areas of subcutaneous fat densification in her gluteal region, bilaterally, in relation to these injections. The hypercalcemia was attributed to increased extrarenal production of active vitamin D by activated macrophages within PMMA-induced granulomas. Hypercalcemia was treated with intravenous hydration, a calcimimetic agent (60 mg daily) and corticosteroid therapy (prednisolone 30 mg daily), resulting in progressive normalization of serum calcium levels and clinical improvement.

Cosmetic enhancement procedures may have delayed side effects that explain the aetiology of hypercalcemia. Removal of this permanent filler is not possible; therefore, long term treatment is necessary to avoid recurrence of hypercalcemia. This case report highlights the challenging management of hypercalcemia in a young patient with impaired kidney function and the need to carefully balance effective calcium control with renal safety.

Abstract citation ID: lvag096.805

EP239 - ECE_2410 - Coexisting causes of secondary osteoporosis: systemic mastocytosis and partial hypogonadism in a male patient with Y-chromosome mosaicism

Vasilis Gioxaris[1], Maria-Eleni Chondrogianni[1,2,3], Anna Papadopoulou[4,5], Nektaria Papadopoulou-Marketou[1], Symeon Tournis[6] and Eva Kassi[1,2,3]
[1]*Endocrine Unit, 1st Department of Propaepeudic Internal Medicine, Laiko Hospital, National and Kapodistrian University of Athens, Athens, Greece;* [2]*Department of Biological Chemistry, Medical School, National and Kapodistrian University of Athens, Athens, Greece;* [3]*Center of Excellence for Rare Endocrine Diseases (C.E.R.E.D.), General Hospital of Athens, LAIKO, National and Kapodistrian University of Athens, European Reference Network on Rare Endocrine Conditions (ENDO-ERN), Athens, Greece;* [4]*Division of Endocrinology, Metabolism & Diabetes, First Department of Pediatrics, Medical School, National and Kapodistrian University of Athens, 'Aghia Sophia' Children's Hospital, Athens, Greece;* [5]*Department of Clinical Biochemistry, National and Kapodistrian University of Athens Medical School, University General Hospital "Attikon", Athens, Greece;* [6]*Laboratory for Research of the Musculoskeletal System 'Th. Garofalidis', Medical School, National and Kapodistrian University of Athens, KAT General Hospital, Kifissia, Athens, Greece*

Introduction: Osteoporosis is a global health problem. Among men with osteoporosis, 50%-80% have secondary osteoporosis, which is frequently under-recognized. Male hypogonadism may represent a cause of secondary osteoporosis. Systemic mastocytosis is another uncommon but clinically significant cause and may present with severe skeletal involvement. We report a patient with known hypogonadism in whom the assessment for secondary osteoporosis revealed systemic mastocytosis.

Case presentation: A 62-year-old man with a medical history of hypertension, nephrolithiasis, previous knee arthroplasty and Y chromosome mosaicism presented with acute back pain following minimal trauma after lifting a 15-kg weight. Cytogenetic investigation due to azoospermia revealed a rare mosaic karyotype pattern of 45,X/46,XY/ 47,XY, +mar (Y).

The molecular analysis of Y-chromosome markers (DYS1, DYS222, DAZ) confirmed loss of Y chromosomal material. He had previously received testosterone replacement therapy during puberty.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

The imaging revealed a vertebral fracture at L1 and kyphoplasty was performed. Nine days later, he experienced sudden back pain and further imaging demonstrated new vertebral fractures at T12, L4, and L5. Thus, he underwent an additional kyphoplasty. Given the occurrence of multiple low-trauma vertebral fractures, the patient was evaluated for secondary causes of osteoporosis other than his partial hypogonadism (testosterone levels = 2.33 ng/ml (normal range: 1.93-7.40)). The workup revealed elevated serum tryptase levels (34.9 μg/L) and hypothyroidism. The patient underwent a bone marrow biopsy, which together with serum tryptase levels, confirmed the diagnosis of systemic mastocytosis. Treatment with levothyroxine, and midostaurin was initiated. Although bisphosphonates remain the cornerstone of therapy for mastocytosis-associated osteoporosis, the patient expressed significant concern regarding the risk of acute phase reactions when informed of bisphosphonates' side effects. Therefore, denosumab therapy was initiated, considering evidence suggesting it may also reduce serum tryptase levels.

New bone mineral density measurements will be evaluated in February 2026, one year after the treatment initiation.

Conclusions: This case highlights the importance of investigating secondary causes of osteoporosis in patients presenting with osteoporosis, as more than one contributing factors may coexist.

References

1. Ebeling PR, Nguyen Hanh H, Aleksova Jasna, Vincent Amanda J, Wong Phillip, Milat Frances. Secondary osteoporosis. *Endocr Rev*. 2022;43(2):240-313. https://doi.org/10.1210/endrev/bnab028
2. Orsolini G, Gavioli I, Tripi G, et al. Denosumab for the treatment of mastocytosis-related osteoporosis: a case series. *Calcif Tissue Int*. 2017;100(6):595-598. https://doi.org/10.1007/s00223-017-0241-z

Abstract citation ID: lvag096.806

EP241 - ECE_3851 - Screening for MEN1 mutations in high-risk primary hyperparathyroidism: age and glandular involvement as predictors of germline status

Bogdan Radu Dițescu[1], Iulia Florentina Burcea[1,2], Dobre Ramona[1,2], Andra Caragheorgheopol[3], Elena Emanuela Braha[4] and Cătălina Poiană[1,2]

[1]*First Endocrinology Department, "C.I. Parhon" National Institute of Endocrinology, Bucharest, Romania;* [2]*Department of Endocrinology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, Bucharest, Romania;* [3]*Research Laboratory—Pathology Department, "C.I. Parhon" National Institute of Endocrinology, Bucharest, Romania;* [4]*Department of Genetics, "C.I. Parhon" National Institute of Endocrinology, Bucharest, Romania*

Introduction: Primary hyperparathyroidism (PHPT) most commonly results from single-gland disease, whereas in hereditary syndromes such as Multiple Endocrine Neoplasia type 1 (MEN1) it typically presents as multiglandular involvement, with most patients developing disease by the fifth decade of life. In accordance with current clinical practice guidelines for MEN1, the objective of this study was to evaluate the clinical and biochemical phenotypes of PHPT and to assess the utility of genetic screening in patients diagnosed before the age of 35 or those presenting with multiglandular disease.

Methods: We performed a retrospective analysis of patients diagnosed with PHPT between January 2024 and December 2025 who met at least one of the following criteria: age ≤35 years at diagnosis or evidence of multiglandular parathyroid disease. Clinical characteristics, biochemical parameters, imaging findings, and associated endocrine manifestations were reviewed. All patients underwent germline MEN1 mutation testing.

Results: A total of 13 patients were included and stratified into two groups based on clinical selection criteria. The first group included 7 patients diagnosed with PHPT prior to age 35 (29 ± 5.06 years), while the second group consisted of 6 patients (55.5 ± 10.1 years) presenting with multiglandular parathyroid disease. In the early-onset group, 85.7% of patients had a single parathyroid adenoma at diagnosis, while 14.3% presented with double adenomas. The mean serum calcium level for this subgroup was 10.41 ± 0.47 mg/dL, with a mean parathyroid hormone (PTH) concentration of 138.92 ± 63.48 pg/mL. In contrast, among patients with multiglandular involvement, 66.6% had two affected glands and 33.3% had three parathyroid adenomas. This group demonstrated higher biochemical severity, with a mean serum calcium level of 11.67 ± 0.58 mg/dL and a median PTH concentration of 220.5 pg/mL. Across the entire cohort, systemic evaluation revealed pituitary tumors in 76.9% of patients, neuroendocrine tumors in 30.7%, and adrenal tumors in 38.4%. MEN1 germline mutations were identified in 28.5% of patients diagnosed before age 35 and in 50% of those with multiglandular parathyroid disease.

Conclusions: Multiglandular parathyroid involvement appears to be a stronger clinical predictor for MEN1 mutations than isolated young age at onset. The high prevalence of associated endocrine tumors supports a MEN1-like phenotype across the cohort, underscoring the importance of genetic evaluation and raising the possibility of syndromic phenocopies.

Abstract citation ID: lvag096.807

EP242 - ECE_2607 - "Serum inflammation-based scores (SIBs) in primary hyperparathyroidism: association with biochemical severity and postoperative outcomes"

Karol Ciszek[1], Dorota Pach[1], Marta Opalinska[1], Jacek Podlewski[2], Marcin Barczynski[3], Aleksander Konturek[3] and Alicja Hubalewska-Dydejczyk[1]

[1]*Chair and Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland;* [2]*Dover Fueling Solutions, Kraków, Poland;* [3]*Department of Endocrine Surgery, Faculty of Medicine, Jagiellonian University Medical College, Kraków, Poland*

Primary hyperparathyroidism (PHPT) is a chronic endocrine disorder increasingly associated with low-grade inflammation, partly caused by persistently elevated parathyroid hormone (PTH) levels. Serum inflammation-based scores (SIBS), obtained from routine blood tests, are widely used as markers of inflammation in various clinical settings; however, their role in primary hyperparathyroidism remains poorly defined. The aim of this study was to assess the association between SIBS and the biochemical severity of primary hyperparathyroidism, to evaluate gender differences in these markers, and to analyze their changes after parathyroidectomy.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

This retrospective single-center study included patients with primary hyperparathyroidism treated between 2020 and 2025 in our clinic. Of the 279 initially identified patients, 153 with complete preoperative laboratory data were included in the analysis. The analyzed inflammation-based scores included the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and the systemic immune-inflammation index (SII: platelets × neutrophils/lymphocytes). Associations between serum calcium, PTH, and SIBS were assessed using correlation analyses and multivariable linear regression models. Postoperative follow-up data were available for 19 patients, allowing for paired pre-post comparisons using Student's t-test or the Wilcoxon signed-rank test, as appropriate. P value $< .05$ was considered statistically significant.

The final cohort consisted of 153 patients (127 females, 26 males). Due to the non-normal distribution of the data, non-parametric analyses were used. Male patients demonstrated significantly higher MLR and NLR values compared to females ($P = .0014$ and $P = .024$, respectively). Significant associations were observed between SIBS and biochemical markers of PHPT. Serum calcium levels showed positive correlations with NLR ($P < .001$), MLR ($P = .002$), and SII ($P < .001$). Similarly, PTH levels positively correlated with NLR ($P < .001$), MLR ($P < .001$), and SII ($P < .001$). In multivariate analysis, MLR was independently associated with PTH, age, and male sex. All inflammation-based scores showed a numerical decrease after parathyroidectomy; however, a statistically significant reduction was observed only for PLR (mean change −34.2, $P = .046$). Changes in MLR, NLR, and SII did not differ significantly, most likely due to the limited number of patients with available postoperative complete blood count with differential.

Serum inflammation-based scores are associated with the biochemical severity of primary hyperparathyroidism. Sex-related differences were observed, with higher MLR and NLR values in male patients. Although SIBS tended to decrease after parathyroidectomy, larger studies with bigger follow-up are needed to confirm postoperative changes and clarify their clinical relevance.

Abstract citation ID: lvag096.808

EP243 - ECE_2783 - Limited predictive performance of scoring models for sporadic multiglandular parathyroid disease in patients referred for fluorocholine PET/CT

Katerina Zajickova[1,2], Josef Vcelak[1,3], Petr Libánský[4], Dana Michalska[2] and David Zogala[5]
[1]Institute of Endocrinology, Prague, Czech Republic; [2]General University Hospital and First Faculty of Medicine, III. Internal Clinic, Endocrinology and Metabolism, Prague 2, Czech Republic; [3]First Faculty of Medicine, First Faculty of Medicine, Charles University, Prague 2, Czech Republic; [4]3rd Department of Surgery, Surgery, Motol University Hospital, Prague 5, Czech Republic; [5]General University Hospital and First Faculty of Medicine, Nuclear Medicine, Prague 2, Czech Republic

Multiglandular parathyroid disease (MGD) is a less common presentation of sporadic primary hyperparathyroidism (PHPT), occurring in approximately 10%-20% of patients compared to single gland hyperparathyroidism (SGD). Equivocal parathyroid imaging is associated with a higher prevalence of MGD in PHPT, making focused, limited parathyroidectomy challenging.

We present a cohort of 54 patients with PHPT (mean calcium 2.77 mmol/l, parathyroid hormone (PTH) 102.1 ng/l and age 64.0 years) who underwent fluorocholine PET/CT (FCH) due to inconclusive neck ultrasound, MIBI scintigraphy or persistent PHPT. Thirteen of 54 patients had MGD (24.1%) based on postoperative histology. The diagnostic performance of three preoperative MGD prediction models (CaPTHUS, the Washington University Index (WUI) and the Luo nomogram) was evaluated.

There were no differences in preoperative parameters, including serum calcium, phosphate, creatinine, and PTH levels, between patients with MGD and SGD. The CaPTHUS test correctly identified 10 patients (76.9%) with MGD and six patients (14.6%) with SGD. The WUI correctly identified three patients (23.1%) with MGD and 30 patients (73.2%) with SGD. The Luo nomogram failed to identify any cases of MGD. FCH identified 42.8% of patients with MGD, and its positive predictive value increased to 50% when combined with WUI-based stratification.

The equivocal standard parathyroid imaging and milder disease presentation were likely the reasons why the preoperative prediction scoring models could not reliably distinguish sporadic MGD from SGD in our patient cohort. The positive predictive value of FCH in diagnosing MGD was better than the three prediction models. The diagnostic value of combining FCH with selected biochemical indices for predicting MGD warrants validation in larger patient populations. Currently, the extent of parathyroidectomy in patients with equivocal imaging relies on surgeon expertise because preoperative differentiation of MGD from SGD is difficult.

Abstract citation ID: lvag096.809

EP244 - ECE_1302 - Unmasking a hereditary cause of aggressive hyperparathyroidism

Leire Perez Garcia[1], Maria del Carmen Fernandez Lopez[2], Leire Isasa Rodriguez[2] and Leire Agea Diaz[1]
[1]Hospital Universitario Araba, Vitoria-Gasteiz, Spain; [2]Hospital Universitario Cruces, Barakaldo, Spain

Background: Parathyroid carcinoma is a rare cause of primary hyperparathyroidism and may occur as part of Hyperparathyroidism–Jaw Tumor (HPT-JT) syndrome, an autosomal dominant disorder caused by pathogenic germline variants in *CDC73*.

Case presentation: A 59-year-old man presented to the emergency department in January 2019 with progressive asthenia, polydipsia and severe hypercalcemia (albumin-corrected calcium 16.02 mg/dL). Labs showed markedly elevated PTH (1363 pg/mL) and severe 25-hydroxyvitamin D deficiency (6 ng/mL). He reported constitutional symptoms since September 2018 and a history of nephrolithiasis requiring lithotripsy 10 and 20 years earlier.

Emergency management included intravenous hydration, furosemide, zoledronic acid, and calcitonin, achieving calcium levels of 8-10.6 mg/dL. Cervical computed tomography revealed a 30 × 26 × 48 mm solid mass posterior to the right thyroid lobe, suggestive of parathyroid carcinoma.

In February 2019, he underwent right hemithyroidectomy with en bloc resection of the right superior parathyroid tumor. Histology confirmed a 3-cm oncocytic parathyroid carcinoma with vascular invasion, capsular and adipose infiltration, necrosis, mitotic index 4/10 HPF, and Ki-67 index 10%. A peritumoral

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hyperplastic parathyroid gland was also identified. Preoperative PTH was 1681 pg/mL, decreasing to 145 pg/mL postoperatively.

Persistent normocalcemic hyperparathyroidism (PTH 300 pg/mL) prompted reoperation in September 2019, excising the inferior and half of the left superior hyperplastic parathyroid glands. Post-reintervention, he achieved stable normocalcemia (8.2-9.3 mg/dL), normal phosphate, high-normal PTH (60-150 pg/mL), and adequate vitamin D status.

Genetic testing revealed a heterozygous *CDC73* frameshift variant (c.687_688delAG; p. R229Sfs*37), recently reported in association with HPT-JT syndrome. One daughter was affected and required surgery, another tested negative.

Follow-up: Despite high risk of hungry bone syndrome, only initial phosphate supplementation and monthly cholecalciferol were needed. Postoperative hypothyroidism required levothyroxine 50 µg daily since 2020. A stable 15-mm lesion in the left second rib, consistent with a brown tumor, was observed on serial magnetic resonance imaging (MRI) between 2020 and 2024. Bilateral Bosniak I renal cysts were observed (largest 3 cm in left kidney, stable 2019-2024). Serial imaging showed no local recurrence (neck ultrasound 2025; MRI 2024), and dental panoramic radiography revealed no jaw tumors (2022). Bone densitometry showed normal lumbar and femoral osteopenia (2023).

Conclusions: This case highlights the diagnostic and therapeutic challenges of parathyroid carcinoma associated with HPT-JT syndrome and underscores the importance of genetic testing and long-term multidisciplinary follow-up.

Abstract citation ID: lvag096.810

EP245 - ECE_2602 - Teriparatide as an effective treatment for refractory hypocalcemia in Autoimmune Polyglandular Syndrome Type 1

Rita Pinto Ribeiro[1], Patrícia Brito[1], Bruna Silva[2], Adriana de Sousa Lages[1], Bárbara Araújo[1], Joana Maclel[1], Diana Borges Duarte[1], Juliana Sá[1], Sara Esteves Ferreira[1] and Olinda Marques[1]

[1]Endocrinology Department, Unidade Local de Saúde de Braga, Braga, Portugal; [2]Endocrinology Department, Unidade Local de Saúde Tâmega e Sousa, Penafiel, Portugal

Introduction: Autoimmune Polyglandular Syndrome Type 1 (APS-1) is a rare inherited disorder characterized by the triad of chronic mucocutaneous candidiasis, hypoparathyroidism, and adrenal insufficiency. Management of hypocalcemia in APS-1 can be challenging, particularly when malabsorption limits oral calcium and active vitamin D efficacy. Teriparatide, a recombinant PTH (1-34) analog, is not approved for hypoparathyroidism but has been used off-label in selected refractory cases.

Case report: Female, 26-year-old, followed in the Endocrinology Department since age 18 for APS-1, comprising primary adrenal insufficiency, primary hypoparathyroidism, premature ovarian insufficiency, autoimmune hepatitis, ectodermal dystrophy of dental enamel and nails, and exocrine pancreatic insufficiency. She was on calcium, calcitriol, azathioprine, hydrocortisone, fludrocortisone, estradiol, progesterone, and pancreatin.

Since 2017, she has experienced recurrent episodes of symptomatic hypocalcemia despite high-dose calcitriol (2,25 µg/day) and calcium carbonate (4500 mg/day), typically triggered by diarrheal exacerbations. She reported a long-standing history of alternating diarrhea and constipation.

In 2024, she presented to the Emergency Room with facial and extremities paresthesias and muscle stiffness. One month earlier, she started complaining of nausea, vomiting, and diarrhea, and the subsequent symptomatic hypocalcemia was treated with intravenous calcium gluconate(IV calcium) and increased oral calcium dose.

At readmission, biochemical evaluation revealed hypokalemia, hypocalcemia, hypomagnesemia and normal serum phosphorus, and she started IV calcium and electrolyte correction. During the first 15 days of hospitalization, repeated attempts to discontinue IV calcium and maintain oral therapy alone resulted in recurrent severe hypocalcemia.

On day 16, teriparatide 20 µg once daily was initiated as an off-label treatment for refractory and severe hypocalcemia. Within two days, IV calcium supplementation was successfully discontinued, and the patient transitioned to oral therapy, with diarrhea resolution. Following discharge, oral calcium carbonate and calcitriol doses were progressively reduced.

Ten months later, she remains clinically stable with normal calcium, phosphorus, and calciuria on calcium carbonate 3000 mg/day, calcitriol 1 µg/day, and teriparatide 20 µg every other day.

Conclusions: This case supports the use of teriparatide as a potential therapeutic option for refractory hypocalcemia due to hypoparathyroidism in APS-1, especially when malabsorption limits conventional therapy. It should be reserved for selected patients under close monitoring. However, the optimal treatment duration remains uncertain, as long-term safety data are still limited.

Abstract citation ID: lvag096.811

EP246 - ECE_2850 - The therapeutic challenge of chronic hypoparathyroidism: a case report of real-life experience with palopegteriparatide

Giulia Del Sindaco[1], Angela Pagnano[1,2], Lucrezia Ghisleni[1,2], Giulia Carosi[1] and Giovanna Mantovani[1,2]

[1]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]Department of Clinical Sciences and Community Health, Dipartimento di Eccellenza 2023-2027, Università Degli Studi Di Milano, , Milan, Italy

The management of chronic hypoparathyroidism remains a therapeutic challenge. Therapy aims to prevent hypocalcemic symptoms, maintain serum calcium levels in the low-normal range, and avoid hypercalciuria, a major concern in this disease. Many patients fail to achieve biochemical control with conventional therapy and experience persistent symptoms with impaired quality of life. Moreover, even in the presence of normocalcemia, unpredictable calcium fluctuations and long-term complications, such as renal impairment, extraskeletal calcifications, and neuropsychiatric disorders, may occur. In this context, emerging therapies based on recombinant PTH or PTH agonists represent a promising approach.

We report the paradigmatic case of a patient who underwent multiple therapeutic strategies over years.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

The patient is a 47-year-old woman who underwent total thyroidectomy at the age of 20 for Graves–Basedow disease unresponsive to medical treatment. Since the diagnosis of hypoparathyroidism, she never achieved satisfactory clinical or biochemical control despite multiple treatment attempts, and she continued to experience hypocalcemic symptoms. In addition to conventional therapy with high-dose calcium supplementation and active vitamin D, up to 7-8 gr of calcium and 2-2.5 mcg of calcitriol daily, she was previously treated with PTH replacement therapy (PTH(1-34) and subsequently PTH(1-84)). Over the years, she experienced several episodes of laryngospasm and severe tetany requiring hospitalization and intravenous calcium administration. She also developed hypercalciuria, nephrocalcinosis, and nephrolithiasis, leading to the introduction of thiazide diuretics. Notably, even during PTH replacement therapy, calcium and calcitriol could never be discontinued because of inadequate biochemical and clinical control, and hypercalciuria persisted.

TransConPTH (palopegteriparatide) is a sustained-release prodrug of PTH(1-34) designed to provide physiological PTH levels over 24 h in adults with hypoparathyroidism. The patient started palopegteriparatide at a dose of 18 mcg daily in July 2025, reporting improved well-being within the first days of treatment. With progressive dose escalation, conventional therapies were gradually down-titrated, allowing complete withdrawal of calcitriol in November 2025. Serum calcium and phosphate levels remained within the low-normal range, no hypocalcemic symptoms were reported, and hypercalciuria normalized after three months of therapy. Bone turnover markers remained stable at the last biochemical assessment. The current palopegteriparatide dose is 42 mcg daily, and no adverse events have been reported to date.

In conclusion, in our experience, palopegteriparatide significantly improved the management of chronic hypoparathyroidism compared with conventional therapy and previous PTH replacement strategies. By restoring physiological PTH activity, palopegteriparatide represents a promising treatment for achieving clinical and biochemical control in chronic hypoparathyroidism.

Abstract citation ID: lvag096.812

EP248 - ECE_2437 - Skeletal lesions in prostate cancer: when primary hyperparathyroidism is the culprit

Teodora Vintilă[1], Alexandru Florescu[1,2], Irina Puscasu[1], Andra Berigoi[1], Stefana Bilha[1,2] and Cristina Preda[1,2]
[1]*Saint Spiridon County Hospital, Iași, Romania;* [2]*Iași, Romania*

Skeletal involvement is a defining feature of advanced prostate cancer (PC) and is commonly regarded as a surrogate of metastatic spread, often guiding staging and therapeutic decisions. While this assumption is frequently justified, it may obscure alternative causes of bone involvement, particularly in the presence of coexisting endocrine disorders. Emerging evidence suggests that primary hyperparathyroidism (PHPT) represents a source of diagnostic ambiguity when skeletal lesions coexist with metabolic bone disease in PC.

We report the case of a 75-year-old man with PC (Gleason score 7), treated with androgen deprivation therapy, in whom pelvic magnetic resonance imaging during oncologic follow-up revealed multiple skeletal lesions suspicious for metastatic disease. The most prominent lesion (41 × 16 mm) was located in the right inferior pubic ramus, with additional indeterminate lesions in the sacrum and iliac bones.

Subsequent evaluation revealed hypercalcemia, prompting endocrinological assessment. Biochemical testing was consistent with PHPT, with elevated PTH (1741 pg/mL), hypercalcemia (13.3 mg/dL), hypercalciuria (367.2 mg/24 h), and low–normal vitamin D levels (20.5 ng/mL). Neck ultrasound and sestamibi scintigraphy identified a large hyperfunctioning left inferior parathyroid lesion. In parallel, bone scintigraphy demonstrated extensive skeletal involvement, with multiple hyperfixating foci affecting the skull, right radius, lumbar spine, sacrum and pelvis resulting in a heterogeneous pattern. In the oncologic context, this appearance was initially interpreted as highly suggestive of widespread metastatic disease.

The patient underwent parathyroidectomy, with histopathology confirming an atypical parathyroid adenoma. One year postoperatively, biochemical parameters normalized (PTH 25.95 pg/mL, corrected calcium 8.3 mg/dL, alkaline phosphatase 58 U/L). Follow-up bone scintigraphy demonstrated marked regression of tracer uptake at previously involved sites, no new hyperfixating lesions, and persistent extra-articular uptake at the level of the hands, a scintigraphic finding consistent with brown tumors. Together with biochemical normalization, this evolution supported the retrospective diagnosis of parathyroid-related bone disease. Bone mineral density improved at axial sites (+40.1% lumbar spine, +16.7% femoral neck), with persistent cortical impairment at the distal radius.

This case illustrates how PHPT can function as a major diagnostic confounder in patients with PC, in whom skeletal lesions are frequently framed as metastatic disease. Beyond a diagnostic pitfall, it raises a clinically relevant question regarding the systematic evaluation of calcium–PTH homeostasis in this population. Proactive parathyroid assessment may be clinically justified in selected PC patients with skeletal involvement or biochemical abnormalities to prevent cancer overstaging and avoid therapeutic escalation driven by metabolically reversible bone pathology.

Abstract citation ID: lvag096.813

EP249 - ECE_2720 - The paradox of diagnosis: evaluating osteoporosis knowledge and health literacy among female patients

Birgul Genc, Berna Evranos Ogmen, Reyhan Ersoy, Oya Topaloglu and Bekir Cakir
Endocrinogy and Metabolism, Ankara Bilkent Şehir Hastanesi, Ankara, Türkiye

Objective: This study aimed to evaluate the knowledge levels and socio-demographic characteristics of female patients regarding osteoporosis and to determine whether a formal diagnosis of the disease correlates with higher health literacy.

Methods: This descriptive, cross-sectional study included 396 female participants aged 30 and over. Data were collected through face-to-face interviews using a standardised demographic questionnaire and a modified 36-item osteoporosis knowledge questionnaire. Participants were divided into two groups based on their medical history: those diagnosed with osteoporosis ($n = 66$) and those without ($n = 330$). Anthropometric measurements

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(BMI) and laboratory findings (serum calcium and vitamin D) were also recorded.

Results: The mean age of the osteoporosis group was significantly higher (63.23 ± 14.41 years) compared to the non-osteoporosis group (50.70 ± 11.56 years, $P < .001$). Patients with osteoporosis were more likely to be from disadvantaged socioeconomic backgrounds, with significantly higher illiteracy rates (28.78% vs 10.30%, $P = .0001$). Despite their diagnosis, the mean total osteoporosis knowledge scores showed no statistically significant difference between the two groups (45.8 ± 15.8 vs 41.67 ± 16.8, $P = .066$), indicating a shared deficiency in disease awareness. Furthermore, the osteoporosis group exhibited significantly lower serum calcium levels ($P = .048$) and alarmingly low rates of calcium and Vitamin D supplementation.

Conclusions: A clinical diagnosis of osteoporosis does not inherently lead to improved disease knowledge or better health practices. Current management appears to be focused on pharmacological treatment, neglecting the essential role of patient education. There is an urgent need for structured, literacy-level-appropriate educational programs to bridge the implementation gap and improve long-term bone health outcomes, particularly among socio-economically disadvantaged populations.

Keywords osteoporosis, osteoporosis knowledge, disease awareness, health literacy

Abstract citation ID: lvag096.814

EP250 - ECE_2401 - Severe refractory hypocalcaemia in a breast cancer patient—multiple concurring mechanisms

Daniel Grigorie[1,2], Diana Felicia Coles[3,4] and Alina Sucaliuc[1]
[1]*Romania, Bucharest, Romania;* [2]*"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania;* [3]*"CI Parhon" National Institute of Endocrinology, Bucharest, Romania;* [4]*"Carol Davila" University of Medicine and Pharmacy, Doctoral School, Bucharest, Romania*

Background: Hypocalcaemia, in contrast to hypercalcaemia, is a rare complication of malignancy, often multifactorial, severe and prolonged, particularly in the context of antiresorptive therapy and extensive skeletal involvement and complicates oncologic management.

Case presentation: We report the case of a 52 years old woman with metastatic hormone receptor–positive breast cancer, who developed severe, refractory hypocalcaemia following a single 120 mg dose of denosumab. She was receiving oncologic therapy with ribociclib, letrozole and goserelin. The patient had total thyroidectomy 2 years earlier and reported inconsistent supplementation with 600 mg calcium and 400 IU vitamin D, being asymptomatic. Prior to denosumab serum calcium was 8.4 mg/dL (8.6-10.6 mg/dL), PTH 37.8 pg/mL (15-65 pg/mL). Five days after denosumab administration, she presented with a severe, life-threatening tetanic crisis with opisthotonus and marked QTc prolongation, with a nadir serum calcium of 3 mg/dL (0.75 mmol/L). Despite intravenous and oral calcium (up to 3.6 g calcium carbonate daily) and alfacalcidol (3 µg/day), hypocalcaemia remained refractory for over two months, with levels reaching 6.4 mg/dL at admission in our department; normal phosphate, magnesium and renal function, elevated alkaline phosphatase (563 U/L, NR 35-105 U/L), and an inappropriately normal parathyroid hormone level (50.7 pg/mL). Imaging revealed disseminated, predominantly osteoblastic bone metastases. Reviewing the chart of the surgery we identified hypoparathyroidism—Ca 7 mg/dL, PTH 4 pg/mL, which evolved to parathyroid insufficiency, after a year Ca 7.2 mg/dL, PTH 50 pg/mL. Switching to calcitriol (1.5 µg/day) and higher calcium dose (4.2 g/day) resulted in gradual normalization of calcium levels and QTc interval, with complete recovery from hypocalcaemia after approximately 95 days. However, inconsistent outpatient monitoring later led to transient hypercalcaemia, hypercalciuria, and renal function decline.

Discussion: Denosumab-induced suppression of bone resorption represented the main precipitating factor. Extensive osteoblastic metastases are less common than osteolytic metastases in breast cancer but they acted as a major facilitating factor, promoting accelerated bone formation and mineralization with increased skeletal calcium sequestration. Parathyroid insufficiency post-thyroidectomy made a significant contribution by limiting compensatory parathyroid hormone response.

Conclusions: Although uncommon, malignancy-associated severe hypocalcaemia may be inherently life-threatening when multiple concurring mechanisms coexist: denosumab administration, osteoblastic metastases and reduced parathyroid reserve.

Abstract citation ID: lvag096.815

EP252 - ECE_3548 - Effect of denosumab on osteoporosis prevalence in simultaneous pancreas and kidney recipients

Jana Brunová and Simona Kratochvílová
Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Introduction: Organ transplant recipients especially after simultaneous pancreas and kidney (SPK) are at increased fracture risk compared to general population. The recommended treatment of osteoporosis in solid organ transplant recipients includes vitamin D, calcium supplementation and bisphosphonates. Denosumab is the possible therapeutic option for patients with impaired renal function.

Aim of study: We investigated the bone mineral density (BMD) development in SPK patients, who originally started with denosumab therapy for osteoporosis in lumbar spine and/or proximal femur

Methods: Our retrospective study comprises 34 subjects after SPK, (12 M, 22 W, mean age 44 ± 9.6 y at the beginning of therapy), transplanted between 1994-2024. Dual energy X-ray absorptiometry scans (DXA) were performed with the Lunar Prodigy apparatus. The mean therapy duration was 37.2 ± 24.2 months (3.1y). Fracture history was present in 15/34 (44%) patients.

Results: L spine T score improved in the whole group from −1.4 ± 1.3 to −0.7 ± 1.5 ($P < .001$). The values of proximal femur T score increased from −2.9 ± 0.6 to −2.7 ± 0.8 after the therapy ($P < .05$). Mean increase in BMD of L-spine was 8.2 ± 6.9%, of the proximal femur raised by 3.6 ± 7.2%. The denosumab therapy decreased the prevalence of osteoporosis in all patients from 34/34 (100%) to 18/34 (53%), in L spine from 7/34 (20%) to 4/34

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(12%), proximal femur from 32/34 (94%) to 17/34 (50%) and in neck from 28/34 (82%) to 20/34 (59%).

Summary: The denosumab treatment significantly improved the BMD values at L spine and proximal femur sites in SPK recipients treated for osteoporosis. The prevalence of osteoporosis decreased by 47% in whole group.

Funding: Supported by MZO 0002301002301

Abstract citation ID: lvag096.816

EP253 - ECE_3885 - Adherence to the mediterranean diet as a predictor of bone health in adults with cystic fibrosis

María Del Carmen Andreo-Lopez[1], Victoria Contreras-Bolívar[1], Francisco Casas-Maldonado[1], Silvia Merlos-Navarro[2], Casilda Olveira[3], Gabriel Olveira[3], José Manuel Vaquero-Barrios[4], Manuel García-Amores[5], Diego Becerra-García[1] and Manuel Muñoz-Torres[1]
[1]Hospital Universitario San Cecilio, Granada, Spain; [2]Hospital Universitario Virgen de las Nieves, Granada, Spain; [3]Hospital Universitario Regional de Málaga, Granada, Spain; [4]Hospital Universitario Reina Sofía, Córdoba, Spain; [5]Hospital Universitario de Jaén, Jaén, Spain

Background: Cystic fibrosis–related bone disease (CFBD) is an increasingly prevalent complication and is associated with a higher risk of fragility fractures and mortality. Beyond areal bone mineral density (aBMD) assessed by dual-energy X-ray absorptiometry (DXA), advanced imaging techniques such as trabecular bone score (TBS) and three-dimensional DXA (3D-DXA) allow a more detailed evaluation of bone microarchitecture and compartmental structure. However, the impact of modifiable nutritional factors, including adherence to the Mediterranean diet, on these advanced bone parameters in adults with cystic fibrosis (CF) remains poorly characterised.

Objective: To evaluate whether adherence to the Mediterranean diet is associated with bone structural parameters assessed by conventional DXA, TBS, and 3D-DXA in adults with CF.

Methods: A case–control study including 32 adults with CF and 70 healthy controls matched for age, sex, and body mass index was conducted. Bone health was assessed using DXA to obtain aBMD, TBS to estimate trabecular microarchitecture, and 3D-DXA to analyse cortical and trabecular compartments. Clinical and biochemical data were collected. Adherence to the Mediterranean diet was assessed using the PREDIMED questionnaire. Multivariable regression models were applied to identify independent associations.

Results: Fragility fractures were present in 22% of adults with CF. Good adherence to the Mediterranean diet was significantly lower in the CF group compared with controls (50% vs 81.2%, $P = .001$). Adults with CF showed a higher prevalence of low aBMD (28.1% vs 5.7%, $P < .001$), impaired trabecular microarchitecture assessed by TBS (31.3% vs 12.5%, $P = .002$), and lower cortical and trabecular parameters evaluated by 3D-DXA (all $P < .01$). In multivariable analyses, adherence to the Mediterranean diet emerged as an independent predictor of aBMD, TBS, and 3D-DXA–derived parameters, explaining between 14% and 60% of their variability.

Conclusions: CF-related bone disease remains highly prevalent in adults with cystic fibrosis. Individuals with CF exhibit impaired bone status across multiple imaging modalities. Higher adherence to the Mediterranean diet is independently associated with more favourable bone structural parameters, suggesting a potential role for dietary patterns in bone health optimisation in this population.

Abstract citation ID: lvag096.817

EP254 - ECE_2618 - "It is not what it seems"-a rare case of Water-clear cell parathyroid adenoma

Zehra Irshad, Dominic Oduro-Donkor and Ranganatha Rao
Coventry, United Kingdom

Background: Water-clear cell parathyroid adenoma (WCCPA) is an exceedingly rare manifestation of primary hyperparathyroidism with only five reported cases to date.[1] Here we describe an interesting case of WCCPA presenting as a stroke mimic.

Case presentation: A 64-year-old African gentleman with background of hypertension presented to Emergency department with acute presentation of slurred speech and balance issues. Initial bloods showed creatinine levels of 136 umol/L (ref 50-104). He had a CT head which did not show any acute pathology and subsequent MRI ruled out acute stroke. He developed confusion and agitation. Blood tests revealed severe hypercalcemia (serum adjusted calcium 4.81 mmol/L, ref 2.17-2.56). Parathyroid hormone was significantly raised at 311 pmol/L (ref 2.0-8.5) with inorganic phosphate levels of 1.58 mmol/L (ref 0.8-1.5), Vitamin D levels of 30 nmol/L (ref > 49) and creatinine levels of 376 umol/L. Initial management included intravenous rehydration and intravenous Bisphosphonate.

CT-TAP showed well-defined enlarged soft tissue leision at the thoracic outlet appearing separate from the right lobe of thyroid. Follow-up ultrasound neck and NM SPECT parathyroid confirmed right-sided parathyroid adenoma. He was admitted under Endocrinology and referred to ENT for parathyroid surgery. He continued to be treated with IV fluids with strict input and output fluid monitoring. Whilst awaiting surgery he was trialled with Calcitonin which did not improve his calcium levels. A right parathyroidectomy was performed, and a histopathological examination confirmed the diagnosis of WCCPA. Post-operatively, the serum calcium and PTH levels of the patient normalised, symptoms resolved and his recovery was uneventful.

Conclusions: WCCPA is a rare albeit significant cause of primary hyperparathyroidism. It is difficult to diagnose as imaging maybe non-specific. This is the first reported case of WCCPA presenting as a stroke mimic with severe hypercalcemia. WCCPA have a unique water-clear cytoplasmic appearance, due to the accumulation of glycogen and intracellular fluid. Histology is key for diagnosis and surgical management has good outcomes. More literature is required to understand lack of response to medical management. Despite their rarity WCCPA are important to understand for early diagnosis and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

treatment to prevent end-stage complications associated with uncontrolled hypercalcemia.

Reference

1. Abdullah AM, Qaradakhy AJ, Ali RM, et al. Water-clear cell parathyroid adenoma: a case report and mini-review of the literature. *Med Int (Lond)*. 2025;5(6):70. https://doi.org/10.3892/mi.2025.269

Abstract citation ID: lvag096.818

EP255 - ECE_2386 - The calcium to magnesium ratio as predictor of renal lithiasis in primary hyperparathyroidism: results from a moroccan cohort

Meryem Eladla, Mohammed Amine Essafi, Zineb El Azime, Hayat Aynaou and Houda Salhi
University Hospital Center Fez Morocco, Endocrinology, Fez, Morocco

Background: Hypercalciuria plays a key role in the development of renal lithiasis in primary hyperparathyroidism, however kidney stones do not occur in all hypercalciuric patients, suggesting the involvement of additional factors . The objective of our study was to evaluate the association between the calcium-to-magnesium ratio and renal lithiasis in this population.

Methods: We conducted a retrospective descriptive and analytical study including patients with hypercalcemic primary hyperparathyroidism managed in the Department of Endocrinology, Diabetology, and Nutrition at Hassan II University Hospital, Fez, between January 2020 and January 2025. Among diagnosed cases, 85 patients met the inclusion criteria and were divided into two age- and sex-matched groups: patients without renal lithiasis (Group 1) and patients with renal lithiasis (Group 2).

All patients underwent a complete biological evaluation including serum calcium, phosphate, magnesium levels, 24-hour urinary calcium excretion, renal function, and calculation of the Ca/Mg ratio. Renal lithiasis was confirmed by renal ultrasonography. Patients with normocalcemic, secondary or tertiary hyperparathyroidism, estimated glomerular filtration rate <30 mL/min, prior medical or surgical treatment, or incomplete records were excluded. An elevated Ca/Mg ratio was defined as >6.35. Statistical analysis was performed using SPSS version 26. Multivariate logistic regression was used to identify independent predictors of renal lithiasis, with $P < .05$ considered significant.

Results: 85 patients were included: 54 in Group 1 and 31 in Group 2. Compared with Group 1, patients with renal lithiasis had higher body mass index and parathyroid hormone levels, and lower estimated glomerular filtration rate, while serum calcium and magnesium levels were comparable between groups. Multivariate analysis showed a significant association between an elevated Ca/Mg ratio and renal lithiasis (OR $\approx$ 3.2, $P < .01$), and an inverse association between serum magnesium levels and renal lithiasis (OR < 1, $P < .05$). Parathyroid hormone levels were not significantly associated with renal lithiasis ($P = .06$). The Ca/Mg ratio and 24-hour urinary calcium showed sensitivities of 78% and 75%, and specificities of 79% and 47%, respectively.

Conclusions: The calcium-to-magnesium ratio is associated with renal lithiasis in primary hyperparathyroidism and demonstrates better specificity than 24-hour urinary calcium excretion. This ratio may represent a simple and practical tool for lithiasis risk stratification in PHPT. In parallel, serum magnesium appears to be inversely associated with renal lithiasis, supporting its protective role. These findings warrant confirmation through prospective studies.

Abstract citation ID: lvag096.819

EP256 - ECE_3404 - Clinical features and treatment strategy of primary hyperparathyroidism during pregnancy

Ekaterina Bibik, Shuainat Labazanova, Tatiana Kokorina, Anna Eremkina, Svetlana Vorotnikova and Natalia Mokrysheva
Endocrinology Research Centre, Moscow, Russia

Background: Primary hyperparathyroidism (PHPT) during pregnancy remains an important clinical problem that requires management and monitoring of the multidisciplinary team. Clinical symptoms of PHPT in pregnant women are often non-specific, leading to diagnostic delays. Biochemical profile of patients correlates with an increased risk of maternal and fetal complications. Drug treatment are limited and may be prescribed based on individual risk-benefit assessment, parathyroidectomy (PTE) seems more beneficial for pregnant patients with symptomatic disease.

Aim: To describe clinical features of PHPT and treatment outcomes in pregnant women.

Results: We managed 30 women (median age 34 [30; 40] years), who were referred to our Centre, among them 28 at 20.5 [16; 24.5] week gestation (min 5, max 34) and two in the postpartum period. 3 patients had confirmed MEN1 syndrome. At initial presentation, the key biochemical parameters were as follows: iPTH 105.5 pg/ml [78.5; 145.8], albumin-adjusted serum calcium (Ca) 2.85 mmol/l [2.69; 2.95], ionized Ca 1.42 mmol/l [1.4; 1.52], phosphorous 0.76 mmol/l [0.7; 0.83], 24-h urinary Ca 10.4 mmol [8.4; 12.5]. The complications of PHPT included nephrolithiasis (50%), bone disorders (17%), non-classical features were gestational diabetes (23%) and hypertension (6%).

10 women received conservative treatment (gr1), 50% of them were operated on after childbirth and 16 underwent PTE in 2 trimester because of severe disease (gr2). A conservative management in all cases included low-calcium diet and rehydration, taking cholecalciferol. 2 patients received cinacalcet with a positive effect before delivery/PTE. One pregnancy occurred during denosumab therapy. Surgery included selective PTE with confirmed parathyroid adenomas (84%), atypical parathyroid tumor (12%) or cancer (4%).There were miscarriages in 2 women and single case of surgical abortion at 21 weeks gestation because of congenital heart defect. One patient underwent emergency C-section because of preeclamplsia,in other cases, the delivery was on time. The total frequency of fetal/newborn complications was 20% in the gr1 and 6% in the gr2, among them hypocalcemia ($n = 1$), congenital pneumonia ($n = 2$), intrauterine fetal death in twins ($n = 1$) were observed.

Conclusions: PHPT during pregnancy can present with various clinical manifestations. Optimal management should be individualized, taking into account gestational age and the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

severity of hypercalcemia. Surgical intervention appears to offer greater benefits, particularly in symptomatic cases of PHPT.

Abstract citation ID: lvag096.820

EP257 - ECE_1892 - Hypercalcaemic crisis due to a water-clear cell parathyroid adenoma

Christina Millou, Christopher Harrold, Reshma Agrawal and David Howe
Endocrine and Diabetes, Wisdem Center, University Hospital of Coventry and Warwickshire, Coventry, United Kingdom

We report a case of water-clear cell adenoma associated with primary hyperparathyroidism. Primary hyperparathyroidism (PHPT) is a leading cause of hypercalcaemia, most commonly due to parathyroid adenomas. The typical cell type in parathyroid adenoma is the chief cell, followed by oxyphilic cell and water-clear cells are extremelly rare and often large.

Case presentation: A 64-year-old man presented with dizziness, unsteady gait and slurred speech and was diagnosed with an acute cerebrovascular event complicated by confusion and expressive aphasia. Investigations revealed severe hypercalcaemia and acute kidney injury.

Initial biochemistry showed adjusted calcium 4.81 mmol/L (ref. range 2.17-2.56 mmol/L), creatinine 395 µmol/L (ref. range 59-104 µmol/L), and PTH 311.2 pmol/L (ref. range 2.0-8.5 pmol/L), consistent with PTH-dependent hypercalcaemia. Vitamin D was low 30 nmol/L (ref. range > 49 nmo/l). Renal ultrasound was normal. Neck ultrasound demonstrated a 3.1×2.4 cm thyroid nodule, but a parathyroid adenoma could not be excluded.

Despite aggressive intravenous fluids, hypercalcaemia persisted. Denosumab 120 mg was administered, leading to biochemical improvement. Cinacalcet was commenced and the patient was discharged.

Two months later he re-presented with confusion and weakness after stopping cinacalcet. Calcium was again elevated (3.54 mmol/L) with PTH 146 pmol/L. Intravenous fluids and pamidronate produced only transient benefit. A SPECT-CT scan localized a lesion posterior to the right lower thyroid pole, consistent with a right inferior parathyroid adenoma.

The patient underwent urgent parathyroidectomy after informed consent was obtained. Post-operatively, PTH suppressed to 0.8 pmol/L and calcium rapidly normalized. At discharge, adjusted calcium was 2.18 mmol/L with PTH 8.1 pmol/L, confirming biochemical cure.

Histopathology: The resected tumor weighed 14.25 g and measured $48 \times 32 \times 21$ mm. Microscopy revealed a thinly encapsulated parathyroid neoplasm composed predominantly of water-clear cells, with focal chief and oncocytic cell population. No capsular thickening or lymphovascular invasion was identified. The morphology is diagnostic of water-clear cell parathyroid adenoma.

Discussion: Parathyroid adenomas account for 75%-80% of PHPT. Water-clear cell adenomas are rare, usually large, and may be difficult to localize on sestamibi imaging. Although often considered biochemically indolent, this case demonstrates that WCCA can present with life-threatening hypercalcaemic crisis.

Abstract citation ID: lvag096.821

EP258 - ECE_1779 - When osteoporosis is not the whole story: late-onset multiple acyl-CoA dehydrogenase deficiency in a postmenopausal woman

Sevkican Gunes, Gamze Bilik Oyman, Ümmü Mutlu, Hulya Hacisahinogullari, Meryem Karaca, Tugba Kalayci and Ayse Kubat Uzum
Istanbul, Türkiye

Background: Osteoporosis is frequently diagnosed in postmenopausal women, yet secondary etiologies account for nearly one-third of cases. Progressive myopathy or accompanying neuromuscular manifestations should prompt a systematic evaluation for underlying metabolic disorders.

Case presentation: A 57-year-old woman was referred for evaluation of osteoporosis. She was frail and wheelchair-dependent due to progressive proximal muscle weakness over three years, accompanied by diffuse musculoskeletal pain. Although inflammatory myopathy was suspected, myositis autoantibodies were negative, electromyography showed a myopathic pattern, and muscle biopsy was non-specific; nonetheless, she received intravenous immunoglobulin, rituximab, and high-dose corticosteroids.

Menopause age was 50 years, had no family history of osteoporosis, did not smoke or consume alcohol. Laboratory evaluation demonstrated normal creatinine, calcium, phosphorus, parathyroid hormone, vitamin D, thyroid function, and 24-hour urinary calcium. Creatine kinase and transaminase levels were mildly elevated. Dual-energy X-ray absorptiometry revealed a lumbar spine T-score of −1.8 and a femoral neck T-score of −3.3, with FRAX-estimated risks of 19% for major osteoporotic fracture and 6.4% for hip fracture. Vertebral imaging revealed mild height loss at L3. Denosumab therapy was initiated, but multiple vertebral fractures occurred eight months later, following a fall, prompting the addition of teriparatide.

Given the prominent myopathy, adult-onset metabolic myopathies were considered. Lactate and ammonia levels were normal. There is no ketonuria. Tandem mass spectrometry showed elevated multi-chain acyl carnitine (C4, C5, methyl-glutaryl, C14:2) levels, and urinary organic acid analysis revealed elevated ethyl-malonate, a pattern consistent with multiple acyl-CoA dehydrogenase deficiency(MADD). Pompe disease was excluded by normal alpha-glucosidase activity, while McArdle and Cori diseases were considered unlikely based on clinical features. The only manifestation attributable to MADD was proximal myopathy. Echocardiography revealed no evidence of cardiac involvement. Molecular genetic testing revealed a homozygous pathogenic ETFDH variant (c.1130T > C), thereby establishing the diagnosis of MADD.

Treatment with riboflavin, coenzyme Q10, and levocarnitine was initiated along with a low-fat, frequent-meal diet. Within one month, the patient achieved independent ambulation with a 75% reduction in ethylmalonate levels. At six months, there was a marked and sustained improvement in muscle strength and pain, accompanied by an approximately 25% increase in bone mineral density.

Conclusions: This case underscores the need for a systematic and individualized approach to osteoporosis, particularly when accompanied by progressive myopathy. Late-onset metabolic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

disorders, including MADD, should be included in the differential diagnosis, as delayed recognition may result in prolonged diagnostic uncertainty and exposure to unnecessary treatments.

Keywords osteoporosis, multiple acyl-CoA dehydrogenase deficiency, metabolic myopathy

Abstract citation ID: lvag096.822

EP259 - ECE_2188 - CD4+ T cells senescence decreases bone density by changes in genes related to calcium and phosphorus homeostasis

Daniel Cabello-Rivera[1], Rosa Plaza-Clavero[1], Luna Ballesteros-Arias[1], Juan Francisco Aranda[2], Manuel Naves Díaz[3], Juan A. Ardura[1], Arancha R. Gortazar[1] and Maria Del Nogal Avila[1]

[1]*Instituto de Medicina Molecular Aplicada (IMMA) Nemesio Díez, Facultad de Medicina, Universidad San Pablo-CEU, CEU Universities, Urbanización Montepríncipe, Boadilla del Monte 28660, Spain;* [2]*Department of Genetics, Physiology and Microbiology, Faculty of Biology, Complutense University of Madrid, C. de José Antonio Novais, 12, Madrid 28040, Spain;* [3]*Bone and Mineral Research Unit, Hospital Universitario Central de Asturias, Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo 33011, Spain*

Introduction: Bone serves as the primary reservoir of calcium and phosphorus in the body and undergoes continuous remodeling. During aging or in conditions of calcium and phosphorus imbalance caused by physiological or pathological processes, bone resorption may increase, negatively impacting bone density. Calcium and bone homeostasis are regulated by several hormones, including PTH, calcitonin, calcitriol, and FGF23, produced in different organs. Inflammaging, a state of low-grade chronic inflammation associated with aging, is considered a risk factor for age-related diseases such as osteoporosis. Accumulation of senescent cells during aging can impair tissue function through the development of a Senescence-Associated Secretory Phenotype (SASP). Mice lacking expression of the mitochondrial gene *Tfam* specifically in CD4+ T cells exhibit T cell senescence and a premature aging phenotype. In this study, we investigated how senescent CD4+ T cells influence bone remodeling.

Materials and Methods: Gene expression was analyzed by real-time PCR in tibiae from CD4-TFAM mice ($Tfam^{fl/fl}$ $Cd4^{Cre/Cre}$) and control littermates, kindly provided by Dr. Mittelbrunn's research group (Centro de Biología Molecular Severo Ochoa, Madrid, Spain). Bone morphology was assessed using micro-computed tomography (micro-CT). Additionally, MLO-Y4 cells, an osteocyte model, were treated with 1% serum from CD4-TFAM or control mice, and gene expression was analyzed by real-time PCR.

Results: CD4-TFAM mice exhibited significantly lower bone mineral density and compromised bone structural integrity compared with controls. In bone tissue, the OPG/RANKL ratio and expression of osteocyte (osteocalcin) and osteoblast markers (alkaline phosphatase and Runx2) were reduced in CD4-TFAM mice. Expression of hormone receptors such as PTH1R and VDR was also significantly lower, whereas FGF23 expression was higher in CD4-TFAM mice. MLO-Y4 cells treated with serum from CD4-TFAM mice showed significantly increased RANKL expression, while VDR expression remained unchanged compared to cells treated with control serum.

Discussion: Mice with senescent CD4+ T cells displayed reduced bone mineral density and impaired structural integrity, likely due to enhanced osteoclastic activity at the expense of osteoblast function, combined with diminished responsiveness to hormonal regulation resulting from decreased receptor expression.

Abstract citation ID: lvag096.823

EP260 - ECE_2678 - Epidemiology and clinical management of autosomal dominant hypocalcemia type 1 (ADH1): a systematic literature review

Tariq Ahmad[1], Nipith Charoenngam[2], Kelly Roszko[3], Chukwuebuka Dominic Igbelina[4], Nicholas Parr[4], James Frampton[4], Marissa Betts[4], Arun Mathew[5], Lyndsay Smith[5] and Heather Falvey[5]

[1]*University of California San Francisco, Benioff Children's Hospital, Oakland, CA, United States;* [2]*Endocrine Unit, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States;* [3]*Skeletal Disorders and Mineral Homeostasis Section, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD, United States;* [4]*Thermo Fisher Scientific, Inc., Waltham, MA, United States;* [5]*BridgeBio Pharma, Inc., San Francisco, CA, United States*

Introduction: Autosomal dominant hypocalcemia type 1 (ADH1) is a genetic form of hypoparathyroidism in which gain-of-function variants in the calcium-sensing receptor (CaSR) gene cause low parathyroid hormone (PTH) levels, hypocalcemia, hypercalciuria and hyperphosphatemia, leading to neuromuscular symptoms and renal complications. This PRISMA-compliant systematic review identified available evidence on epidemiology, management, humanistic and economic costs of ADH1.

Methods: Studies reporting on the epidemiology, clinical management, humanistic burden, or economic costs of ADH1 were eligible. Searches covered Embase, MEDLINE, PsycInfo, EconLit, and Cochrane databases (September 24, 2025).

Results: Eight studies were identified; three on epidemiology and five on clinical efficacy and/or safety of treatments. No humanistic or economic cost studies were found. ADH1 prevalence per 100 000 people was 6.4 in UK BioBank, 3.9 in US DiscovEHR and 0.6 in Norway (any ADH). Encaleret, an investigational oral calcilytic and negative allosteric modulator of CaSR, was evaluated in a phase 2b study with two 5-day inpatient periods, a 24-week outpatient period, and long-term extension ($N = 13$; NCT04581629). Encaleret significantly increased mean albumin-corrected serum calcium and intact PTH and decreased mean serum phosphate and 24-hour urinary calcium compared with baseline (all $P < .05$). Kidney function remained stable. No serious adverse events (SAE) were reported. Findings were sustained over 42 months (open-label). In a pharmacokinetic study ($N = 5$; NCT02204579), the calcilytic NPSP795 induced dose-dependent increases in mean serum PTH concentrations at 15- and 210-minutes post-administration ($P < .05$). Symptomatic cholelithiasis was reported in one patient during the 2-week follow-up. In a retrospective cohort study ($N = 6$), patients treated with subcutaneous PTH infusion via pump over

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

0.8-5.5 years showed increases in mean serum calcium and magnesium and reduced seizures vs baseline treatment with calcium/vitamin D analogs and/or bolus PTH injection ($P < .05$), but with no significant changes in mean serum phosphate or calcium–phosphate product. No SAEs were reported. In a case series ($N = 5$; median follow-up: 5 years), patients treated with calcium carbonate, calcitriol and/or PTH injection had similar median serum calcium, phosphate and magnesium concentrations to untreated patients. In another case series, of patients treated with calcium, calcitriol, thiazide diuretics or dihydrotachysterol ($N = 25$; with any ADH; mean treatment duration: 7.1 years), one patient experienced impaired kidney function and one patient died.

Conclusions: ADH1 is a rare, serious, understudied condition. Available clinical evidence is limited, though investigational calcilytics such as encaleret are associated with promising biochemical improvements in small studies. Gaps remain regarding long-term outcomes and the humanistic and economic burden of ADH1.

Abstract citation ID: lvag096.824

EP261 - ECE_2131 - The effect of denosumab on IGF-1 and bone turnover markers in patients with severe osteoporosis

Mariana Agapito Fonseca[1,2], Marta Vaz Lopes[2,3], Teresa Alegria Neto[2], Catarina Isabel Lopes[2], Miguel António Duarte[2], Mariana De Griné Severino[2,3], Ema Lacerda Nobre[2,3], Ana Gomes[2,3], Francisca Costa[1], Eva Alves[1,3], Francisco Sampaio[1,3] and Ana Paula Barbosa[1,2,3]
[1]Fracturary Osteoporosis Multidisciplinary Clinic, ULS Santa Maria, Lisbon, Portugal; [2]Diabetes and Metabolism Department, ULS Santa Maria, Endocrinology, Lisbon, Portugal; [3]Lisbon, Portugal

Background: Insulin-Like Growth Factor-1 (IGF-1) is the main growth factor in the bone matrix and regulates the expression of receptor activator of nuclear factor kappa-B ligand (RANKL). In osteoporosis, IGF-1 declines in serum and bone, highlighting its predominant anabolic effect *in vivo*. Denosumab is a monoclonal antibody that binds RANKL, preventing osteoclast differentiation, leading to fracture risk reduction. This mechanism of action is linked to that of IGF-1, which could lead to potential alterations in serum IGF-1 levels in osteoporotic patients under denosumab. Therefore, the authors aimed to analyze the variation of IGF-1 levels in patients under denosumab and its relationship with known bone turnover markers.

Methods: Retrospective single-center analysis of female patients with osteoporosis and fragility fractures treated with denosumab. Data were obtained from electronic health records and included age at the beginning of denosumab, duration of therapy, IGF-1 and bone turnover markers (BTM) [Procollagen-1 N-terminal Propeptide (P1NP), bone alkaline phosphatase (BALP), C-terminal telopeptide (CTX) and osteocalcin] before treatment and at the time of its interruption or at the last appointment.

Results: The study included 37 female patients. The mean age at the beginning of denosumab was $71,8 \pm 11,7$ years old, with mean duration of therapy of $37,3 \pm 17,0$ months. Treatment with denosumab was associated with a statistically significant reduction in all four BTM, with CTX showing the greatest decrease (57,5%), followed by osteocalcin (53,2%), P1NP (48,1%) and BALP (34,3%). IGF-1 levels reduced by 7,5% (mean level before denosumab 100,7 ng/mL, after denosumab 93,2 ng/mL), without attaining statistical significance ($P = ,413$).

Conclusions: In this population, treatment with denosumab led to the expected decrease in all bone turnover markers, with the biggest expression in CTX, in agreement with the inhibition of bone resorption. It also led to a decrease in serum IGF-1, accompanying the BTM trend, but without statistical significance.

Although serum IGF-1 levels do not always directly represent bone IGF-1 levels, these preliminary results of a small cohort point to a lack of effect of denosumab on the bone anabolic action of IGF-1.

Abstract citation ID: lvag096.825

EP262 - ECE_2926 - Real-world clinical assessment of CKD-associated osteoporosis: a single-center experience

Nada Akad[1,2], Mihaela Baranceanu[2], Teodora Nastasa[2], Anca Matei[1,2], Alexandru Florescu[1,2], Maria-Christina Ungureanu[1,2] and Stefana Bilha[1,2]
[1]Universitatea de Medicină şi Farmacie 'Grigore T. Popa' Iaşi, Iaşi, Romania; [2]Endocrinology, Spitalul Clinic Judeţean de Urgenţă Sfântul Spiridon Iaşi, Iaşi, Romania

Chronic kidney disease (CKD) is associated with complex disturbances in mineral and bone metabolism, collectively referred to as chronic kidney disease–mineral and bone disorder (CKD-MBD). Alterations in calcium, phosphate, parathyroid hormone (PTH), and vitamin D metabolism contribute to impaired bone quality, reduced bone strength, and an increased risk of fragility fractures. Importantly, skeletal involvement in CKD may overlap with, but is not identical to, age-related or postmenopausal osteoporosis, posing diagnostic and therapeutic challenges.

Patients on maintenance hemodialysis have a markedly increased fracture risk, while kidney transplant recipients remain vulnerable despite improved kidney function, due to persistent CKD-MBD and immunosuppressive therapy. Early identification of osteoporosis in these populations is essential for fracture prevention.

We present the real-world clinical assessment of CKD-associated osteoporosis in a tertiary center in Iasi, Romania. Over the past year, we evaluated 78 patients, including 30 patients on hemodialysis (HD)**,** and 48 kidney transplant recipients (KTR)**.**

All patients underwent bone mineral density (BMD) assessment by dual-energy X-ray absorptiometry (DXA), along with evaluation of mineral metabolism parameters, including serum calcium, phosphate, and parathyroid hormone (PTH). Serum 25-hydroxyvitamin D levels and bone turnover markers were additionally assessed when available.

In the HD group (15 men, 15 women; median dialysis vintage 46 months**),** osteoporosis was identified in 13 patients (43.3%), osteopenia in 9 patients (30.0%), low BMD in 3 patients (10.0%), and normal BMD in 5 patients (16.7%). CKD-MBD alterations were observed in 29 of 30 patients. Notably, one patient had a history of multiple fragility fractures (forearm, vertebral, and ankle), and another presented with vertebral fractures at the L2-L4 level.

In the KTR group (26 men, 22 women; median time since transplantation 83.5 months), osteopenia was observed in 15 patients (31.3%), osteoporosis in 9 patients (18.8%), low BMD in 7 patients

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(14.6%), while 17 patients (35.4%) had normal BMD. CKD-MBD alterations were noticed in 42 out of 48 patients. No fractures occurred in the KTR group prior to their evaluation.

In conclusion, our real-world data demonstrate a substantial burden of low bone mass and osteoporosis across the CKD spectrum, with the highest prevalence observed in hemodialysis patients and a persistent risk in kidney transplant recipients. These findings support the need for systematic bone health assessment and individualized management strategies in CKD-associated osteoporosis.

Abstract citation ID: lvag096.826

EP263 - ECE_2934 - Lower calcium availability may impact bone density in vegans: results from a cross-sectional study

Johana Gallova, Karolína Mrkáčková, Anna Ouřadová and Jan Gojda
Departement of Internal medicine, Královské Vinohrady University Hospital and Third Faculty of Medicine, Charles University, Prague, Czech Republic

Background: Plant-based diets have gained substantial popularity in recent years, driven by their perceived health and environmental advantages. Although robust evidence supports their beneficial effects on cardiometabolic outcomes, uncertainties persist regarding their impact on bone health. The present study aimed to compare self-identified vegans with an age- and BMI-matched group of omnivores to assess differences in calcium–phosphate metabolism, renal calcium handling, and bone density.

Methods: Czech participants from the multinational VEGANSCreener study were analysed, including self-identified vegans (VG, $n = 107$, mean age 33.63 ± 6.31 years) and omnivores (OM, $n = 55$, mean age 32.29 ± 9.79 years). Anthropometry, body composition, and resting energy expenditure measured by indirect calorimetry were recorded. Blood samples and 24-hour urine collections were obtained. Serum concentrations of calcium, phosphate, parathyroid hormone, vitamin D, creatinine, and alkaline phosphatase were measured in the institutional laboratory, along with 24-hour urinary calcium and urea excretion. Bone density was assessed using heel ultrasound densitometry. Dietary intake was evaluated using a 4-day prospective food record analysed with validated food composition databases. Between-group comparisons were performed using unpaired non-parametric Mann–Whitney tests. Associations between variables were assessed using Spearman correlation analysis. A P-value < 0.05 was considered statistically significant.

Results: The VG and OM groups were comparable in anthropometric characteristics and resting metabolic rate. Serum calcium concentrations did not differ between groups, while phosphate levels were lower in VG. Moreover, vegans exhibited significantly lower 24-hour urinary calcium excretion compared with omnivores (1.26 ± 0.88 vs 2.12 ± 1.48 mmol/day, $P < .0001$) and higher PTH concentrations (3.28 ± 1.13 vs 2.58 ± 0.83 pmol/L, $P = .0002$), accompanied by lower 24-hour urinary urea excretion (127.5 ± 60.1 vs 197.1 ± 101.6 mmol/day, $P < .0001$). No significant differences in bone density T- or Z-scores were observed between groups, though when performing sex—stratified analyses, we found significant difference in men only. Dietary records showed significantly lower calcium intake in vegans compared with omnivores (823 ± 289 vs 1026 ± 389 mg/day, $P = .0016$). Among participants with available data, calcium supplementation was reported by approximately 10% of vegans.

Conclusions: Despite lower renal calcium excretion and compensatory increased PTH, vegans did not exhibit impaired bone density compared with omnivores. These findings suggest that lower dietary calcium intake, with possible contributions of lower calcium bioavailability, is not necessarily associated with reduced bone health.

Abstract citation ID: lvag096.827

EP265 - ECE_2034 - Primary hyperparathyroidism due to abnormal giant single-gland and multigland disease: 2 case reports of a second-level endocrinological centre

Antonino Russo[1], Luca Fabris[2], Michele Zuolo[2], Giacomo Faccioli[2], Simone Zanella[3], Enzo Bonadies[3], Francesco Antonio Ciarleglio[4] and Vito Racanelli[1]
[1]*Azienda Sanitaria Universitaria Integrata del Trentino (ASUIT), Trento;* [2]*General Surgery Department, Azienda Sanitaria Universitaria Integrata del Trentino (ASUIT), "Valli del Noce Hospital", Cles, TN, Italy;* [3]*General Surgery Department, Azienda Sanitaria Universitaria Integrata del Trentino (ASUIT), "Santa Maria del Carmine Hospital", Rovereto, TN, Italy;* [4]*General Surgery Department, Azienda Ospedaliera di Perugia, Ospedale di Perugia, Perugia, Italy*

Introduction: Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia, affecting approximately 1% of adults in the general population. The clinical history and pathway of 2 particular cases of PHPT are described below.

Observations: Case Report 1

A 57 year-old female was admitted to the emergency department in September 2023 reporting abdominal pain. Laboratory admission profile exhibited indicated PHPT (table 1). Neck ultrasound identified one suspected rounded area below the lower pole of thyroid's left lobe. Sestamibi scan, however, showed two areas of high uptake of tracer caudally to the left lobe of the thyroid. She was submitted to surgery and intraoperative-PTH assay confirmed the removal of pathological parathyroid (PTH 866→79 pg/mL, 20 min after removal). The postoperative course was regular and calcium at discharge was normal (9.2 mg/dl). Histopathology revealed the presence of a single giant left adenoma (oncocytic variant, 7 gr, 5.1 cm diameter). A second lesion adjacent to adenoma was also removed, which was histologically found to be a reactive lymph-node.

Case report 2

A 78 year-old female was admitted to the emergency department in March 2024, reporting anemia with chest discomfort. Laboratory admission profile indicated PHPT (table 1). Neck ultrasound identified two suspected areas at the middle-inferior third of thyroid's right lobe and posteriorly at the middle third of thyroid's left lobe . She further underwent Sestamibi scan, that confirmed the enlargement of the right and left lower parathyroids. Therefore, she was referred for elective surgery. Intraoperative PTH assay confirmed the removal of two pathological parathyroids (PTH 171→73 pg/mL, 20 min after removal of both lesions). The postoperative course was uneventful and calcium at discharge was normal (9.9 mg/dl). Histopathology revealed a left parathyroid adenoma (mainly

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

oxyphilic cells, 3 g, 3.5 cm diameter) and a right parathyroid adenoma (mainly chief cells; 3 g, 2.5 cm diameter).

Conclusions: These case reports emphasize the peculiarity of PHPT presentation related to abnomal single-gland (1) and multigland (2) disease. The first case highlights how preoperative instrumental assessment can be distorted by the morphological characteristics of large adenomas. The second case allows us to understand how PHPT can sometimes be sustained by double adenomas with different histopathological characteristics.

	Range	Case 1	Case 2
Creatinine (mg/dl)		*1.17*	*0.62*
Calcium (mg/dl)	*8.5-10.5*	***12.4***	***12.0***
Phosphate (mg/dl)	*2.6-4.5*	***1.8***	***1.9***
Urinary Calcium (mg/24 h)	*100-250*	***426***	***295***
PTH (pg/ml)	*15-65*	***597***	***320***
25-OH Vitamin D (ng/ml)	*20-100*	*32*	*10*

Abstract citation ID: lvag096.828

EP267 - ECE_3686 - Normocalcemic primary hyperparathyroidism: characterization, complications, and follow-up

Joana Vinhais, Beatriz R. Pereira, Ana Cláudia Martins, David Verissimo, Catarina Ivo, Mafalda Marcelino, Dolores Passos, Luis Lopes, João Jácome de Castro and João Nunes Silva
Serviço de Endocrinologia, Hospital das Forças Armadas, Lisboa, Portugal

Background/Aims: Normocalcemic primary hyperparathyroidism (PHPT) is diagnosed by persistent elevation of PTH with normal calcium concentration and exclusion of secondary causes of hyperparathyroidism. As its incidence increases, accurate diagnosis and appropriate management are crucial to prevent complications.

Aimed to characterize patients with normocalcemic PHPT evaluated in our hospital, the incidence of complications and evolution to hypercalcemia.

Methods: We retrospectively analysed every patient with raised PTH since 2015 and a minimum follow-up of 2 years in our department. Patients with chronic kidney disease (CKD; GFR < 60 mL/min/m^2), vitamin D deficiency and hypercalcemia were excluded.

Results: Among 1337 patients with elevated PTH and normal total calcium, 812 were excluded due to CKD or vitamin D deficiency, and 487 due to incomplete data or follow-up < 2 years.

We analysed 38 patients with normocalcemic PHPT. Average age was 68.7 years; 52.6% were female. Mean PTH was 111.2 pg/mL (15-68), total calcium 9.8 mg/dL (81-10.4), phosphate 3.1 mg/dL (2.5-4.5), alkaline phosphatase 80 U/L (30-120) and 25-OH vitamin D 42 ng/mL (30-100).

Thirty patients (79%) had target organ involvement. Regarding skeletal manifestations, 12 patients had osteoporosis in densitometry (three were taking bisphosphonates before diagnosis), and seven sustained fractures. Nephrolithiasis was identified in 13 patients, and eight exhibited hypercalciuria. Five patients were diagnosed before age 50.

Regarding the number of complications: 21 patients had one complication; Eight patients had two complications, and one patient had three complications.

Average follow-up time was 5.8 years, and five patients (13%) progressed to mild hypercalcemia.

One patient was submitted to parathyroidectomy but maintained normocalcemic PHPT, although showed improvement of complications.

Conclusions: Differentiating normocalcemic PHPT from secondary hyperparathyroidism is not always straightforward. In this cohort, eight patients presented hypercalciuria, which can also represent a secondary cause of hyperparathyroidism.

In our cohort, most patients remained normocalcemic during the follow-up, consistent with an overall stable biochemical course of the disease. However, skeletal and renal complications were frequent, highlighting the importance of establishing the diagnosis and properly manage normocalcemic PHPT.

Many patients had incomplete diagnostic workup, suggesting underdiagnosis of this condition. The reduced number of surgically treated patients indicates difficulties in differential diagnosis and lesion localization.

Abstract citation ID: lvag096.829

EP268 - ECE_1875 - Effect of teriparatide on trabecular bone score

Dan Peretianu[1]
[1]*Endocrinology, Medical Center Povernei, Bucharest, Romania*

Objective: To investigate the importance of trabecular bone score (TBS) in the follow-up of anti-osteoporotic therapy with teriparatide.

Material/Method: A. DEXA: GE-Lunar Prodigy Pro # 500074. TBS: iNsight®, version 3.0.2.0.

B. Patients: 138 patients women (only one man) were analyzed correlatively with BMD and TBS before and after teriparatide, 20 microg/day, between 6 months to 4 years. 269 tests were performed. **C.** Percentage difference calculation: (x-y)*100/x, where "x" is the original score value and "y" is the current score value.

Results: Data are displayed in the order: analysis time, number, BMD score ante, BMD score post, BMD percentage increase, *P*-value, TBS score ante, TBS score post, TBS percentage increase, *P*-value:

Post teripratid	Number	Age on onset	Current age	DMO score ante-T	DMO score post T	Increase %	*P*	TBS score ante-T	TBS score post -T	Increase %	*P*
6 months	63	66.45	66.95	−1.49	−1.19	20.63	.08	−3.03	−2.75	9.35	.09
12 months—1 year	78	66.70	67.70	−1.86	−1.43	22.42	.001	−3.30	−2.61	20.6	.05
18 months—1,5 year	29	66.49	67.99	−1.58	−0.96	38.89	.02	−2.95	−2.68	9.14	.31

(*continued*)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Continued

Post teripratid	Number	Age on onset	Current age	DMO score ante-T	DMO score post T	Increase %	P	TBS score ante-T	TBS score post -T	Increase %	P
24 months—2 years	62	65.70	67.70	−1.83	−1.20	34.14	.0000	−3.16	−2.93	7.34	.148
30 months—2,5 years	11	66.25	0.00	−1.77	−0.99	44.09	.009	−2.39	−2.02	15.66	.256
36 months—3 years	20	68.26	71.26	−1.66	−0.88	46.72	.0013	−3.31	−2.74	17.21	.037
42 months—3,5 yeras	5	69.08	72.58	−2.17	−1.27	71.15	.040	−2.76	−1.94	42.40	.073
48 months—4 years	1	52.00	56.00	−0.85	−1.18	−38.24	.33	−3.40	−3.28	3.68	.887

Observations: 1. Increase in BMD scores is much greater and statistically significant than the increase in TBS scores. This is because TBS scores were much more altered than BMD scores. **2.** The apparent decrease in TBS growth at 2 years (20.6% −1 y, 9.14%-1,5, v 7.34% at 2 y) would suggest that this would be the time to stop therapy. However, at 2.5, 3, and later at 3,5 years the TBS score increases surprisingly very much: 15.66%, 17.21% and 42.4%. **3.** No adverse effects were observed after 2 years administration.

Conclusions: 1. Although teriparatide (usual administration) does not appear to be more active on bone microarchitecture (TBS) than on bone material accumulation (BMD),

2. The administration of teriparatide over the 2-year period brings benefits, certified by the correlative increase in BMD and TBS scores.

Abstract citation ID: lvag096.830

EP269 - ECE_1912 - Post-stroke fracture risk: intracerebral haemorrhage vs ischaemic stroke—a systematic review and meta-analysis

Chrislyn Ng[1,2], Connor Burley[3], Jakub Mesinovic[4], Peter Ebeling[1], Gabrielle Stokes[3,5,6], Frances Milat[1,3,5] and Mícheál Ó. Breasail[1]

[1]Monash University, Clayton, Australia; [2]Department of Endocrinology, Monash Health, Clayton, Australia; [3]Monash Health, Clayton, Australia; [4]Deakin University, Burwood, Australia; [5]Hudson Institute of Medical Research, Melbourne, Australia; [6]Clayton, Australia

Background: Stroke can be divided into two subtypes—intracerebral haemorrhage (ICH) and ischaemic stroke (IS), of which ICH constitutes 28.8% of strokes and contributes to significant mortality and morbidity. Heightened fracture risk in stroke survivors is a well-established physical complication. The mechanisms for this are multifactorial, culminating in skeletal fragility and falls. Despite this, there is inconsistent evidence surrounding post-stroke fracture rates depending on stroke aetiology.

Objective: Examine the current literature in post-stroke fracture outcomes in both stroke subtypes.

Methods: A systematic review was conducted in accordance to PRISMA guidelines, with PROSPERO registration. We searched Ovid MEDLINE, Scopus, Cochrane Database and Embase up to November 2025 for observational studies reporting post-stroke fracture outcomes in adults with confirmed ICH, with comparisons to IS. Additionally, backward citation screening was carried out. Risk of bias was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist. A meta-analysis is currently underway.

Results: Fifteen total studies were identified through screening methods. Five analysed cumulative incident fractures, three provided sub-analysis of fracture rates at multiple fracture locations, four focused solely on hip fractures, and one focused particularly on "'low-trauma" fractures. The remaining two studies utilised stroke subtype as a co-variate only and thus did not present meaningful data. Results across the included studies were inconsistent in establishing whether IS or ICH is associated with a greater fracture risk, with only four reporting a statistically significant difference. These included three reporting increase fracture rate in the ICH cohort. Two of these studies, Zheng et al. and Lee et al., compared each stroke subtype against a matched non-stroke control group rather than conducting a direct comparison between ICH and IS. Whereas the study Lisabeth et al. reported increased overall fracture rates in the ICH with a hazard ratio of 1.93 (95% CI: 1.11-3.34) when directly compared to IS. Interestingly, one study reported higher fracture rates in the alternative stroke subtype.

Conclusions: There is some evidence suggests that ICH may be associated with higher fracture risk than IS, however a formal meta-analysis is currently pending. Based on the included studies, it is clear that both stroke subtypes are associated with increased fracture risk and in turn poor bone health outcomes. The limited number of studies comparing stroke subtypes highlights the need for more robust and well-designed studies. Overall, these results support the need for implementation of a generic approach to post-stroke bone health assessment and fracture prevention.

Abstract citation ID: lvag096.831

EP270 - ECE_2535 - Proximal humeral cortical thickness measured by MRI accurately predicts low bone mineral density in acromegaly

Sebnem Burhan[1], Yigitcan Kartal[2], Ozge Polat Korkmaz[3], Mutlu Niyazoğlu[1,4] and Esra Hatipoglu[3,4]

[1]Department of Endocrinology and Metabolism, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye; [2]Department of Radiology, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye; [3]Pituitary Disorders Research Center, University of Health Sciences, Istanbul, Türkiye; [4]Department of Neurosurgery, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye

Objective: In acromegaly, Dual-Energy X-ray Absorptiometry (DXA) assessed bone mineral density (BMD) is often misleading. Although it is still useful for guideline-recommended BMD monitoring, it cannot be relied on alone, so it should be complemented by other bone assessments. The aim of this study was to investigate the diagnostic value of humeral cortical thickness measured from shoulder magnetic resonance imaging (MRI) in patients with acromegaly and to determine its performance

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Materials and Methods: Twentythree patients with acromegaly followed in the endocrinology clinic were included in the study. Patients with postmenopausal status, cases with age >65 years, or known hypogonadism were excluded. A single radiologist, blinded to DXA results, measured average humeral cortical thickness (HCT). HCT was measured by calculating the difference between the outer and inner cortical margins at 10 cm and 12 cm distal to the humeral head by using T1-weighted coronal shoulder images (1.5 Tesla). DXA was also performed within one months of the MRI. Patients were divided into two groups based on lumbar spine DXA T-scores: normal BMD (T-score ≥ -1.0) and low BMD (T-score < -1.0). Data analysis included between-group comparisons, Spearman correlation and ROC curve analysis.

Results: The acromegaly cohort ($n = 23$;13 females,10 males; age 48 ± 9.4 years) had a median IGF-1 of 186 ng/mL[153-269] and median GH of 1.10 ng/mL[0.50-1.88]. Seventeen patients (70%) were in remission, and 13 (58%) were receiving medical therapy. The mean HCT of patients in the low BMD group (4.81 ± 1.23 mm) was statistically significantly lower than the normal BMD group (6.22 ± 0.99 mm) ($P = .014$). A positive correlation was found between HCT and DXA T-scores ($r = 0.54$, $P < .01$). ROC analysis demonstrated excellent diagnostic performance of CBT on MRI, with an area under the curve (AUC) of 0.988 (95% CI: 0.955-1.00, $P < .001$). The optimal cut-off point was identified; a cut-off of 5.24 yielded 100% sensitivity and 92.9% specificity.

Conclusions: Proximal HCT measured from shoulder MRI is a reliable, radiation-free biomarker for assessing BMD in acromegaly patients. It holds significant potential as a complementary tool to DXA, particularly in cases where bone structural changes due to growth hormone excess may confound DXA measurements. The opportunistic use of this technique can provide additional and valuable information about bone health in patients undergoing shoulder MRI for different indications.

Keywords acromegaly, humeral cortical thickness, dual-energy X-ray absorptiometry (DXA), osteoporosis, magnetic resonance imaging (MRI)

Abstract citation ID: lvag096.832

EP273 - ECE_3747 - Hyperphosphatemic familial tumoral calcinosis: a case report of a severe disease course

Vit Zikan[1,2], Aleš Panczak[3], Dana Michalska[1], Kateřina Hirschfeldová[3], Renata Vlasakova[1] and Ivan RaskaJr[1]

[1]First Faculty of Medicine, Third Internal Clinic, Clinic of Endocrinology and Metabolism, General University Hospital, Charles University, Prague, Czech Republic; [2]First Faculty of Medicine, Third Department of Medicine-Department of Endocrinology and Metabolism, General University Hospital, Charles University, Prague, Czech Republic; [3]Faculty of Medicine 1, Institute of Biology and Medical Genetics, General University Hospital, Charles University, Prague, Czech Republic

Hyperphosphatemic familial tumoral calcinosis (HFTC) is a rare disorder characterized by hyperphosphatemia and ectopic deposition of calcium–phosphate crystals, caused by loss of function of fibroblast growth factor 23 (FGF23). We report the case of a 50-year-old man with HFTC and a 35-year history of progressive ectopic calcifications.

Laboratory testing revealed elevated serum phosphate (1.97 mmol/L; reference range 0.65-1.61) and low plasma intact FGF23 (13.42 ng/L; reference range 23.2-95.4). Genetic analysis identified a pathogenic variant in the FGF23 gene consistent with HFTC. NaF-PET demonstrated increased osteoblastic activity predominantly in multiple extra-osseous soft-tissue calcifications (elbows, pelvis, hips, and feet), with minor subcutaneous calcifications in the lower legs. Bilateral renal calcifications, including nephrolithiasis and parenchymal calcifications, were also present.

Management included phosphate-lowering strategies (dietary restriction, phosphate binders, acetazolamide) and surgical excision of symptomatic lesions. The patient experienced repeated relapses of calcified masses, mainly around the elbows, pelvis, and hips, requiring more than 40 surgical procedures. Complications included non-healing skin defects and a high risk of infectious complications necessitating continuous wound care. Additional complications comprised recurrent bilateral nephrolithiasis with left-sided pyelolithiasis requiring ureteral stenting, occlusion of the distal left anterior tibial artery with further vascular calcifications and treated arterial hypertension.

This case highlights the importance of a multidisciplinary approach. However, treatment options remain limited, with evidence largely restricted to case reports and small cohorts, and no clearly effective causal therapy currently available.

Keywords acetazolamide, ectopic calcifications, fibroblast growth factor 23, hyperphosphatemic tumoral calcinosis, phosphate

Abstract citation ID: lvag096.833

EP275 - ECE_2017 - A rare cause of fragility fractures: tumor-induced osteomalacia due to a phosphaturic mesenchymal lesion hidden in the foot

Eider Pascual-Corrales[1], María Eugenia Reguero Callejas[2], Fausto González Lizán[3] and María del Carmen Sanz Pascual[3]

[1]Endocrinology and Nutrition, Hospital Universitario Ramón y Cajal, Madrid, Spain; [2]Pathology, Hospital Universitario Ramón y Cajal, Madrid, Spain; [3]Traumatology, Hospital Universitario Ramón y Cajal, Madrid, Spain

Introduction: Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome caused by fibroblast growth factor 23 (FGF23)-secreting mesenchymal tumors, leading to renal phosphate wasting, hypophosphatemia and osteomalacia. Tumor localization is often challenging, particularly when circulating FGF23 levels are within the reference range, delaying diagnosis and treatment.

Case presentation: We report the case of a 62-year-old man referred for evaluation of severe hypophosphatemia and multiple low-impact fractures. His relevant past medical history included obesity treated with sleeve gastrectomy. Since October 2024, he developed progressive generalized bone pain, proximal muscle weakness and multiple insufficiency fractures affecting the feet, calcaneus and sacrum. Laboratory evaluation revealed persistent hypophosphatemia (1.7-2.3 mg/dL; reference range 2.7-4.5 mg/dL) despite supplementation, reduced tubular phosphate reabsorption (66.7%; reference range 80%-94%), elevated alkaline phosphatase (176 U/L; reference range 53-128 U/L), normocalcemic hyperparathyroidism (PTH 121.1 pg/mL; reference range 17.3-74.1 pg/mL), 25-hydroxyvitamin D insufficiency (20.0 ng/mL), low-normal 1,25-dihydroxyvitamin D (31.8 pg/mL) and elevated bone turnover markers (β-CTX and P1NP).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Notably, FGF23 concentrations were repeatedly within the normal range.

Bone mineral density showed osteoporosis at the lumbar spine (T-score −3.3) and osteopenia at the hip (T-score −2.0). Bone scintigraphy revealed focal uptake in the posterior right fifth rib and areas of stress-related bone remodeling in the right lower extremity, including a prior calcaneal fracture, while pelvic MRI confirmed an insufficiency fracture of the left sacral ala. Extensive imaging studies, including 18F-FDG PET/CT, neck ultrasound, parathyroid scintigraphy and CT scans, were initially inconclusive. However, 68Ga-DOTA-TOC PET/CT demonstrated a focal, intensely somatostatin receptor-avid lesion (SUVmax 8.2, Krenning 3-4) at the base of the right foot between the second and third toes. MRI of the foot confirmed a hypervascular interdigital soft tissue mass measuring approximately $20 \times 17 \times 14$ mm. Ultrasound-guided core needle biopsy revealed a benign mesenchymal neoplasm with histological and immunohistochemical features consistent with a phosphaturic mesenchymal tumor.

The lesion was surgically treated in December 2025 with wide excision and extensive margins. The pathology report of the surgical specimen confirmed the diagnosis of a phosphaturic mesenchymal tumor. Biochemical abnormalities, including hypophosphatemia, resolved after surgery, allowing discontinuation of phosphate supplementation.

Conclusions: This case highlights the diagnostic challenges of tumor-induced osteomalacia, particularly in patients with normal circulating FGF23 levels. Somatostatin receptor-based imaging using 68Ga-DOTA peptides remains the preferred modality for tumor localization. Early recognition and complete surgical resection are essential to achieve biochemical cure and prevent progressive skeletal morbidity.

Abstract citation ID: lvag096.834

EP277 - ECE_1183 - FRAX prediction with and without bone mineral density: a comparison and the factors influencing the discordant results in osteoporosis treatment decisions in Sri Lanka

Shahini Winson Gnanathayalan, Mahisha Chandrasekaran, T.G. Athukorala, Uditha Bulugahapitiya and Manilka Sumanatilleke
Endocrinology and Diabetes, National Hospital of Sri Lanka, Colombo, Sri Lanka

Background: The Fracture Risk Assessment Tool (FRAX) estimates an individual's 10-year fracture probability using clinical risk factors, with bone mineral density (BMD) as an optional contributor. Incorporating BMD may refine risk estimates, but its impact on treatment decisions in the Sri Lankan setting remains unclear. The objective of the study was to evaluate the level of agreement between treatment recommendations generated by FRAX with BMD and FRAX without BMD, using Sri Lankan intervention thresholds.

Methods: A cross-sectional analysis was conducted among adults aged 40-90 years who underwent dual-energy X-ray absorptiometry(DXA) for osteoporosis screening at a tertiary hospital in Sri Lanka in 2023-2024. FRAX probabilities were calculated using the Sri Lankan model, both with and without femoral neck BMD. Participants were categorized into treatment or non-treatment groups based on national thresholds (≥9% for major osteoporotic fracture risk[MOFR] and ≥3% for hip fracture risk[HFR]). Concordance was defined as identical treatment recommendations from both FRAX approaches. Clinical variables were compared between concordant and discordant groups.

Results: Of the 309 participants included, 88.0% were women. Treatment was recommended for 94 individuals(30.4%) using FRAX with BMD and 82 individuals(26.5%) using FRAX without BMD. Overall concordance was 82.5%(255/309). The median age was 61 years in the concordat group and 66 years in the discordant group. Discordance was significantly more frequent among older adults, particularly those aged >60 years($P <$ .001), and among individuals whose FRAX scores without BMD were close to intervention thresholds($P <$ .001). A greater proportion of patients with DXA-defined osteoporosis showed discordant classifications compared with those with osteopenia or normal BMD. Sex, BMI, and other clinical risk factors including secondary osteoporosis did not differ significantly between the two groups. In the discordant subset, treatment was suggested for 32 participants(59.3%) using FRAX with BMD compared with 22 participants(40.7%) using FRAX without BMD. These differences were not influenced by sex or BMI, but treatment recommendations based on FRAX with BMD were significantly more common among younger participants($P <$ .001) and those with osteoporosis on DXA($P <$ .001).

Conclusions: FRAX calculations with and without BMD yield consistent treatment recommendations for most patients. However, agreement diminishes in older adults and in those whose BMD-free FRAX estimates fall near intervention thresholds. These findings highlight the importance of obtaining BMD in borderline cases and in elderly patients to improve fracture-risk precision, while supporting the cost-effectiveness of using FRAX without BMD in resource-poor settings with limited DXA access.

Abstract citation ID: lvag096.835

EP280 - ECE_1881 - Chronic cholecalciferol supplementation and adequate vitamin D status are associated with reduced risk of long COVID

Luigi Di Filippo, Umberto Terenzi, Simona Bolamperti, Simonetta Bossoni, Marco Campaniolo, Licia Gifuni, Mauro Doga and Andrea Giustina
Institute of Endocrine and Metabolic Sciences, Università Vita-Salute San Raffaele, IRCCS Ospedale San Raffaele, Milan, Italy

Vitamin D deficiency has been associated with worse COVID-19 outcomes and with the persistence of post-acute sequelae, but the impact of vitamin D supplementation on Long COVID remains poorly defined. We investigated the association between chronic cholecalciferol supplementation, circulating 25-hydroxyvitamin D [25(OH)D] concentrations, and the risk of Long COVID.

This retrospective observational study included patients with confirmed COVID-19 between March 2020 and May 2021 previously followed at a tertiary Endocrine Department. Long COVID was defined according to NICE criteria as the persistence of at least two symptoms for more than 12 weeks after recovery. Patients receiving chronic cholecalciferol supplementation

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

were compared with non-supplemented individuals. A 1:1 matched analysis for age, sex, comorbidities, and acute COVID-19 severity was performed, together with dose-specific analyses for daily cholecalciferol intake ≥750 IU and ≥1000 IU.

Overall, 132 patients were included (median age 56 years; 49% male), of whom 50 (38%) were chronically supplemented with cholecalciferol for a median duration of 38 months. Long COVID was diagnosed in 30 patients (22.7%). Long COVID occurred less frequently among supplemented patients compared with non-supplemented individuals (14% vs 28%, $P = .086$). The difference became statistically significant in patients receiving ≥1000 IU/day (10.5% vs 27.6%, $P = .039$) and showed a similar trend for doses ≥750 IU/day (12.5% vs 28.6%, $P = .051$). Baseline 25(OH)D concentrations were significantly lower in patients with Long COVID (17.5 vs 24 ng/mL, $P = .023$).

In the matched cohort ($n = 86$), Long COVID occurred in 22.1% of patients and was significantly less frequent in those supplemented with cholecalciferol (11.6% vs 32.6%, $P = .036$). In this matched cohort, baseline 25(OH)D concentrations showed a strong predictive performance for Long COVID (AUROC 74.3%, $P = .005$). Similar findings were confirmed in matched analyses restricted to patients receiving ≥1000 IU/day (8.5% vs 34.2%, $P = .018$). In multivariate logistic regression analyses, chronic cholecalciferol supplementation emerged as an independent protective factor against Long COVID in both the entire cohort (OR 0.31, $P = .038$) and the matched cohort (OR 0.22, $P = .017$), while lower 25(OH)D concentrations independently predicted Long COVID occurrence. Obesity emerged as an independent risk factor only in the non-matched cohort.

In conclusion, chronic cholecalciferol supplementation, particularly at daily doses ≥750-1000 IU and associated with adequate 25(OH)D concentrations, was independently associated with a lower risk of Long COVID. These findings suggest that maintaining sufficient vitamin D status through long-term supplementation may represent a simple, safe, and low-cost strategy to mitigate post-COVID sequelae and support recovery.

Abstract citation ID: lvag096.836

EP281 - ECE_2614 - Successful management of gestational hypercalcemia due to CYP24A1 mutations with intermittent intramuscular calcitonin: a multigenerational family case

Sean Godfrey[1], Nadejda Kotlyarevska[1] and Maya Y. Peltsverger[1,2,3]

[1]Novant Health New Hanover Regional Medical Center, Wilmington; [2]Internal Medicine, Novant Health NHRMC, Wilmington, United States; [3]Novant Health New Hanover Regional Medical Center, Wilmington, United States

Background: Loss-of-function mutations in CYP24A1, encoding vitamin D 24-hydroxylase, impair vitamin D catabolism and cause vitamin D-dependent hypercalcemia. Pregnancy triggers symptomatic hypercalcemia in 81.8% of affected women, with high rates of obstetric complications including preterm delivery, preeclampsia, and fetal loss.[1] Therapeutic options are limited, as bisphosphonates are contraindicated. We report a multigenerational family demonstrating genotype-phenotype correlation and successful management with intermittent intramuscular calcitonin.

Case presentation: Two sisters with biallelic CYP24A1 pathogenic variants [c.62delC (p.Pro21Argfs8) and c.1186C > T (p.Arg396Trp)] and a variant of uncertain significance [c.1219T > A (p.Tyr407Asn)] developed pregnancy-associated hypercalcemia. The index patient presented with symptomatic hypercalcemia refractory to conservative measures. She was managed with intravenous normal saline, low-calcium diet, strict vitamin D and sunlight restriction, and intermittent intramuscular calcitonin throughout gestation. This multimodal approach maintained serum calcium within safe range (11.4 mg/dL), prevented calcitonin tachyphylaxis, and was associated with stable renal function, absence of acute kidney injury, and well-controlled blood pressure.[2]

In contrast, her older sister, treated only with intravenous fluids during both pregnancies, experienced recurrent hospital admissions for nephrolithiasis, persistent hypercalcemia (10-11.5 mg/dL), preeclampsia, and preterm delivery. Their mother, a monoallelic carrier, remained asymptomatic, demonstrating attenuated disease expression consistent with the 5.6% symptomatic hypercalcemia rate in heterozygous carriers.[1] The father, also a monoallelic carrier, had nephrolithiasis only.

The index patient's newborn developed neonatal hypercalcemia due to inherited CYP24A1 deficiency. Genetic testing revealed inheritance of a single pathogenic variant [c.62delC (p.Pro21Argfs8)], with absence of the c.1186C > T variant, confirming monoallelic carrier status. Monoallelic carriers can develop symptomatic hypercalcemia (5.6% rate) and have increased risk of nephrolithiasis (19.4%) and nephrocalcinosis (4.9%).[1,3]

Conclusions: This familial case demonstrates the autosomal recessive inheritance pattern of CYP24A1 deficiency with clear genotype-phenotype correlation. Biallelic mutations confer high risk of pregnancy-triggered hypercalcemia and obstetric complications, while monoallelic variants are associated with milder or asymptomatic phenotypes. Intermittent intramuscular calcitonin, combined with dietary and environmental vitamin D restriction and hydration, represents an effective and safe strategy for managing gestational hypercalcemia.[1,4,5] This approach may reduce maternal complications including acute kidney injury, hypertension, and preeclampsia compared to conservative management alone. Early diagnosis, family screening, and tailored perinatal management are essential for optimizing outcomes in both mothers and newborns with CYP24A1 deficiency. Neonates inheriting CYP24A1 mutations require lifelong monitoring and strict avoidance of vitamin D supplementation.[1,3]

Abstract citation ID: lvag096.837

EP282 - ECE_3085 - Management of patients with hypoparathyroidism treated with teriparatide: the long-term clinical experience of Padova's Endocrinology Department

Giacomo Contini, Giacomo Voltan, Carlo Mogno, Michela Ferrarese and Valentina Camozzi

Endocrine Disease Unit, University-Hospital of Padova, Padova, Italy

Introduction: Chronic hypoparathyroidism is traditionally managed with calcium and calcitriol supplements, but these treatments often fail to ensure adequate control of serum calcium levels and do not effectively prevent complications. In more

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

severe cases, treatment with 1-34PTH (teriparatide) can be used; in Italy, this is authorized under Law 648/1996 and reserved for patients who meet specific criteria. However, even teriparatide does not always allow for optimal disease control, requiring multiple daily administrations and failing to guarantee prevention of hypocalcemic crises. Here we report our clinical experience with four patients with postsurgical hypoparathyroidism who have been treated for years with 1-34PTH.

Patient presentation: Katy, 51 years old, with significant comorbidities including nephrocalcinosis due to medullary sponge kidney and breast cancer; despite replacement therapy, there was poor control of hypercalciuria, and the patient experienced numerous episodes of hypocalcemia requiring IV calcium infusions; she showed temporary improvement with 1-84PTH, which was later discontinued.

Rossana, 29 years old, with class II obesity, had difficulties absorbing the drug due to the thickness of subcutaneous fat, only partially resolved by using longer needles; after weight loss, she developed iatrogenic hypercalcemia.

Maria, 60 years old, initially benefited from 1-84PTH but, after switching to 1-34PTH, experienced several episodes of severe hypocalcemia.

Luana, 51 years old, with symptomatic atrophic gastritis and intolerance to calcium supplements, experienced multiple hypocalcemic crises.

Conclusions: The experiences reported highlight the complexity of managing hypoparathyroidism, with recurrent crises, a negative impact on quality of life, and difficulties related to comorbidities. 1-84PTH, which is no longer available, had provided benefits to several patients. Recently, palopegteriparatide has been approved, allowing for once-daily administration and showing excellent results in trials, but it is not yet reimbursed in Italy, limiting access and leaving 1-34PTH as the only option, which remains off-label and not fully effective.

Abstract citation ID: lvag096.838

EP283 - ECE_1620 - Outpatient parathyroidectomy for primary hyperparathyroidism in the Canadian public health care system: a safe and cost-saving practice

Camille Klotz[1], Florence Bénard[2], Dan Moldoveanu[2], Marie-Josée Bégin[3], Rondeau Geneviève[4] and Frédéric Mercier[2,5]
[1]*Faculty of Medecine, University of Montréal, Montreal, Canada;* [2]*Surgical Oncology, Surgery, Centre Hospitalier Universitaire de Montréal (CHUM), Montreal, Canada;* [3]*Endocrinology, Medecine, Centre Hospitalier Universitaire de Montréal (CHUM), Montréal, Canada;* [4]*Montréal, Canada;* [5]*Oncologic, Endocrine and Digestive Surgery, Surgery, Hôpital Privé Jean Mermoz, Lyon, France*

Primary hyperparathyroidism (PHPT) accounts for 80%-90% of outpatient-diagnosed hypercalcemia and is associated with complications like osteoporosis, nephrolithiasis and renal impairment. PHPT is caused by a single parathyroid adenoma and the preferred treatment consists in a focused parathyroidectomy. Although it can be safely performed as an outpatient procedure in selected patients, this practice remains uncommon in Canada, despite its potential for substantial cost savings for the public health care system.

The aim of this case series was to evaluate the safety and economic relevance of outpatient focused parathyroidectomy. This observational study was conducted at the Centre Hospitalier de l'Université de Montréal (Québec, Canada) between 2023 and 2025. Twenty-five patients who underwent outpatient parathyroidectomy were included. Most patients were female (76%), with a mean age of 60 years old. Patients were carefully selected preoperatively; classified II or III on the American Society of Anesthesiologists scale. All adenomas were localized preoperatively using technetium-99m sestamibi scintigraphy or 18F-choline positron emission tomographic imaging.

Mean preoperative ionized calcium and parathyroid hormone (PTH) levels were 1.46 mmol/L and 17.8 pmol/L, respectively. Patients were directly admitted to the operating room the day of surgery. Mean operative time was 35 minutes. Immediate postoperative biochemical assessment showed mean PTH of 2.67 pmol/L. PTH levels decreased by an average of 75%, consistent with biochemical cure, as a PTH reduction of 50% or more, with return to the normal range, is an established early marker of success. Two patients experienced complications that did not delay discharge: a right vocal cord paralysis and an intraoperative bleeding requiring vein repair.

Twenty patients were discharged with oral calcium supplementation according to preoperative calcium or postoperative PTH levels. One patient discharged without supplementation developed asymptomatic hypocalcemia on postoperative day one, which resolved with oral calcium by day two. At 48 h postoperatively, calcium and PTH levels had normalized in all but one patient due to a second adenoma not identified on initial imaging. Two postoperative emergency visits were recorded in the first 48 h; one for suspected acute renal insufficiency that was an erroneous laboratory and one for diffuse paresthesia despite normocalcemia.

From a health economic perspective, outpatient parathyroidectomy was associated with cost reduction estimated to thousands of dollars per patient, primarily due to avoidance of postoperative hospitalization.

In conclusion, outpatient focused parathyroidectomy is a safe approach for PHPT in carefully selected patients and offers significant cost savings for the public health care system.

Abstract citation ID: lvag096.839

EP284 - ECE_1270 - Multiple myeloma and primary hyperparathyroidism: a case of dual pathologies co-existing for the presentation of hypercalcaemia

Pei Shan Yeo[1,2]
[1]*Singapore, Singapore;* [2]*Endocrinology, Tan Tock Seng Hospital, Singapore, Singapore*

Hypercalcaemia of varying severity is a common electrolyte disturbance that can affect up to 1%-2% of the general population. Depending on its degree of elevation and symptoms, severe hypercalcaemia is considered an endocrinology emergency. These patients are often referred to endocrinologists for management in such settings.

Apart from instituting acute measures for calcium lowering, it is crucial to dissect the aetiology of hypercalcaemia to treat the underlying cause and consider multiple pathologies appropriately. A rare case of dual pathology leading to hypercalcaemia due to multiple myeloma and primary hyperparathyroidism is presented in this middle-aged Chinese man. This 52-year-old man

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

was referred to our service for the medical management of calcium lowering therapy in the context of hypercalcaemia of malignancy with the classical presentation of low back pain, anaemia, acute renal impairment and hypercalcaemia. A myeloma panel done revealed newly diagnosed multiple myeloma. However, on review of the biochemistry, an elevated serum calcium level associated with hypophosphatemia and an inappropriately elevated PTH level was not in keeping with the aetiology of multiple myeloma. Subsequent investigations revealed a left lower hyperfunctioning parathyroid adenoma on Sestamibi scan. He also suffered complications of osteoporosis from the underlying primary hyperparathyroidism. Hypercalcaemia persisted despite chemotherapy for multiple myeloma. The patient eventually underwent a focused left inferior parathyroidectomy with resolution of hypercalcaemia.

This case serves to illustrate several learning points including (a) careful interpretation of biochemistry studies for calcium metabolism; (b) consideration for alternative diagnoses and/or dual pathologies to tie in the clinical presentation, initial management and progress of the patient; (c) ordering and prioritisation of treatment with dual pathologies; and (d) multidisciplinary care. These learning points are crucial in the holistic management of our patient to diagnose the presence of both medical conditions that warrant different treatment plans to resolve the hypercalcaemia.

Abstract citation ID: lvag096.840

EP286 - ECE_3654 - Assessing bone health and factors associated with low bone mineral density in Turner and Klinefelter syndromes

Rita Pinto Ribeiro[1], Patrícia Brito[1], Eduarda Mourão Rodrigues[2], Adriana de Sousa Lages[1], Ana Margarida Monteiro[1], Catarina MacHado[1], Catarina Matos[1], Juliana Sá[1], Maria Joana Santos[1], Marta Alves[1], Maria Pereira[1], Vera Fernandes[1], Olinda Marques[1] and Sara Esteves Ferreira[1]

[1]Endocrinology Department, Unidade Local de Saúde de Braga, Braga, Portugal; [2]Escola de Medicina da Universidade do Minho, Braga, Portugal

Background: Turner Syndrome (TS) and Klinefelter Syndrome (KS) are two chromosomal disorders associated with primary hypogonadism, predisposing affected individuals to low bone mineral density (BMD) and osteoporosis. Although hormone replacement therapy (HRT) plays a central role in the management of bone health in these populations, BMD outcomes are influenced by multiple factors beyond gonadal hormone deficiency. The aim of this study was to evaluate the factors influencing BMD in TS and KS patients by analyzing the relationship between BMD outcomes and clinical, biochemical, and therapeutic variables in these populations.

Methods: We conducted a retrospective study of adult patients with TS and KS followed at our center between 2011 and 2025. Data on BMD, hormone replacement therapy, parameters of phosphocalcium metabolism, and other relevant clinical and biochemical variables were collected. Patients were classified into low and normal BMD groups based on BMD measurements. Statistical analyses were performed to assess associations between BMD status and the studied variables.

Results: We included 17 TS and 25 KS adult patients. In TS patients, delayed HRT initiation was associated with low BMD ($P = .023$). BMI showed significant positive correlations with femoral absolute BMD ($r = 0.684$, $P = .005$) and femoral T-score ($r = 0.621$, $P = .018$), whereas time from TS diagnosis to HRT initiation was negatively correlated with femoral T-score ($r = -0.551$, $P = .027$). Growth hormone therapy showed no significant impact on bone health.

In KS, low BMD patients had a later diagnosis and were older than those with normal BMD ($P = .019$ and $P = .006$, respectively). They also initiated testosterone therapy later ($P = .005$). Femoral BMD showed positive correlations with testosterone therapy dose ($r = 0.610$, $P = .035$), vitamin D ($r = 0.436$, $P = .030$), and phosphorus levels ($r = 0.763$, $P = .001$).

Conclusions: This study highlights the critical role of timely HRT initiation in preserving bone health in TS and KS. Additionally, vitamin D status appears to influence BMD in KS, underscoring the need for optimized monitoring. These findings provide valuable insights for improving BMD preservation and management strategies in these populations.

Abstract citation ID: lvag096.841

EP287 - ECE_1128 - Turner syndrome mosaicism (45,X/46,XY) presenting with severe osteoporosis and secondary hyperparathyroidism: a multidisciplinary case study

Madina Sagimbayeva, Aigul Durmanova, Diana Kurgambekova and Zhaniya Tazhigulova

Corporate Fund "University Medical Center", Department of Endocrinology, General Therapy Program 2, Astana, Kazakhstan

Introduction: Turner syndrome (TS) is a chromosomal disorder caused by partial or complete monosomy of the X chromosome, affecting 1 in 2000-2500 live female births. Mosaic forms containing Y-chromosome material (45,X/46,XY) are uncommon and frequently associated with atypical phenotypes, gonadal dysgenesis, and complex metabolic complications. Early recognition of such genetic variants is essential for preventing progressive skeletal and endocrine deterioration.

Case presentation: We report a 36-year-old woman with Turner syndrome mosaicism (45,X/46,XY) who presented with progressive skeletal deformities, chronic pain, and multiple pathological fractures. Her height was 130 cm, and she exhibited primary amenorrhea and characteristic Turner features, including short stature, webbed neck, and gonadal dysgenesis. She became wheelchair-dependent in 2023 due to progressive bone fragility. Genetic karyotyping confirmed mosaicism 45,X[12]/46,XY[13], with 48% X monosomy and 52% Y-chromosome presence.

Clinical Data Included: Endocrine investigations revealed hypophosphatemia (0.27-0.38 mmol/L), elevated parathyroid hormone levels (256.7 pg/mL), and vitamin D deficiency (28.5 ng/mL). Thyroid function tests indicated subclinical hypothyroidism (TSH 5.3 mIU/L). Imaging findings included generalized osteoporosis, multiple pelvic and femoral neck fractures in consolidation, and bilateral hip osteoarthrosis (CT and DEXA scan). Despite long-term treatment with denosumab, calcium, and vitamin D supplementation, bone mineral density showed no improvement. FISH analysis confirmed Y-chromosome mosaicism in 65% of lymphocytes, providing a genetic explanation for the severe skeletal phenotype.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Discussion: The presence of Y-chromosome material in Turner mosaicism may intensify skeletal fragility and endocrine dysfunction through disrupted gonadal steroidogenesis and mineral metabolism. Secondary hyperparathyroidism and phosphate imbalance further exacerbate bone loss. This case illustrates the diagnostic challenges of mosaic TS in adulthood, especially when initial manifestations mimic isolated metabolic bone disease. Multidisciplinary evaluation involving endocrinology, genetics, and orthopedics was crucial for accurate diagnosis and individualized management.

Conclusions: Turner syndrome mosaicism (45,X/46,XY) with Y-chromosome inclusion represents a rare but clinically significant cause of severe, treatment-resistant osteoporosis. Early cytogenetic testing should be considered in patients with unexplained osteoporosis, primary amenorrhea, and short stature. Timely initiation of hormone replacement therapy, phosphate correction, and careful surveillance for gonadal neoplasia are key to improving quality of life and reducing morbidity.

Keywords Turner syndrome, mosaicism, osteoporosis, secondary hyperparathyroidism, genetic endocrinology

Abstract citation ID: lvag096.842

EP289 - ECE_3799 - Recognizing X-linked hypophosphatemia: the role of family screening in patients with short stature

Mihaela Maria Vlad[1], Carmen Dorogi[2] and Bianca Maler[2]
[1]2nd Internal Medicine, "Victor Babes" University of Medicine and Pharmacy, Timişoara, Romania; [2]Endocrinology, "Pius Brinzeu" Emergency County Hospital, Timişoara, Romania

Background: X-linked hypophosphatemia (XLH) is a rare inherited disorder caused by pathogenic variants in the *PHEX* gene. It is characterized by increased fibroblast growth factor 23 (FGF-23) activity, leading to renal phosphate wasting, hypophosphatemia, reduced 1,25$(OH)_2$ vitamin D synthesis, and impaired bone mineralization. Clinical manifestations include growth failure, skeletal deformities, dental abnormalities, muscle weakness, and chronic pain. Diagnostic delay is frequent, particularly in adults and in patients initially evaluated for isolated short stature.

Case presentation: We report three members of the same family diagnosed with XLH, emphasizing the pivotal role of targeted family screening. The diagnostic process was initiated in **Case 1**, a 43-year-old woman with lifelong disproportionate short stature, who had previously been misdiagnosed with pituitary dwarfism and later achondroplasia. Persistent hypophosphatemia identified during routine evaluation raised the suspicion of XLH. Upon further questioning, the patient reported multiple relatives with short stature. Subsequent construction of a detailed family pedigree revealed a pattern consistent with X-linked dominant inheritance, prompting systematic family screening. **Case 2**, the nephew of Case 1, had been diagnosed at 2 years of age with familial hypophosphatemic rickets resistant to vitamin D and treated with active vitamin D analogues and phosphate supplementation until the age of 7 years. **Case 3**, the mother of Case 2, had never undergone endocrinological evaluation despite marked short stature and skeletal deformities. All three patients presented with chronic musculoskeletal pain, disproportionate short stature, waddling gait, genu varum, and poor dentition. Biochemical evaluation demonstrated persistent hypophosphatemia, normal serum calcium, low-normal 1,25$(OH)_2$ vitamin D levels, elevated or high-normal alkaline phosphatase, increased urinary phosphate excretion, and reduced tubular phosphate reabsorption. Radiological examination revealed pseudofractures in Case 2. Genetic testing confirmed a pathogenic *PHEX* mutation in all affected family members.

Management and Outcomes: Cases 1 and 3 received conventional therapy with active vitamin D analogues and oral phosphate, with limited clinical improvement. Case 2 initiated treatment with burosumab, resulting in normalization of serum phosphate levels and improvement in biochemical parameters, while clinical symptoms improved modestly.

Conclusions: This case series demonstrates that recognition of hypophosphatemia in a single patient with short stature should prompt thorough family history assessment, pedigree analysis, and targeted family screening. Early identification of XLH allows timely treatment and may prevent irreversible skeletal complications and long-term impairment in quality of life.

Abstract citation ID: lvag096.843

EP291 - ECE_3271 - Adult-onset familial hypomagnesemia with secondary hypocalcemia: an atypical presentation of a rare disorder

Ana Margarida Sobral[1], Alice Monsanto[1], Bárbara Jesus[1], Adriana Duarte[1], Mariana Coelho[1], Sofia Lopes[1], Mafalda Martins Ferreira[2], Mariana Lavrador[1], Joana Reis Guiomar[1], Carolina Moreno[1], Daniela Guelho[1] and Leonor Gomes[1]
[1]Coimbra, Portugal; [2]Serviço de Endocrinologia da Unidade Local de Saúde São José, Lisboa, Portugal

Introduction: Familial hypomagnesemia with secondary hypocalcemia (FHSH) is a rare autosomal recessive disorder (prevalence < 1/million) caused by mutations in the *TRPM6* gene (chromosome 9q22), which encodes a magnesium-permeable ion channel expressed in the renal tubules and intestine.

Clinical manifestations include seizures and neurodevelopmental delay, typically presenting in childhood. Biochemically, it is characterized by severe hypomagnesemia and consequent hypocalcemia refractory to calcium supplementation. Treatment consists of magnesium replacement.

We report an atypical case diagnosed only in adulthood, representing the first case described in the literature with these characteristics.

Case report: A 22-year-old man presented to the emergency department with abdominal pain, vomiting, diarrhea, and episodes of absence. His medical history was notable for attention deficit hyperactivity disorder (ADHD). Physical examination at admission was unremarkable.

An electroencephalogram excluded epileptic activity, and brain computed tomography revealed calcifications of the basal ganglia.

Laboratory evaluation showed: Ca^{2+} 6.3 mg/dL; albumin 5.2 g/dL; Mg^{2+} < 0.6 mg/dL (1.8-2.6); PO_4^{3-} 5.4 mg/dL (2.5-4.5); 25-hydroxyvitamin D 19 ng/mL; and inappropriately low parathyroid hormone levels (PTH 16 pg/mL [9-72]).

The patient was admitted to the Endocrinology Department and treated with calcium carbonate 1500 mg twice daily and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

intravenous magnesium sulfate. Calcium carbonate was discontinued after normalization of serum magnesium levels. At discharge, laboratory results showed Ca^{2+} 10.1 mg/dL and Mg^{2+} 1.9 mg/dL under magnesium aspartate 1229.6 mg three times daily.

Family history revealed that his brother had epilepsy and hypomagnesemia since the age of 2 years and was on magnesium supplementation. Genetic testing for causes of hypomagnesemia identified a homozygous *TRPM6* variant, c.3179T > A p.(Ile1060Asn). Family members were referred for genetic counselling and are currently waiting for test result.

The patient is currently asymptomatic, with normal calcium levels and well-controlled magnesium levels on magnesium aspartate 1229.6 mg twice daily.

Conclusions: FHSH is a rare cause of hypomagnesemia, usually diagnosed in childhood. This case illustrates a late-onset presentation, highlighting the importance of considering a genetic etiology in adults with unexplained hypomagnesemia and hypocalcemia.

FHSH should be considered in patients with refractory hypocalcemia and neurological symptoms, as early diagnosis and treatment may prevent potentially irreversible neuromuscular and metabolic complications.

According to the literature review, this is the first reported case with adult-onset manifestations leading to diagnosis. The identified variant has been described in only one other case, also reported in Portugal, with no evidence of familial relationship or consanguinity between the two cases.

Abstract citation ID: lvag096.844

EP292 - ECE_2450 - A Rare cause of osteopenia and non-cirrhotic portal hypertension in a premenopausal breast cancer patient: gaucher disease

Ece Gül Köse Hamidi[1], Deniz Türküm Atikcan[1], Merve Şenay Özçalık[1], Ozlem Turhan Iyidir[1], Asli Nar[1], Arzu Oguz[2] and Neslihan Başçıl Tütüncü[1]
[1]*Endocrinology and Metabolism, Department of Endocrinology and Metabolism, Baskent University Faculty of Medicine, Ankara, Türkiye;* [2]*Oncology, Department of Oncology, Baskent University Faculty of Medicine, Ankara, Türkiye*

Introduction: Gaucher disease is an autosomal recessive lysosomal storage disorder caused by β-glucocerebrosidase deficiency. Although it is the most common lysosomal storage disease, adult-onset cases remain rare and are frequently diagnosed late due to heterogeneous and often subtle clinical manifestations. Skeletal involvement, including osteopenia and osteoporosis, represents one of the earliest and most prevalent features, yet is commonly misattributed to primary or secondary causes. In premenopausal women with breast cancer receiving aromatase inhibitor (AI) therapy, bone loss is expected, which may obscure the presence of underlying rare disorders. The coexistence of cytopenias and organomegaly should prompt further investigation.

Case presentation: A 43-year-old premenopausal woman was referred for evaluation of reduced bone mineral density. She had been diagnosed with early-stage, hormone receptor–positive breast cancer and treated with left mastectomy followed by ovarian suppression with goserelin and adjuvant letrozole. Dual-energy X-ray absorptiometry revealed diffuse lumbar osteopenia, with osteoporosis at L4 (T-score −2.5), and femoral osteopenia. Laboratory evaluation showed mild anemia (Hb 11.7 g/dL), leukopenia (3.82×10^3/μL) and persistent thrombocytopenia ($96\text{-}112 \times 10^3$/μL). Biochemistry was largely unremarkable, with normal calcium–phosphate balance and adequate vitamin D levels. Abdominal ultrasonography demonstrated marked splenomegaly (192 mm) and features consistent with non-cirrhotic portal hypertension, while hepatic veins remained patent and no evidence of cirrhosis was observed.

The combination of osteopenia, cytopenias, splenomegaly and portal hypertension raised suspicion for a lysosomal storage disorder. Enzymatic testing revealed markedly reduced leukocyte β-glucocerebrosidase activity (0.80 nmol/mg/h) and significantly elevated plasma chitotriosidase (452 μmol/L·h), consistent with Gaucher disease. Genetic confirmation via *GBA* mutation analysis was planned.

Discussion: While AI therapy commonly induces bone loss in premenopausal breast cancer patients, the presence of systemic features in this case indicated an alternative etiology. Gaucher disease is associated with bone marrow infiltration, increased bone resorption and impaired bone formation, predisposing patients to early osteopenia and fractures. Delayed diagnosis may result in irreversible skeletal damage and progressive organ involvement.

Conclusions: This case highlights that osteopenia in premenopausal breast cancer patients should not be attributed solely to oncological therapy when accompanied by cytopenias and organomegaly. A holistic assessment of systemic findings is essential to identify rare yet treatable conditions such as Gaucher disease, enabling timely intervention and prevention of long-term complications.

Abstract citation ID: lvag096.845

EP293 - ECE_2725 - Clinical features of long-standing postoperative hypoparathyroidism with multiple complications

Madina Bakirzhan[1,2], Anna Bazarova[1,2], Malika Kozhemzharova[1,2] and Zhannat Taubaldiyeva[1,2]
[1]*Astana Medical University, Astana, Kazakhstan;* [2]*Endocrinology, Multidisciplinary City Hospital No.1, Astana, Kazakhstan*

Relevance: Long-standing postoperative hypoparathyroidism is a rare endocrine disorder with significant clinical interest due to its chronic course and systemic complications. Prolonged use of active vitamin D metabolites carries a high risk of renal and extraskeletal complications. Renal complications, including nephrocalcinosis and nephrolithiasis, occur in 20%-40% of patients. This case demonstrates the severe consequences of conventional therapy and highlights the need for reconsideration of treatment strategies.

Aim: To analyze the clinical course of long-standing postoperative hypoparathyroidism with systemic complications, evaluate limitations and risks of standard therapy using active vitamin D metabolites, and emphasize the need for transition to parathyroid hormone therapy to prevent progression and preserve organ function.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Case description: Hypoparathyroidism affects approximately 20-40 per 100 000 population, mainly postoperative. In Kazakhstan, reliable epidemiological data are limited due to restricted access to specialized care, insufficient laboratory diagnostics, and absence of national registries.

Standard therapy with active vitamin D metabolites does not replicate parathyroid hormone effects and causes chronic hypercalciuria and elevated calcium–phosphate product, mechanisms underlying renal and extraskeletal complications.

The patient has a 20-year history of endocrine disease. At 23, she underwent total thyroidectomy for diffuse toxic goiter, complicated by persistent hypoparathyroidism and hypothyroidism, requiring lifelong hormone replacement.

Pregnancy at 32 occurred with chronic hypocalcemia, requiring careful monitoring and therapy adjustment. From age 34, she received alfacalcidol 3-5 μg/day, maintaining normocalcemia.

At 46, nephrocalcinosis and a left renal calculus were detected; at 48, nephrolithiasis exacerbation led to acute kidney injury (eGFR 24 mL/min). Surgery was performed, and alfacalcidol reduced to 2 μg/day. At 49, partial renal recovery (eGFR 58 mL/min) was observed, but recurrent hypocalcemia required an increase to 3 μg/day. At 50, a right renal calculus was identified. At 52, brain MRI revealed basal ganglia calcifications.

Conclusions: Even with normocalcemia, conventional therapy with active vitamin D metabolites does not prevent severe systemic complications. Progressive nephrocalcinosis, recurrent nephrolithiasis, renal function decline, and cerebral calcifications highlight the limited efficacy of this approach. Transition to recombinant parathyroid hormone therapy is pathogenetically justified, clinically appropriate, and may help prevent further progression of systemic complications while preserving organ function.

Abstract citation ID: lvag096.846

EP295 - ECE_1593 - The prevalence and clinical presentation of transient primary hyperparathyroidism

Yanmei Qi, Renata Marques Jones and Xiangbing Wang
Rutgers University-Robert Wood Johnson Medical School, New Brunswick, United States

Background: Primary hyperparathyroidism (PHPT) has become a common endocrine disorder and surgery is the only cure for symptomatic patients. Rarely, hypercalcemia and elevated intact parathyroid hormone (iPTH) may spontaneously normalize without intervention, a phenomenon termed transient PHPT (tPHPT). The prevalence of tPHPT remains unknown and the etiologic spectrum is evolving. We present 2 cases of tPHPT: one representing the longest reported follow-up of adenoma-associated tPHPT, and another highlighting a novel post-viral etiology.

Case presentation: Case 1: A 60-year-old man presented with new-onset hypercalcemia (11.6 mg/dL), elevated iPTH (124 pg/mL), vitaminD deficiency (15.2 ng/mL), and hypercalciuria (24-hour urine calcium 604 mg). Imaging indicated a left parathyroid adenoma. Immediately prior to planned parathyroidectomy, repeated testing revealed spontaneous normalization of calcium (9.6 mg/dL) and iPTH (64 pg/mL). Consequently, surgery was cancelled. Over a 12-year follow-up (the longest reported in literature), calcium and iPTH remained normal, with most recent calcium 9.7 mg/dL and iPTH 71 pg/mL. Imaging confirmed adenoma size reduction and subsequent stability. BMD remained normal, and the patient remained asymptomatic.

Case 2: A 60-year-old woman presented with asymptomatic hypercalcemia (serum calcium 11.4 mg/dL, ionized 6.1 mg/dl) and inappropriately high-normal iPTH (57 pg/mL). No history of malignancy or thiazide, lithium, vitamin D, and calcium supplements. Renal function, vitamin D status, and calcium-sensing receptor sequencing were normal. Imaging revealed a multinodular goiter without parathyroid findings. Notably, she had recovered from COVID-19 infection 4-6 weeks prior to calcium (11.6 mg/dL) and iPTH (110 pg/mL) peak. Without intervention, biochemical markers normalized within seven months (calcium 9.1 mg/dL, iPTH 38 pg/mL), followed by alkaline phosphatase normalization six months later. Remission has persisted for >3 years.

Discussion/Conclusions: The estimated global prevalence of tPHPT is 0.0016% (67 cases reported since 1946), markedly lower than the 0.4% (2/500) frequency identified in our center.

Proposed pathogenic mechanisms include adenoma infarction or hemorrhage (~93%), immune-mediated inflammation/injury, and possible parathyroiditis.

Case 1 strongly suggests adenoma auto-infarction; the 12-year follow-up validates a conservative approach but underscores the need for surveillance. Conversely, Case 2 lacked structural pathology but was temporally linked to SARS-CoV-2, suggesting a distinct mechanism of post-viral parathyroiditis causing transient PTH leakage. The absence of secondary causes and sustained remissions support a self-limited process. To our knowledge, this is the first documented tPHPT case with a post-viral etiology.

Recognizing tPHPT is critical to avoid unnecessary parathyroidectomy. Pre-operative biochemical re-assessment is vital, particularly in new-onset or short-duration hypercalcemic PHPT. For confirmed tPHPT, observation is appropriate, though long-term monitoring remains crucial given the potential of recurrence.

Abstract citation ID: lvag096.847

EP300 - ECE_2883 - Primary hyperparathyroidism masquerading as tertiary hyperparathyroidism in a renal transplant recipient

Huriya Siddique[1], Shahroz Azhar[1], Arfa Ahmed Assad[1], Sidra Safdar[2], Muhammad Murtaza Shafqat[1] and Hira Irfan[1]
[1]*Endocrinology, Internal Medicine & Endocrinology, Pakistan Kidney and Liver Institute & RC, Lahore, Pakistan;* [2]*Clinical Trial Unit, Department of Oncology and Radiotherapy, Mayo Hospital Lahore, Lahore, Pakistan*

Background: Persistent hypercalcaemia following renal transplantation is most commonly attributed to tertiary hyperparathyroidism, reported in approximately 17%-50% of transplant recipients. However, alternative aetiologies should be actively considered. We describe a renal transplant recipient with persistent hypercalcaemia who was ultimately diagnosed with primary hyperparathyroidism due to an ectopic mediastinal parathyroid adenoma.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Case presentation: A 48-year-old male underwent a living-related renal transplant after nine years of haemodialysis for end-stage renal disease secondary to long-standing uncontrolled hypertension. Post-transplant recovery was uneventful, and he achieved stable graft function on an immunosuppressive regimen.

Three years post-transplant, he presented with generalized bone pain and weakness. Biochemical evaluation revealed persistent hypercalcaemia (11.06 mg/dL) with elevated intact parathyroid hormone (iPTH) levels (148.9 pg/mL) and mildly elevated phosphate levels. Renal function and vitamin D levels were within normal limits. These findings initially suggested tertiary hyperparathyroidism. However, parathyroid ultrasonography was unremarkable.

The combination of persistent hypercalcaemia, elevated iPTH levels, and normal ultrasonographic findings raised suspicion for an ectopic parathyroid source. A contrast-enhanced CT scan of the neck and chest did not identify ectopic parathyroid tissue. Given the high index of suspicion, a Tc-99m sestamibi parathyroid scan with early and delayed imaging was performed, demonstrating focal tracer uptake in the superior mediastinal region, consistent with an ectopic mediastinal parathyroid adenoma. The patient was referred to thoracic surgery for resection and remains under close endocrinology follow-up.

Conclusions: This case illustrates a rare but important diagnostic pitfall in renal transplant recipients presenting with persistent hypercalcaemia. Elevated parathyroid hormone levels after transplantation should not be automatically attributed to tertiary hyperparathyroidism. Although uncommon, primary hyperparathyroidism—particularly due to ectopic parathyroid adenomas—remains a crucial differential diagnosis, especially when conventional imaging is inconclusive. Functional imaging with Tc-99m sestamibi plays a pivotal role in localising ectopic parathyroid tissue and preventing diagnostic delay, inappropriate management, and prolonged patient morbidity.

Abstract citation ID: lvag096.848

EP301 - ECE_2983 - Performance of diagnostic modalities in primary hyperparathyroidism: single-center expert experience

Fatma Nur Korkmaz
Kayseri, Türkiye

Introduction: In patients with primary hyperparathyroidism(PHPT) requiring treatment, parathyroid localization is performed using neck ultrasonography(USG), Parathormone washout(PTHW) and/or fine-needle aspiration biopsy(FNAB), parathyroid sestamibi scintigraphy(MIBI), and -dimensional contrast-enhanced neck tomography(4D-CT). Parathyroid adenomas(PA) may mimic lymph nodes or thyroid nodules on imaging; therefore, accurate localization requires combined evaluation of multimodal imaging and biopsy techniques.

Aim: The aim was to evaluate the diagnostic accuracy of imaging methods used to determine localization in patients diagnosed with PHPT.

Method: Patients with PHPT between March 2024 and January 2026 were retrospectively reviewed. The patients' demographic characteristics, laboratory parameters, imaging modalities (USG, MIBI scintigraphy, 4D-CT), vertebral radiographs, bone mineral density measurements of the femur, spine, and distal radius), indications for treatment were evaluated. The indications for surgery were determined according to the criteria defined in the Fifth International Workshop on the Evaluation and Management of Primary Hyperparathyroidism. The diagnostic algorithm is shown in Figure 1.

Results: The clinical and laboratory characteristics of the patients are presented in Table 1. Three of the four patients diagnosed with MEN belonged to the same family. Figure 2 summarizes the results of the localization studies. PTHW was not performed because one patient had a preliminary diagnosis of parathyroid carcinoma, three patients had not accepted PTHW procedure, and six patients had previously performed MIBI studies that were positive and concordant with USG. Using USG ± PTHW/FNAB or MIBI, the PA was localized in 80.5% of the patients (47 + 7 out of 67 patients). Among three patients with negative USG findings, only one underwent surgery based on MIBI uptake, confirming parathyroid adenoma on pathology (1/67 false negative USG).

The correlation of MIBI and USG results is presented in Table 2 in PTHW(+) patients. According to this, 3/3 lesions in the right upper gland, 4/5 lesions in the right lower gland, 3/7 lesions in the left upper gland, and 7/8 lesions in the left lower gland were detected. False-negative uptake was observed in 6 out of 23 cases.

One patient with negative USG was truly diagnosed with PA with MIBI. Another patient was diagnosed with PA on the neck by USG and FNAB, while MIBI revealed an ectopic PA localization. Surgery was performed in 21 patients, with 20 diagnosed with PA and 1 with parathyroid carcinoma.

Conclusions: PTH washout demonstrates high diagnostic accuracy, while FNAB and MIBI are less reliable. MIBI, however, may offer additional value in cases with multiple lesions.

Figure 1

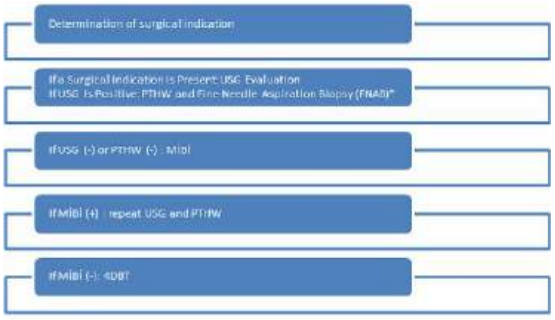


Figure 1.**Diagnostic algorithm.**
* In patients who had previously undergone MIBI imaging at an external center, PTH washout and FNAB were not performed. Note: At the stage deemed appropriate for surgery, MIBI and/or 4D-CT imaging was performed regardless of ultrasonographic or PTH washout positivity.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Table 1

Table 1 The clinical and laboratory characteristics of the patients

Parameter[†]	Total (n=65)	Normal Range	Localization (-) (n=9)	Localization (+) (n=56)	P value
Age, years, mean±SD	55.65 ± 14.01	–	57.44 ± 9.18	55.15 ± 14.86	0.656*
Sex, n (F/M)	53/13	–	8/1	43/12	0.671**
Postmenopausal F, n	33	–	6	26	0.693**
Male >50 years, n	10	–	1	9	–
Diagnosis, n (%)					
PHPT	57 (86.5)	–	6	49	0.110**
NPHPT	9 (13.5)	–	3	6	–
BUN, mg/dL	14.0 (5–40)	8–23	14.0 (5–27)	13.0 (5–40)	0.809*
Creatinine, mg/dL	0.70 (0.47–3.05)	0.59–0.80	0.645 (0.50–1.14)	0.71 (0.50–3.05)	0.412*
PTH, pg/L	175.7 (54–1436)	15–65	103 (54–226)	145 (50–1436)	0.128*
cCa, mg/dL	10.9 (9.7–19.2)	8.6–10.2	10.6 (9.7–11.1)	10.9 (9.8–19.2)	0.180*
Phosphorus, mg/dL	2.5 (1.4–4.4)	2.4–4.5	2.8 (2.0–4.0)	2.5 (1.4–4.4)	0.279*
ALP	96 (44–195)	–	114 (58–181)	95 (44–195)	0.293*
25 OH Vit D, ng/L	18.7 (6.1–55.4)	30–80	18.7 (6.1–55.4)	18.7 (6.1–55.4)	0.972*
Urinary Ca, mg/24 h	283 (86.3–1134)	100–300	388 (108–496)	283 (86–1134)	0.328*
Nephrolithiasis, n (%)	19 (28.8)	–	4 (66.7)	8 (19)	0.019**
Hypercalciuria, n (%)	31 (47.0)	–	5 (83.4)	17	0.145**
Osteoporosis, n (%)	28 (42.4)	–	3 (50)	19	0.462**
Surgical indication	2 (1–4)	–	2 (1–3)	2 (1–4)	0.450*
Treatment, n (%)					
Surgery (MI/TP)	21 (28.8)	–	0	21 (37.5)	
IV bisphosphonate	4 (6)	–	4 (44.4)	0	
Thiazide	1 (1.5)	–	1 (11.1)	0	<0.1**
Cinacalcet	1 (1.5)	–	0	1 (1.8)	
Follow-up, n (%)	14 (20.9)	–	4 (44.4)	7 (12.5)	
Planned surgery	17 (25.5)	–	0	17 (30.4)	
Continuing evaluation	8 (11.9)	–	1 (11.1)	6 (10.7)	
PA size, mm	13.5 (6–39)	–	10 (8–16)	14 (7–39)	0.115*
Nodule number	0.5 (0–7)	–	1 (0–3)	0 (0–7)	0.303*
USG findings, n (%)					
– No lesion	3 (4.5)	–	2 (22.2)	1 (1.8)	
– Right upper	5 (7.6)	–	0	5 (9.1)	
– Right lower	25 (37.9)	–	3 (33.3)	21 (38.2)	0.017**
– Left upper	12 (18.2)	–	0	12 (21.8)	
– Left lower	19 (–)	–	2 (22.2)	16 (3)	
– Multiple	3 (4.5)	–	2 (22.2)	1 (1.8)	
PTH washout (n=55, 83.4%)	Negative	–	6 (66.7)	3 (5.4)	<0.001**
	Positive	–	0	45 (80.4)	
PTH washout, pg/mL	2778 (2–>5000)	–	13.5 (2–19)	3866 (5–5001)	<0.001*
MIBI (n=41, 60.6%)	Positive	–	4 (44.4)	7 (12.5)	0.182**
	Negative	–	4 (44.4)	26 (46.4)	
FNAB (n=41, 60.6%)	PA / concordant	–	0	10 (15.6)	0.638
	Non-PA diagnosis	–	6 (66.7)	23 (43.1)	

[†]Parameters are presented as median (minimum–maximum) unless otherwise specified. * Student t-test, ** Fisher's Exact test, # Mann–Whitney U test

Abbreviations: SD =standard deviation; MI = Minimally invasive parathyroidectomy; TTP = Total thyroidectomy and parathyroidectomy; PA = Parathyroid adenoma; USG = Ultrasonography; MIBI = Sestamibi scintigraphy; FNAB = Fine needle aspiration biopsy; PHPT = Primary hyperparathyroidism; NPHPT = Normocalcemic PHPT; cCa = Albumin-corrected calcium; PTH = Parathyroid hormone; ALP = Alkaline phosphatase

Figure 2

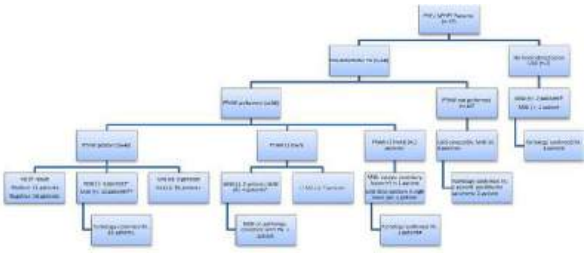


Figure 2: the results of the localization studies

PTH washout was not performed in two patients who refused the procedure and in one patient due to suspected malignancy.[#]One patient underwent surgery based on positive MIBI findings, and pathology confirmed parathyroid adenoma (PA). As the remaining patients were not operated on, true or false MIBI positivity could not be determined.*In two patients, multiple PA-suspected lesions were detected on ultrasonography (USG) while MIBI was negative.**In one patient, USG localized a left superior lesion, whereas MIBI showed right inferior uptake. After left superior minimally invasive parathyroidectomy, pathology confirmed PA and remission was achieved. In one patient with MIBI positivity concordant with USG localization but negative PTH washout, surgery was performed and pathology confirmed PA. In the remaining patients, diagnostic accuracy could not be assessed due to lack of pathology. # Cervical lesion was identified by USG and FNAB, while ectopic lesion was detected by MIBI; all pathological results of both lesions were consistent with PA. Abbreviations: PHP, primary hyperparathyroidism; NPHPT, normocalcemic primary hyperparathyroidism; USG, ultrasonography; PTHw, parathyroid hormone washout; FNAB, fine needle aspiration biopsy; MIBI, sestamibi parathyroid scintigraphy; 4D-CT, four-dimensional computed tomography; PA, parathyroid adenoma.

Table 2

Table 2 Correlation of Parathyroid Scintigraphy and Ultrasonography Localization in PTH Washout–Positive Patients

		USG				
		Right Superior	Right Inferior	Left Superior	Left Inferior	Multiple
MIBI	Negative	0	1	3	1	1
	Right Superior	3	0	0	0	0
	Right Inferior	0	4	1	0	0
	Left Superior	0	0	3	0	0
	Left Inferior	0	0	0	7	0

Abstract citation ID: lvag096.849

EP302 - ECE_3831 - A diagnostic masquerader: CYP24A1-related vitamin D–dependent hypercalcaemia presenting as recurrent nephrolithiasis over three decades

Maliha Iqbal[1], Saba[2,3,4], Al-BahraniAli[2] and Amie Thompson[2]

[1]Maidstone, Maidstone Hospital, United Kingdom; [2]Clinical Metabolism, Clinical Metabolism, Maidstone Hospital, Maidstone, United Kingdom; [3]Diabetes and Endocrinology, Maidstone and Tunbridge Wells NHS Trust, Maidstone, United Kingdom; [4]Diabetes and Endocrinology, Maidstone Hospital, Maidstone, United Kingdom

Background: Primary hyperparathyroidism (PHPT) is a common cause of hypercalcaemia and nephrolithiasis; however, rare disorders of vitamin D metabolism can mimic this presentation. Autosomal recessive infantile hypercalcaemia type 1 (ARIH1), caused by pathogenic variants in *CYP24A1*, leads to impaired degradation of active vitamin D metabolites, resulting in PTH-independent hypercalcaemia, hypercalciuria, and renal stone disease. Diagnosis is often delayed due to atypical biochemical features.

Case presentation: We describe a 63-year-old male with a history of recurrent renal stone disease since 1988. Over more than 20 years, he was reviewed multiple times in endocrine clinics for suspected PHPT. Biochemistry consistently showed mildly elevated or high-normal adjusted serum calcium (2.57-2.91 mmol/L) with parathyroid hormone (PTH) levels not suppressed but in the lower half of the reference range at 2.1-3.6 pmol/L (reference range: 1.6-6.9 pmol/L). Serum phosphate was intermittently low-normal, renal function remained preserved, and 24-hour urinary calcium was persistently elevated (10.5-11.3 mmol/24 h), with calcium-creatinine clearance ratios around 0.03, excluding familial hypocalciuric hypercalcaemia. Vitamin D levels were normal to high-normal, and extensive evaluation excluded malignancy, granulomatous disease, and paraproteinemia. There was no history of calcium or vitamin D supplementation.

Family history revealed a sister who underwent parathyroid surgery for hypercalcaemia in later life. Given long-standing PTH-independent hypercalcaemia dating back to the late 1990s, a disorder of vitamin D metabolism was suspected. Measurement of vitamin D metabolites demonstrated elevated 1,25-dihydroxyvitamin D with suppressed 24,25-dihydroxyvitamin D and markedly elevated metabolite ratios. Genetic testing confirmed a homozygous pathogenic variant in *CYP24A1*, establishing the diagnosis of ARIH1.

Management and Outcome: The patient was advised to avoid vitamin D supplementation, excessive dietary calcium, and prolonged sun exposure, with emphasis on maintaining good hydration. He was referred for genetic counselling, with discussion of cascade testing for family members. Shared care with a tertiary metabolic bone service was established, with consideration of cinacalcet as a potential future therapeutic option. Renal function remains stable.

Conclusions: This case highlights the importance of considering *CYP24A1*-related hypercalcaemia in patients with long-standing nephrolithiasis, hypercalcaemia, hypercalciuria, and low-normal PTH. Early recognition can prevent unnecessary surgery and guide appropriate long-term management and family screening.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.850

EP303 - ECE_1917 - Management of osteoporosis in stroke patients: a systematic review of clinical practice guidelines

Chrislyn Ng[1,2], Mariam Mohammad Rahim[1,2], Jakub Mesinovic[3], Ayse Zengin[1], Anne Trinh[1,2,4], Peter Ebeling[1,5], Frances Milat[1,4,6], Gabrielle Stokes[1,2,4] and Mícheál Ó. Breasail[1]

[1]Monash University, Clayton, Australia; [2]Monash Health, Clayton, Australia; [3]Deakin University, Burwood, Australia; [4]Hudson Institute of Medical Research, Melbourne, Australia; [5]Monash Health, Melbourne, Australia; [6]Department of Endocrinology, Monash Health, Clayton, Australia

Background: Stroke is a leading cause of mortality and morbidity worldwide, with stroke survivors suffering a wide range of post-stroke complications. Osteoporosis is a well-established complication post-stroke due to accelerated bone and muscle loss. While this is a significant driver of fractures, osteoporosis post-stroke remains substantially underdiagnosed and undertreated.

Objective: To evaluate current clinical guidelines and recommendations for osteoporosis screening, prevention and treatment post-stroke.

Methods: A systematic review was conducted and reported in accordance to PRISMA guidelines, with PROSPERO registration. We searched OVID MEDLINE, Embase, Emcare and Web of Science databases up to 05/01/2026 with a complementary search for websites of major international societies, national professional bodies specialising in the care of stroke and/or osteoporosis and Guidelines International Network (GIN). Identified guidelines were appraised using the AGREE-II (Appraisal of Guidelines for Research and Evaluation) tool.

Results: Nine clinical guidelines across five countries were identified, including guidelines from the United Kingdom ($n = 3$), the United States ($n = 3$), Singapore ($n = 1$), Malaysia ($n = 1$) and South Africa ($n = 1$). Five were osteoporosis guidelines that included information on post-stroke osteoporosis, while the remaining 4 guidelines were stroke guidelines that identified osteoporosis as a post-stroke complication. All osteoporosis guidelines nested stroke as a risk factor for osteoporosis and fractures among other neurological conditions, with no additional stroke-specific information on fracture prevention and treatment of osteoporosis. Among the four stroke guidelines, fracture risk assessment was recommended as part of stroke rehabilitation but no specific details about stroke-specific fracture risk assessment. Three of four stroke guidelines recommended improving levels of physical activity and vitamin D and calcium supplementation to avert post-stroke osteoporosis. Appraisal of identified guidelines using the AGREE-II is currently underway.

Conclusions: Despite the documented high fracture rates post-stroke, health professionals do not have adequate guidance to support the management of osteoporosis in this setting. Although acknowledged as a secondary cause of osteoporosis, stroke-specific guidance remains largely lacking from osteoporosis clinical practice guidelines. While the included stroke clinical practice guidelines included offered more targeted guidance on the screening and prevention of osteoporosis, these represent a small fraction of stroke guidelines worldwide. Providing specific recommendations post-stroke related to bone health in national osteoporosis guidelines should be a priority given the high burden of fracture in the patient population.

Abstract citation ID: lvag096.851

EP304 - ECE_1814 - Tumor-induced osteomalacia of the left maxillary sinus: diagnostic challenges

Daniel Grigorie and Alina Sucaliuc

National Institute of Endocrinology, Bucharest, Romania

Background: Tumor-induced osteomalacia (TIO) is an ultrarare paraneoplastic syndrome due to overproduction of fibroblast growth factor 23 (FGF23), which produces significant patient morbidity and poses diagnostic challenges, with an initial misdiagnosis rate of more than 95%. Biochemical features of TIO are represented by hypophosphatemia, increased or inappropriately normal levels of FGF23, and low to low normal circulating calcitriol. TIO-causing tumors have been observed in soft tissue and bone in many different locations, around 10% in the head.

Case presentation: A 57-years old woman was admitted to our endocrinology department to investigate an non-suspicious thyroid nodule, reporting a 10 months history of progressive and severe bone and muscle pain, proximal muscle deficit, mobility limitation and difficult gait and upright posture, with a preliminary diagnostic of secondary bone lytic lesions, treated with zoledronate a month before admission. The medical history included: total right hip replacement for osteoarthritis seven yrs before, osteoporosis treated with risedronate (LS Z-score = −2.9 SD), bilateral sacroiliitis by RMI and positive HLA-B27, CT head, thorax and abdomen: multiple lytic lesions in the ribs, pelvis, femoral neck, and multiple hot spots on bone scintigraphy; negative tumor markers and testing for multiple myeloma. A month before, in another hospital: P 1.39 mg/dl, AlkPhos 330 U/L (35-105). At admission: P: 1.7-1.9 mg/dl; AlkPhos 345 U/L; Ca: 8.9 mg/dl; PTH 91.48 pg/ml; 25OHD 36 ng/ml; normal renal, thyroid, adrenal function. P urine 0.58 g/24 h; TmP/GFR = 0.52 mmol/l (0.80-1.35 mmol/L); FGF-23 = 153 pg/ml (23.2-95.4); calcitriol = 30.5 pg/ml (19.9-79.3). Calcitriol 3 mcg and 3 g phosphate per day were recommended with progressive improvement of clinical, biochemical and radiographic osteomalacia. After 6 mo the treatment was interrupted for 2 weeks: *P* = 1.90 mg/dl, AlkPhos = 166 U/L; P urine 0.27 g/24 h; calcitriol = 9.14 pg/ml; FGF-23 = 254.80 pg/ml; TmP/GFR = 0.5 mmol/l. LS BMD increased by 50% after 6 mo and bone scan was normal after 1 year. As SPECT-CT was negative for tumor we performed genetic testing for XLH/FGF23, but no clinically relevant variants were detected. A PET CT Ga-68 DOTATATE identified an increased uptake focus on posterior wall of the left maxillary sinus. A maxillary sinus MRI and an appointment with an oral surgeon were scheduled.

Conclusions: This case has several particularities: a rather short history, frequent misdiagnosis, good response to conventional therapy, but delayed healing of osteomalacia due to zoledronate and the necessity of genetic testing in the absence of initial tumor localization.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.852

EP306 - ECE_1758 - Stabilization of exostotic bone lesions following bisphosphonate therapy: a small clinical case series

Michail Savvas Magklis[1,2,3], Maria Chrysoula Tatarida Palla[1,2,3], Christos Yapijakis[1], Eleni Koniari[1], Katerina Firfilioni[1,2], Eleni Papanikolaou[1,2] and George Chrousos[1,2,3]

[1]National and Kapodistrian University of Athens, Athens, Greece; [2]Clinical and Translational Research Endocrine Unit, National and Kapodistrian University of Athens, Athens, Greece; [3]National and Kapodistrian University of Athens, University Research Institute of Maternal and Child Health and Precision Medicine, University Research Institute of Maternal and Child Health and Precision Medicine, Athens, Greece

Background: Exostoses and osteochondroma-like lesions may arise in a range of bone remodeling disorders, including Paget disease of the bone and inherited osteodysplasias, leading to pain, functional impairments, and repeated surgical interventions. Currently, no established medical therapy directly targets exostosis formation or progression and the management is surgical.

Objective: To describe clinical and radiographic outcomes following bisphosphonate therapy in patients with heterogeneous bone disorders presenting with exostotic lesions.

Methods: We report an observational case series of three patients with exostosis-prone bone disorders with genetically determined osteodysplastic syndromes, who were treated with bisphosphonate therapy for pain, functional limitation, osteoporosis, and progressive exostotic burden. Clinical outcomes included pain relief, improvement of mobility and quality of life, and no further need for surgical intervention. Radiographic follow-up was assessed using routine clinical imaging.

Results: All three patients experienced substantial symptomatic improvement within months of therapy initiation, with marked reduction in pain and improved functional capacity. During follow-up of >20 y for two patients and >3 y for the third patient, no recurrence of symptomatic exostoses or emergence of new exostotic lesions was observed. Radiographic assessment suggested stabilization of exostotic bone changes compared with prior clinical course. Treatment was well tolerated, with no clinically significant adverse effects reported.

Conclusions: In this small, heterogeneous case series, bisphosphonate therapy was associated with symptomatic improvement and apparent stabilization of exostotic bone lesions. Although causality cannot be established, these observations suggest that modulation of bone turnover may influence exostosis-related manifestations across different bone remodeling disorders. Further systematic studies are warranted to define disease-specific efficacy, optimal timing, and long-term outcomes.

Abstract citation ID: lvag096.853

EP307 - ECE_2986 - Therapeutic challenges in the management of Paget's disease of bone: effectiveness of denosumab

Iulia-Alexandra Voinea[1], Eugenia Petrova[1,2], Andra Cocoloș[1,2], Gabriela Voicu[3] and Adina Ghemigian[1,2]

[1]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [2]Department of Endocrinology, C.I.Parhon National Institute of Endocrinology, Bucharest, Romania; [3]Nuclear Medicine Laboratory, C.I.Parhon National Institute of Endocrinology, Bucharest, Romania

Background: Denosumab, a monoclonal antibody that inhibits bone resorption, is approved for osteoporosis, bone metastases, and giant cell tumor of bone. This report highlights denosumab as an effective therapy option in Paget's disease of bone (PDB) with unsustained response to bisphosphonate therapy.

Methods: A 49-year-old female has been under follow-up for five years for PDB associated with a pathogenic SQSTM1 mutation. Initial laboratory assessment included serum calcium, alkaline phosphatase (ALP), and bone turnover markers (P1NP and beta-crosslaps). Disease extent was evaluated by bone scintigraphy. Sequential antiresorptive therapy with zoledronic acid and denosumab was administered, with ongoing clinical and biochemical monitoring.

Results: At diagnosis, serum calcium, ALP, P1NP, and beta-crosslaps were increased: 10.3 mg/dL (N:8.4-10.3), 392 U/L (N:35-104), 203.4 ng/mL (N:14.28-58.92), and 0.67 ng/mL (N:0.162-0.436), respectively. Bone scintigraphy revealed left ulna involvement. The first administration of zoledronic acid induced a very good clinical and biochemical response. Twelve months after the second zoledronic acid infusion, the ulna lesion enlarged and pain reappeared. Bone turnover markers rebounded. Under denosumab therapy, bone turnover was suppressed, with resolution of symptoms. Biochemical monitoring showed partial escape from denosumab suppression at six months, with recurrent pain. Calcium supplementation during the first two months was required to prevent hypocalcemia and secondary hyperparathyroidism.

Conclusions: This case underscores the need for individualized antiresorptive strategies in PDB. Denosumab effectively controlled disease activity and symptoms. Biochemical rebound suggests that shorter dosing intervals may be required. Long-term clinical and biochemical monitoring remains essential.

References

1. Singer FR, Bone HG III, Hosking DJ, et al. Paget's disease of bone: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(12):4408-4422. https://doi.org/10.1210/jc.2014-2910
2. Schwarz P, Rasmussen AQ, Kvist TM, et al. Paget's disease of the bone after treatment with denosumab: a case report. *Bone*. 2012;50(5):1023-1025. https://doi.org/10.1016/j.bone.2012.01.020

Abstract citation ID: lvag096.854

EP310 - ECE_2211 - Pseudohypoparathyroidism clinical puzzle: a case report

Alla Shepelkevich[1], Diana Baalbaki[1] and Zhanna Kirilenko[2]

[1]Endocrinology, Belarusian State Medical University, Minsk, Belarus; [2]Minsk City Clinic Endocrinology Center, Minsk, Belarus

Introduction: Pseudohypoparathyroidism (PHP) is a rare genetic disorder characterized by end-organ resistance to parathyroid hormone (PTH), which results in patients developing hypocalcemia and hyperphosphatemia despite increased serum PTH levels. Moreover, its association with Albright Hereditary Osteodystrophy (AHO)—a set of distinctive physical features,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

usually contributes to a prompt diagnosis. We report the case of a patient presenting with AHO phenotype, seizures, history of metatarsal fractures, extensive cerebral calcifications and previously normal calcium-phosphorus levels.

Case report: A 15-year-old male was referred for endocrine consultation after a sudden deterioration in his condition (fatigue, seizures, tetany, facial twitching). Patient's physical features were consistent with AHO (short stature—150 cm, round face, brachydactyly and subcutaneous ossifications) and medical history was remarkable for fractures of 2nd and 3rd metatarsals in one foot and fractures of proximal phalanges in another. The patient was formerly diagnosed with Fahr's syndrome due to abnormal findings on plain CT scan of the head which revealed symmetrical linear and focal calcification in the white matter of the frontoparietal zones and in basal ganglia. There was no documented evidence of previously abnormal laboratory results and his family history was unremarkable. Laboratory testing revealed elevated PTH of 79 pg/ml (14,9-56,9 pg/ml), low serum calcium of 1.16 mmol/L (2.1-2.6 mmol/L), high phosphorus of 1.66 mmol/L (0.81-1.62 mmol/L), high TSH of 10.5 µIU/mL (0.7-4.2 µIU/mL) and low free T4 of 10.1 pmol/L (11-23 pmol/L). According to patient's DEXA, bone mineral density was lower than that of the same age group (Z-score −2.1 in L1-L4 vertebrae). Additionally, X-ray of left hand revealed epiphyseal closure. Based on the presented clinical, laboratory and radiological findings, the diagnosis of PHP was established. Confirmation of PHP with genetic testing was not performed due to its unavailability. Patient was started on a regimen of oral calcium, calcitriol and levothyroxine, leading to significant improvement. On further follow-ups, patient remained asymptomatic with adequate compensation of PHP.

Conclusions: This clinical case emphasizes the importance of repeated phosphocalcic and PTH levels assessment in patients presenting with AHO phenotype and clinical manifestations of hypocalcemia despite previously normal levels to solve the diagnostic puzzle and improve patient's long-term outcomes.

Abstract citation ID: lvag096.855

EP311 - ECE_2906 - When bones tell a genetic story: a young woman with Albright's hereditary osteodystrophy and GNAS mutation causing pseudopseudohypoparathyroidism

Adelola Adekolu-John and Muhammad Athar Iqbal Khan
Rotherham, United Kingdom

When Bones Tell a Genetic Story: A Young Woman with Albright's Hereditary Osteodystrophy and GNAS Mutation Causing Pseudopseudohypoparathyroidism

We present the case of a 22-year-old woman referred with long-standing musculoskeletal deformities and progressive pain. She reported finger and toe abnormalities since childhood, with a 2-3-year history of worsening stiffness and pain affecting the hands, wrists, back, hips, and feet. Additional symptoms included fatigue, mood fluctuation, weight gain, and reduced mobility. There was no history of joint swelling, dysphagia, hearing impairment, or significant endocrine disturbance. She sustained a low-impact ankle fracture the previous year with prolonged healing.

Examination demonstrated brachydactyly, particularly involving the 4th metacarpals and toes, enlarged distal interphalangeal joints of both thumbs, limited MCP movements, asymmetrical hypermobility, and painful restriction of hip movements. Biochemistry revealed persistently normal adjusted calcium (2.39 mmol/L) and phosphate, elevated parathyroid hormone (PTH 8.3 pmol/L), and low 25-OH vitamin D (32 nmol/L). Genetic testing identified a pathogenic GNAS mutation.

The patient exhibited classical features of Albright's hereditary osteodystrophy (AHO), including short stature, brachydactyly, joint abnormalities, and ectopic bone-related symptoms. Given normal calcium and phosphate with raised PTH (likely secondary to vitamin D deficiency), this presentation is most consistent with pseudopseudohypoparathyroidism (PPHP) rather than pseudohypoparathyroidism (PHP).

PHP is characterised by end-organ resistance to PTH, leading to hypocalcaemia, hyperphosphatemia, and elevated PTH, often with AHO features. In contrast, PPHP shows the AHO phenotype without biochemical resistance. Vitamin D replacement was initiated and repeat PTH is planned to clarify the diagnosis. Thyroid and pituitary axes are under evaluation.

This case highlights the importance of integrating genetic, biochemical, and phenotypic data in young patients with unexplained skeletal abnormalities and chronic pain.

Abstract citation ID: lvag096.856

EP313 - ECE_1755 - A case of challenging localization in primary hyperparathyroidism

Jelena Marinkovic Radosevic[1], Lora Kirigin Biloš[1], Velimir Altabas[1,2] and Gorana Mirosevic[1,3]
[1]*University Hospital Centre Sestre Milosrdnice, Department of Endocrinology, Diabetes and Metabolic Diseases "Mladen Sekso", Zagreb, Croatia;* [2]*School of Medicine, University of Zagreb, Zagreb, Croatia;* [3]*School of Dental Medicine, University of Zagreb, Zagreb, Croatia*

Preoperative localization of hyperfunctional parathyroid tissue can, in rare cases, be challenging. Cervical ultrasonography combined with [99mTc]Tc-MIBI scintigraphy typically provides a diagnostic sensitivity of 81%-95%. In patients with discordant findings, fine-needle aspiration (FNA) cytology with parathyroid hormone measurement in the aspirate (FNA-PTH) may help confirm parathyroid origin. [18F]fluorocholine PET/CT is considered a second-line modality with reported sensitivity up to 95%. Although standard CT generally has limited value in detecting enlarged parathyroid glands, it can provide diagnostic support when first-line imaging is inconclusive or negative, or when alternative imaging techniques are unavailable.

We present a case that highlights the challenges in localizing a parathyroid adenoma in a patient with primary hyperparathyroidism. A 57-year-old woman presented with several years of polyuria (4 L/24 h). Her medical history included obstructive sleep apnoea, hyperlipidaemia, osteopenia, and partial empty sella with normal anterior pituitary function. Laboratory evaluation revealed hypercalcaemia (2.7 mmol/L; ref. 2.1-2.5), normal phosphate (0.8 mmol/L; ref. 0.7-1.4), sufficient 25-hydroxyvitamin D (103 nmol/L), normal renal function (creatinine 59 µmol/L), hypercalciuria (12.2 mmol/24 h; ref. <7.9), and elevated PTH (11.4 pmol/L; ref. 1.6-6.9), confirming primary hyperparathyroidism.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Despite clear biochemical evidence of disease, all standard localization studies were negative, including cervical ultrasound with FNA cytology, [99mTc]Tc-MIBI scintigraphy, and [18F]fluorocholine PET/CT. Finally, a conventional neck CT identified a 16 × 8 mm contrast-enhancing lesion posterior and caudal to the right thyroid lobe, suspicious for an enlarged parathyroid gland. Following FNA confirmation of parathyroid tissue, the patient proceeded to surgery, where an enlarged right superior parathyroid gland was identified, together with additional parathyroid tissue adjacent to the inferior pole of the right thyroid lobe. Both lesions were removed. Histopathology confirmed a right superior parathyroid adenoma (1.5 × 0.7 × 0.4 cm) and incidentally revealed a microadenoma (of the right inferior gland (0.3 cm). Postoperatively, calcium and PTH levels normalized.

This case highlights that, in selected patients with primary hyperparathyroidism, conventional CT—despite historically limited sensitivity—may serve as a valuable adjunct when standard imaging fails to localize pathological glands.

Abstract citation ID: lvag096.857

EP314 - ECE_3852 - Unveiling McCune-Albright syndrome: polyostotic fibrous dysplasia and hyperfunctioning endocrinopathies

Natasha Petrovska[1], Cvetanka Volkanovska Ilijevska[1], Marija Zivkovic[1], Irfan Ahmet[1], Bojan Boskovski[2] and Ivica Kocevski[3]

[1]Diabetes and Metabolic Disorders, PHI University Clinic of Endocrinology, Skopje, North Macedonia; [2]University Clinic of Neurology, Skopje, North Macedonia; [3]PHI University Clinic of Neurosurgery, Skopje, North Macedonia

Introduction: Fibrous Dysplasia (FD) is a disorder characterized by the replacement of bone tissue by fibrous tissue and irregularly distributed bone trabeculae, increasing the risk of pathological fractures. It may impact either a solitary bone (monostotic) or multiple bones (polyostotic; PFD). The proximal femur, ribs, and skull base are the most often affected bones. PFD accompanied by café-au-lait skin pigmentation and hyperfunctioning endocrinopathies is identified as McCune-Albright syndrome (MAS).

Case report: We report a case of a 22-year-old male patient presenting with severe headaches, left eye ptosis, and visual field deficits. He was initially assessed at the neurology clinic. MRI scans showed a pituitary macroadenoma with suprasellar and parasellar extension and abnormally expanded bones of the skull and face. The medical history included pathological fractures of both femurs at age of 12 and several corrective surgeries for subsequent bone bowing. Skeletal radiographs showed multiple lytic lesions in the femur and tibia. A 99mTc-MDP full-body scan demonstrated radiotracer uptake in the appendicular and axial bones. The patient was treated with intravenous bisphosphonates since he was 17 years old; however, confirmatory testing for bone disease was not done. The skeletal investigations were indicative of PFD. The presence of café-au-lait skin pigmentation implied MAS. Hormonal analysis confirmed acromegaly and hypopituitarism. After transcranial surgical decompression treatment with Sandostatin LAR was initiated, however, due to an insufficient therapeutic response, a decision was made to switch to Pasireotide every 28 days. Patient remains under our care for regular follow-ups and monitoring.

Conclusions: MAS is a diagnostic challenge and a delayed diagnosis might result in significant consequences. Screening and early detection of endocrinopathies can improve the quality of life of patients with PFD.

Keywords McCune–Albright syndrome, café au lait macules, fibrous Dysplasia

Abstract citation ID: lvag096.858

EP315 - ECE_1462 - Effectiveness of 4DCT for preoperative parathyroid localization in undetectable parathyroid gland from conventional study in Siriraj Hospital

Anchisa Triphob[1], Pradit Rushatamukayanunt[1], Tanakorn Tarapongpun[1], Mongkol Boonsripitayanon[1], Pongthep Pisarnturakit[1], Suebwong Chuthapisith[1], Benjapa Khiewvan[2], Dittapong Songsaeng[2] and Waraporn Imruetaicharoenchoke[1]

[1]Faculty of Medicine Siriraj Hospital, Mahidol University, Head-Neck and Breast Surgery, Surgery, Bangkok, Thailand; [2]Faculty of Medicine Siriraj Hospital, Diagnostic Radiology, Radiology, Mahidol University, Bangkok, Thailand

Objective: To evaluate the effectiveness of four-dimensional computed tomography (4DCT) for preoperative localization of parathyroid glands in patients whose can't localized by conventional imaging (Tc-99m sestamibi SPECT/CT or parathyroid scintigraphy) and undergoing parathyroid surgery at Siriraj Hospital.

Materials and Methods: This retrospective study included patients diagnosed with primary, secondary, or tertiary hyperparathyroidism between 2013 and 2025 whose parathyroid lesions could not be localized by conventional imaging and underwent 4DCT, parathyroid surgery and follow up at Siriraj Hospital. Concordance between 4DCT localization, intra-operative findings, and pathological results was assessed. Clinical characteristics, surgical outcomes, and enhancement patterns based on Hounsfield unit (HU) measurements were analyzed.

Results: A total of 72 patients with total 85 4DCT detected preoperative localization of parathyroid glands were analyzed. Effectiveness of 4DCT preoperative localization, surgical resection and pathological was truly parathyroid gland were 77 of 85 glands (90.6%). No demographic or clinical patient factors were significantly associated with surgical success or failure, although body mass index $\geq$25 kg/m^2 showed trend toward unsuccessful but non-significant. The only significant factor was imaging predictor of true-positive localization was lower non-contrast HU attenuation. Ectopic glands were identified in 31.8% of cases and no significant associated with Unsuccessful surgery.

Conclusions: In this highly selected cohort with non-pre-operative localization parathyroid gland by conventional imaging, 4DCT demonstrated high clinical effectiveness imaging for pre-operative parathyroid localization. Low HU in non-contrast phase was the only significant imaging factor associated with true-positive localization, while no definitive patient-related predictors of surgical success were identified. These findings support the role of 4DCT as a valuable second-line imaging tool in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

complex hyperparathyroidism case, particularly in resource-limited settings.

Keywords parathyroid, 4DCT, hyperparathyroidism, preoperative localization, re-operative parathyroid surgery

Abstract citation ID: lvag096.859

EP317 - ECE_2403 - Giant parathyroid adenomas mimicking parathyroid carcinoma: a case series

Humera Tabassum[1,2,3], Gowry Reddy[1,2,3], Julie Nguyen[1,2,3], Aleksandra Schriber[1,3] and Karyne Vinales[1,2]
[1]*Endocrinology, University of Arizona College of Medicine, Phoenix, United States;* [2]*Phoenix VA Healthcare System, Phoenix, United States;* [3]*Endocrinology, Medicine, Banner—University Medical Center Phoenix, Phoenix, United States*

Background: Giant parathyroid adenomas, defined as lesions weighing >3.5 g, are rare causes of primary hyperparathyroidism. Their size, biochemical derangements, skeletal involvement, and imaging raise concern for parathyroid carcinoma. Accurate diagnosis requires integration of radiologic, histopathologic, and postoperative biochemical data. Hungry bone syndrome is a recognized complication and may be delayed.

Case Series: We report two cases of severe primary hyperparathyroidism caused by giant parathyroid adenomas with biochemical, radiologic, surgical, and pathologic overlap with malignancy.

Case 1 involved a 32-year-old male presenting with left foot pain and hypercalcemia (14.6 mg/dL). Parathyroid hormone (PTH) peaked at 3019 pg/mL with elevated alkaline phosphatase (867 IU/L). Imaging demonstrated a left parathyroid mass with diffuse skeletal FDG uptake and lytic bone lesions concerning for metastatic disease. En bloc resection of a left superior parathyroid mass with hemithyroidectomy was performed due to adherence to surrounding structures. Histopathology revealed an encapsulated hypercellular parathyroid tumor measuring 3.2 cm and weighing 4.3 g, without atypia or capsular, vascular, or perineural invasion. Ki-67 confirmed a low proliferative index, consistent with a giant parathyroid adenoma. Intraoperative PTH declined from 2146 pg/mL to 190 pg/mL. Postoperatively, the patient developed hungry bone syndrome requiring intravenous and oral calcium and calcitriol. PTH decreased to 118 pg/mL at one week and 83 pg/mL at two weeks, followed by a gradual rise (173-232 pg/mL) with normocalcemia, consistent with postoperative PTH rebound. Left foot pain resolved, and alkaline phosphatase improved to 209 IU/L.

Case 2 A 54-year-old female presented with syncope, polyuria, and polydipsia and was found to have hypercalcemia (14.1 mg/dL), elevated alkaline phosphatase (1199 IU/L), and parathyroid hormone (PTH) exceeding 5000 pg/mL. Imaging demonstrated a right parathyroid mass abutting the posterior pole of the right thyroid lobe, showing tracheoesophageal mass effect. She underwent superior parathyroidectomy with intraoperative PTH decline to 36 pg/mL and postoperative normocalcemia. Pathology revealed a hypercellular adenoma weighing 19.2 g, with no evidence of atypia, increased mitoses, necrosis, or capsular, lymphovascular, or perineural invasion. One month later, she re-presented with hypocalcemia (corrected calcium 5.8 mg/dL), elevated PTH (184 pg/mL), and improving alkaline phosphatase (577 IU/L), consistent with delayed hungry bone syndrome.

Conclusions: PTH elevation, tumor size, mass effect, and skeletal imaging abnormalities do not imply malignancy. Integration of imaging, histopathology, and postoperative PTH trends is essential to distinguish giant parathyroid adenomas from carcinoma. Hungry bone syndrome may be severe or delayed, requiring anticipatory calcium management and biochemical surveillance.

Abstract citation ID: lvag096.860

EP318 - ECE_2495 - Giant parathyroid adenoma unmasked by acute pancreatitis and Osteitis Fibrosa Cystica: a case report

Octavian Alexandrescu[1], Ioana Herghea[1,2], Andrei Muresan[1], Dana Terzea[1], Dana Manda[1], Suzana Vladoiu[1], Sorina Schipor[1], Elena Braha[1] and Madalina Daniela Lucia Musat[1,2]
[1]*C. I. Parhon National Institute of Endocrinology, Bucharest, Romania;* [2]*Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

Introduction: Giant parathyroid adenomas (GPAs), defined as parathyroid adenomas weighing more than 3.5 g, are extremely rare clinical entities (approximately 1.5% of all parathyroid adenomas) and are often associated with severe bone disease, such as osteitis fibrosa cystica (OFC). While their pathogenesis remains unclear, GPA can exhibit both benign and malignant biochemical, histological and molecular features.

Case report: We present the case of a 51-year-old Caucasian woman who experienced left thigh muscle weakness and pain, along with difficulty walking, just several weeks before she was admitted to the intensive care unit with loss of consciousness. She was diagnosed with acute pancreatitis due to severe hyperparathyroidism: total serum calcium 18 mg/dL (4.49 mmol/L), serum intact PTH 1504 pg/mL (reference range: 17.3-74.1 pg/mL) and vitamin D deficiency (serum 25-hydroxyvitamin D: 13.13 ng/mL). Neck CT scan identified a $63 \times 40 \times 23$ mm tumor inferior and posterior to the right thyroid lobe, while left femur X-ray demonstrated a distal cystic lesion consistent with OFC. She underwent right inferior parathyroidectomy and histopathology revealed a giant parathyroid adenoma of $6.3 \times 4.1 \times 2.2$ cm, weighing 32.7 g, without atypical features. Immunohistochemistry showed diffuse positive expression of parafibromin/CDC73 and chromogranin A, and a Ki-67 index of 1% in tumor cells. Postoperatively, PTH levels decreased to 20.41 pg/mL and normal calcium levels were maintained with calcitriol and calcium supplements. However, left femur fracture occurred during hospitalization, requiring further orthopedic surgery.

Discussion: Although molecular studies of atypical parathyroid tumors have demonstrated several somatic mutations in cell-cycle control genes, such molecular signatures account for only a small fraction of GPAs. Next-generation sequencing (NGS) for germline and somatic mutations in MEN1, CDC73, VDR and CASR is pending. More likely, coexistent vitamin D deficiency contributed to the giant adenoma and OFC in this case, as the inverse relationship between parathyroid adenoma weight and serum 25-hydroxyvitamin D level was confirmed in a larger number of patients from different parts of the world (Rao DS et al).

Conclusions: This case is remarkable for several reasons: (1) acute pancreatitis that has unmasked the diagnosis of hyperparathyroidism, (2) giant parathyroid adenoma without atypical features coexisted with vitamin D deficiency and (3) OFC

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

complicated by femoral fracture, an otherwise rare occurrence in contemporary hyperparathyroidism.

Abstract citation ID: lvag096.861

EP319 - ECE_2847 - A patient Familial Hypocalciuric Hypercalcaemia (FHH) presenting with moderate hypercalcaemia

Ishara Ranathunga, Chandima Idampitiya and Fathima Pambinezhut
Endocrinology, North Cumbria University Hospitals Nhs Trust—Carlisle Library, Carlisle, United Kingdom

Background: Familial hypocalciuric hypercalcaemia (FHH) is a rare inherited disorder of calcium homeostasis, most commonly caused by inactivating variants of the calcium-sensing receptor (CaSR) gene. It is characterised by lifelong, usually asymptomatic hypercalcaemia, inappropriately normal or mildly elevated parathyroid hormone (PTH) levels, and low urinary calcium excretion. The condition can closely mimic primary hyperparathyroidism (PHPT), and failure to distinguish between the two may result in unnecessary investigations or parathyroid surgery.

Case presentation: A 69-year-old gentleman with persistent hypercalcaemia for 11 years was referred for further evaluation. He had a history of depression and type 2 diabetes. The patient reported long-standing polyuria with normal thirst. There was no history of nephrolithiasis, fractures, skeletal symptoms or known family history of hypercalcaemia. Examination revealed mildly elevated blood pressure but was otherwise unremarkable. Investigations were consistent with elevated adjusted serum calcium levels, with a highest value of 3.09 mmol/L. Serum phosphate levels were within the normal range and PTH levels were inappropriately normal in the context of hypercalcaemia. Vitamin D and renal function were normal. Twenty-four-hour urinary calcium excretion was low at 1.3 mmol/24 h, and fractional excretion of calcium was markedly low at 0.003, strongly suggestive of FHH. Genetic testing subsequently confirmed a pathogenic variant consistent with Familial Hypocalciuric Hypercalcaemia Type 1 (FHH1). A dual-energy X-ray absorptiometry scan and ultrasound urinary tract was arranged as part of baseline assessment.

Discussion: This case emphasises the diagnostic complexity of FHH, particularly in a symptomatic patient when serum calcium concentrations are higher than typically expected. Reliance on serum calcium and PTH levels alone may be misleading, highlighting the importance of fractional calcium excretion. Particularly in patients with acceptable vitamin D levels and retained renal function, a significantly lower fractional excretion of calcium continues to be a crucial differentiator between FHH and PHPT. Although FHH is generally asymptomatic and benign, patients may present with non-specific symptoms such as polyuria or neuropsychiatric complaints, which further complicate clinical assessment. In addition to providing a precise diagnosis, genetic confirmation has consequences for long-term care, counselling, and family screening. Importantly, parathyroidectomy is ineffective in FHH and should be avoided, highlighting the clinical significance of early and accurate diagnosis.

Conclusions: FHH should be considered even in symptomatic patients with longstanding moderate hypercalcaemia. Early recognition and genetic confirmation can prevent unnecessary interventions and ensure appropriate counselling and follow-up.

Abstract citation ID: lvag096.862

EP320 - ECE_2901 - Palopegteriparatide treatment for chronic hypoparathyroidism: a report of three cases

Karmelo Lovric[1], Anja Barac Nekic[2], Karin Zibar Tomsic[2] and Ivana Kraljevic[2,3]
[1]*Department of Endocrinology, General Hospital "Dr. Ivo Pedisic" Sisak, Sisak, Croatia;* [2]*Zagreb, Croatia;* [3]*School of Medicine, University of Zagreb, Zagreb, Croatia*

Background: Chronic hypoparathyroidism (HypoPT) may be associated with persistent hypocalcaemic symptoms and a high treatment burden despite conventional therapy with oral calcium and active vitamin D.

Case presentation: We report three patients with chronic HypoPT (two postsurgical, aged 60 and 70 years, and one autoimmune, aged 40 years) with recurrent symptoms of hypocalcaemia, including paresthesias and muscle cramps, despite long-term intensive conventional treatment. Prior to parathyroid hormone replacement, all patients required high daily doses of oral calcium and calcitriol yet remained incompletely biochemically controlled. Two patients presented with electrolyte instability (total calcium 1.3 and 1.86 mmol/L; phosphate 1.81 and 1.77 mmol/L, respectively); one of them had impaired renal function, while the third patient developed malabsorption following jejunostomy placement.

Results: Following initiation of palopegteriparatide therapy, two patients showed normalisation of serum calcium and phosphate concentrations within the first week of treatment, allowing withdrawal of oral calcium and active vitamin D supplementation. The third patient, previously treated with teriparatide, resulting in more stable calcium concentrations and reduced supplementation requirements, was recently transitioned to palopegteriparatide. Across all patients, hypocalcaemic symptoms were no longer reported during follow-up. No treatment-related adverse events were observed. Renal function improved in a patient who had pre-existing impairment.

Conclusions: This case series illustrates the clinical limitations of conventional therapy in chronic HypoPT and shows that parathyroid hormone replacement may facilitate biochemical stabilization and reduction of treatment burden in selected patients.

Abstract citation ID: lvag096.863

EP323 - ECE_3853 - An unusual presentation of primary hyperparathyroidism: a reversible cause of acute psychiatric symptoms

Marta Almeida, Miguel Marques, Daniel Duarte, Francisca H., Ricardo Capitão and Maria Carlos Cordeiro
Unidade Local de Saúde de Almada-Seixal, Almada, Portugal

Background: Primary hyperparathyroidism (PHPT) may present with neuropsychiatric manifestations, particularly in elderly patients, and can mimic primary psychiatric disorders, potentially delaying diagnosis.

Case presentation: We report the case of a 73-year-old woman with stage G3b chronic kidney disease and a solitary kidney.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

One month prior to admission, she developed new-onset psychiatric symptoms characterized by anxiety and depressive features. She was evaluated by her primary care physician and a psychiatrist, and psychiatric medication was initiated and titrated (benzodiazepines followed by venlafaxine). Despite treatment, the patient experienced progressive cognitive and behavioural deterioration in the weeks preceding hospitalization, including disorientation, confabulation, visual hallucinations, and persecutory delusions. She denied systemic, infectious, or focal neurological symptoms. Physical examination on admission was unremarkable.

Initial laboratory evaluation revealed acute-on-chronic kidney injury (creatinine 2.2 mg/dL; eGFR 22 mL/min/1.73 m^2) and hypoalbuminemia (3.1 g/dL), and no elevation of inflammatory markers. Further investigation prompted by persistent confusional symptoms demonstrated severe hypercalcemia (corrected calcium 13.4 mg/dL) with markedly elevated parathyroid hormone (PTH 886 pg/mL), hypophosphatemia (1.9 mg/dL), and hypomagnesemia (1.3 mg/dL), establishing the diagnosis of PHPT. The patient received aggressive intravenous hydration, resulting in improved renal function and partial correction of hypercalcemia. Bisphosphonates were avoided due to CKD. Cinacalcet was initiated at 30 mg twice daily with biochemical improvement. Localization studies identified a 4 cm right inferior parathyroid lesion on 4D-CT with delayed washout on scintigraphy. Given surgical criteria including symptomatic severe hypercalcemia (>1 mg/dL above upper normal limit), hypercalciuria, and CKD, parathyroidectomy was performed. Intraoperative PTH monitoring demonstrated an appropriate decline from 628 pg/mL preoperatively to 129 pg/mL (79% reduction), predicting surgical success. Histopathology confirmed a parathyroid adenoma. Postoperatively, calcium and PTH levels normalized with complete resolution of neuropsychiatric symptoms. At one-year follow-up, calcium levels remain controlled.

Conclusions: This case highlights PHPT as a reversible cause of acute confusional and psychiatric symptoms in elderly patients. Despite specialist psychiatric evaluation and treatment, the underlying metabolic disorder was initially missed. Serum calcium measurement should be included in the initial metabolic evaluation of new-onset neuropsychiatric presentations, particularly in older adults, to avoid diagnostic delay of this treatable condition.

Abstract citation ID: lvag096.864

EP324 - ECE_1196 - Bone loss after high-dose glucocorticoid therapy in patients with non-idiopathic pulmonary fibrosis interstitial lung disease

Jeeyeun Hwang, Junghae Ko and Mikyung Kim
Internal Medicine, Inje University Haeundae Paik Hospital, Inje University College of Medicine, Busan, South Korea

Background: Interstitial lung disease (ILD) patients often require high-dose steroids, increasing osteoporosis risk. However, data on bone mineral density (BMD) changes in ILD patients from Asian populations, particularly Korea, are scarce. We aimed to evaluate longitudinal changes in BMD, body composition, and bone metabolic markers in a Korean ILD cohort before and after glucocorticoid therapy.

Methods: Eligible participants were ILD patients treated with prednisolone ≥5 mg/day for at least 3 months during the study period (August 2020 to August 2021). BMD was measured at baseline and 12 months. Body composition, bone metabolic markers were measured at baseline, 6 months, and 12 months. BMD changes were analyzed using paired t-tests or Wilcoxon signed-rank tests, and repeated-measures ANOVA was used for body composition and bone metabolic markers.

Results: Non-Idiopathic pulmonary fibrosis ILD patients ($n = 18$) were analyzed. BMD at the lumbar spine, femoral neck, and total hip decreased by 4.3%, 2.0%, and 1.8% (all $P < .05$). Body weight and muscle mass showed no change, whereas body fat percentage increased from 31.6% to 34.9% ($P < .001$). Vitamin D deficiency was 61% (67% men, 58% women).

Conclusions: In this Korean ILD cohort, glucocorticoids induce rapid, lumbar-predominant bone loss. Fat gain with preserved body weight cannot be detected without body composition assessment. The high prevalence of vitamin D deficiency, especially in men, remain a concern in Korean patients with ILD.

Abstract citation ID: lvag096.865

EP325 - ECE_1260 - Two-year outcomes in an adult with x-linked familial hypophosphatemia treated with burosumab

Maria Ponte, Andreia Pataco, Regina Medeiros, Ana Figueiredo, Carolina Chaves, Catarina Senra, Isabel Sousa, João Anselmo and Bernardo Gago Da Câmara Dias Pereira
Ponta Delgada, Portugal

Introduction: X-linked hypophosphatemia (XLH) is a rare disorder caused by inactivating mutations in the phosphate-regulating endopeptidase X-Linked (PHEX) gene, leading to increased serum fibroblast growth factor 23 (FGF23). Elevated FGF23 reduces renal tubular phosphate reabsorption (TmP/GFR), resulting in chronic hypophosphatemia and impaired skeletal mineralization. Burosumab, a new monoclonal antibody that targets FGF23, has demonstrated biochemical, radiographic and functional improvement in children with XLH, but long-term data in adults is still scarce. We report the outcomes of a 54-year-old woman with XLH after 2 years of burosumab therapy.

Case report: A 44 years-old female was referred to the Endocrinology consultation due to hypophosphatemic rickets. She had a medical history since her 3 years old of progressive lower limbs deformities, gait impairment, and growth deceleration, which resulted in severe short stature (-4SD). She also started presenting paresthesia, generalized bone pain and recurrent dental caries. She started cholecalciferol at 6 years old. Adult height was 136 cm, and she subsequently underwent 20 limb-lengthening surgeries, achieving 146 cm. A low-trauma femoral fracture occurred at the age of 26 and evolved into hypertrophic pseudarthrosis. Progressive functional decline resulted in premature retirement. At Endocrinology appointment hypophosphatemia, inappropriately high 1.,25-dihydroxyvitamin D and a TmP/GFR of 2.1 mg/dL (2.6-3.8) were found. Dual X-ray absorptiometry demonstrated a T-score of −3.2SD at the radius, and 1.7 SD to 2.7SD at the lumbar spine. Cholecalciferol was substituted by calcitriol (0.75 mcg/day). Genetic testing identified a heterozygous nonsense variant in PHEX (c.1699C > T,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

p.Arg567*). At age 52, burosumab 60 mg monthly was initiated and calcitriol was discontinued. Biochemical improvement was evident at month 3: serum phosphate increased from 2.1 to 2.7 mg/dL (2.5-4.9) and TmP/GFR to 2.7 mg/dL. The Brief Pain Inventory also demonstrated clinical benefit by the third month, with a reduction in average pain intensity from 6/10 to 2/10. Progressive improvement continued throughout the two-year treatment period. The intensity of the worst pain decreased from 8/10 to 3/10, interference of pain with gait from 9/10 to 5/10, and impact on overall daily activity from 7/10 to 2/10. She formerly relied on crutches for most of her ambulation and is now capable of walking short distances unaided. The hypertrophic pseudarthrosis achieved complete radiographic healing after one year of burosumab therapy.

Discussion: This case illustrates the substantial benefit of starting burosumab in adults with long-standing XLH, allowing normalization of phosphate homeostasis and significant pain and functional improvement.

Abstract citation ID: lvag096.866

EP327 - ECE_3712 - Paget's disease of bone: differential diagnosis of a bone lesion suspicious of osteosarcoma

Nektarios Adamopoulos[1], Grigoris Effraimidis[1,2], Maria Apostolopoulou[1,2], Athanasios Kasotas[1], Dionysios Vrachnis[1], Maria Galani[1], Eleni Georgiou[1], Ioannis Gkountios[1], Anastasia-Konstantina Sakali[1] and Alexandra Bargiota[1,2]

[1]Department of Endocrinology and Metabolic Diseases, University General Hospital of Larissa, Larissa, Greece; [2]Faculty of Medicine, Department of Endocrinology and Metabolic Diseases, School of Health Sciences, University of Thessaly, Larissa, Greece

Introduction: Paget's disease of bone (PDB) is a chronic focal disorder of bone remodeling, often asymptomatic and usually is detected incidentally by elevated alkaline phosphatase (ALP) levels. Rarely benign pagetic lesions with atypical imaging features need to be distinguised from secondary osteosarcoma.

Case: A 63-year-old female patient was referred for evaluation of asymptomatic elevated alkaline phosphatase (ALP) levels, identified on routine laboratory testing. The patient reported progressive sensorineural hearing loss and further work up revealed disproportionately elevated bone—specific ALP, increased Procollagen Type I N-terminal Propeptide (PINP) and Beta-CrossLaps (β-CTX) and radiographic findings consistent with PDB such as mixed osteolytic and osteosclerotic changes of the long bones, a "picture-frame" vertebrae in the lumbar spine, osteosclerotic and osteolytic areas in the pelvis and hip. Bone scintigraphy showed an increased uptake in typical pagetic sites, but also a focal osteoblastic activity at the distal part of the right humerus with extension into adjacent soft tissues raising the suspicion of osteosarcoma. Subsequent cross—sectional imaging of this lesion with a CT and an MRI was non-diagnostic. A CT-guided bone biopsy was performed and the histological findings were typical pagetic bone changes with a mosaic pattern of "irregular cement lines", osteoblastic "rimming" at various spots and the presence of several multinuclear osteoclasts forming a pattern of focal "bite" mark. No histological findings compatible with osteosarcoma were present.

Discussion: Atypical presentation of PDB could be confusing and diagnostically challenging. As in rare cases a malignant transformation to osteosarcoma can be seen. The lifetime risk is low (≤1%), but still much higher compared to the general population and is usually observed in older adults with long standing, metabolically active disease. New focal pain, swelling, or presence of a destructive lytic lesion within a pagetic bone should raise suspicion for Pagetic osteosarcoma, which has a poor prognosis. Multidisciplinary collaboration among internists, radiologists, nuclear medicine physicians, and pathologists is essential for accurate diagnosis and optimal management for PDB.

Abstract citation ID: lvag096.867

EP328 - ECE_3858 - Rare case of secondary hyperparathyroidism as a manifestation of Celiac disease

Ana Pruidze[1], Tea Khurodze[2,3], Elisabed Pkhaladze[1], Vitali Vashakidze[1,4], Basa Gegeshidze[1,5] and Mariam Tevzadze[6]

[1]David Tvildiani Medical University, Tbilisi, Georgia; [2]David Tvildiani Medical Univeristy, Tbilisi, Georgia; [3]Medical House, Tbilisi, Georgia; [4]Gagua Clinic, Tbilisi, Georgia; [5]Caucasus Medical Center, Tbilisi, Georgia; [6]Tbilisi, Georgia

Background: Secondary hyperparathyroidism (SHPT) is a condition in which the parathyroid glands produce excessive amounts of hormone in response to severe hypocalcemia, rather than due to intrinsic parathyroid disease. The combination of hyperparathyroidism and severe osteoporosis in advanced age is frequently associated with parathyroid adenomas. Celiac disease represents a key underlying condition in which both of these endocrine disorders may occur simultaneously. Mainly this disease is associated with gastrointestinal symptoms, but also presents with extraintestinal manifestations, in adults this diagnosis may be delayed. Disturbances in calcium–phosphate homeostasis are a recognized consequence of chronic intestinal malabsorption, which causes parathormone elevation.

Case presentation: A 58-year-old woman presented to our clinic with severe back pain and a history of multiple recurrent fractures, the most recent involving the ribs. Bone densitometry conducted at our clinic demonstrated high-grade osteoporosis. Comprehensive laboratory investigations performed prior to initiation of therapy demonstrated elevated PTH levels, reduced urinary and serum calcium excretion, normal serum phosphorus concentrations, low levels of corrected calcium, severe vitamin D_3 deficiency, and evidence of hypothyroidism. On ultrasound, multiple thyroid nodules were revealed. Further diagnostic investigations were initiated to exclude the presence of a parathyroid adenoma, kidney dysfunction, and malabsorption syndrome. Repeated parathyroid scintigraphy performed on two separate occasions consistently revealed no scintigraphic evidence of adenoma. Laboratory and ultrasonographic evaluations excluded renal dysfunction and nephrolithiasis. Following consultation with a gastroenterologist,further invasive and laboratory studies were indicated. Laboratory investigations demonstrated markedly elevated tTG-IgA and significantly increased chromogranin

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

A levels. After serological confirmation of Celiac disease, duodenal endoscopy with biopsy was conducted, revealing histopathological evidence of villous atrophy. After correcting calcium and vitamin D3 levels with targeted supplementation and initiating a gluten-free diet, the patient was started on anti-osteoporotic therapy.

Conclusions: In patients with hyperparathyroidism and osteoporosis, this case emphasizes the need to consider secondary causes, including systemic conditions like malabsorption, that may drive persistent elevation of parathyroid hormone. Early recognition and management—including a gluten-free diet, supplementation, and appropriate osteoporosis therapy—are essential to prevent further bone complications and improve patient outcomes.

Abstract citation ID: lvag096.868

EP331 - ECE_2704 - Late diagnosis of X-linked hypophosphatemic rickets in an adult: clinical case and experience with burosumab therapy

Alina Alzhaxina, Kristina Baikadamova and Aigul Durmanova
University Medical Center, Astana, Kazakhstan

Introduction: X-linked hypophosphataemic rickets (XLH) is a rare hereditary disease caused by pathogenic mutations in the PHEX gene. It causes chronic hypophosphataemia and abnormal mineralisation of the bones, resulting in progressive skeletal deformity. XLH can be diagnosed in affected individuals early in the course of their disease. However, in some patients, diagnosis is delayed until adulthood, leading to poor functional outcomes.

Case presentation: We present a 23-year-old male patient with severe skeletal deformities, inability to walk independently, chronic lower limb pain, joint contractures, short stature, and premature tooth loss. Symptoms had been present since birth. During childhood, the patient was repeatedly treated for nutritional rickets without any clinical improvement. On physical examination: height—132 cm, body weight—54 kg, marked deformities of the upper and lower limbs, bilateral genu valgum, thoracic scoliosis, and severe functional limitation were observed, requiring wheelchair assistance. The patient had persistent hypophosphataemia (0.61-0.77 mmol/L), normal total serum calcium levels (2.23-2.32 mmol/L) and slightly decreased vitamin D levels (29.4 ng/mL). Alkaline phosphatase activity (ALP) was elevated (266-284 U/L). Whole-exome sequencing revealed a hemizygous pathogenic nonsense mutation (c.500G > A, p.Trp167Ter) in the PHEX gene. Brain MRI showed a congenital hydrocephalus and Arnold-Chiari malformation, type I. Renal ultrasound revealed no dilation of the upper urinary tract, and eGFR was 157.7 mL/min, confirming preserved kidney function.

Results: The patient started burosumab therapy-1.3 mg/kg subcutaneously every 4 weeks.

After starting burosumab, serum phosphate steadily rose from 0.61-0.70 mmol/L to 0.81 mmol/L, while ALP activity was trending downward. The serum calcium levels and the renal function have remain stable within the normal range. The patient reported an improvement in overall well-being and significant pain reduction. No adverse effects were noted.

Discussion: X-linked hypophosphatemic rickets (XLH) remains a diagnostic and therapeutic challenge due to its rarity and variable clinical presentation. Delayed recognition often leads to irreversible skeletal deformities and functional limitations. The introduction of burosumab has changed the treatment paradigm by directly targeting the underlying pathophysiology of phosphate wasting. This case contributes to the growing clinical experience demonstrating the importance of timely diagnosis and access to targeted therapies in improving long-term outcomes for patients with XLH.

Conclusions: Burosumab provides significant biochemical and clinical benefits in patients with severe phenotype of XLH in adults. Additional studies are needed to further study the effects of burosumab and optimal use in the management of adult XLH.

Abstract citation ID: lvag096.869

EP332 - ECE_3864 - Management of hypoparathyroidism in a patient with Fabry disease and advanced chronic kidney disease: a case report on the use of palopegteriparatide

Georgios Kostopoulos, Evangelia Makri, Athanasios Panagiotou and Foteini Adamidou
Endocrinology, Hippokration General Hospital, Thessaloniki, Greece

Background: The concurrence of chronic hypoparathyroidism and severe chronic kidney disease (CKD; estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2) is rare. Palopegteriparatide has been used as replacement therapy for chronic hypoparathyroidism in Europe since its approval in 2023. However, it has not been studied in patients with advanced CKD. We present a case of postsurgical hypoparathyroidism in a patient with Fabry's disease and advanced CKD post-kidney transplantation, treated with palopegteriparatide.

Case presentation: A 59-year-old man with Fabry disease and a history of kidney transplantation with suboptimal graft function (eGFR 22 mL/min/1.73 m^2) was referred for management of chronic hypoparathyroidism. He had previously undergone total thyroidectomy and subtotal parathyroidectomy for multinodular goiter and parathyroid hyperplasia, respectively. Despite treatment with calcium carbonate (4.5 g/day), sevelamer carbonate (2.7 g/day), cholecalciferol (25000IU weekly) and alfacalcidol 1 mcg daily, biochemical evaluation revealed persistent hypocalcaemia (corrected serum calcium 6.8 mg/dL), hyperphosphataemia (serum phosphate 7.1 mg/dL), inappropriately normal PTH levels (27.7 pg/mL), magnesium 3 mg/dl, and 25-hydroxy-vitamin-D 60 ng/ml. Given inadequate biochemical control, high pill burden, and limited therapeutic options due to CKD, initiation of palopegteriparatide at a starting dose of 18 μg/day was undertaken. The patient achieved eucalcemia within ten days (corrected calcium 9.5 mg/dl) and phosphate levels dropped to 5.8-5.1 mg/dl), allowing discontinuation of alfacalcidol and phosphate binders, followed by calcium supplements eight weeks later. Palopegteriparatide dose remained at 18 μg/day and eGFR stabilized at around 25 mL/min/1.73 m^2 over the next four months of follow-up.

Conclusions: This case highlights that palopegteriparatide may be an effective and well-tolerated therapeutic option in select patients with hypoparathyroidism and advanced CKD when conventional therapy fails.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.870

EP334 - ECE_1682 - Complexities in the management of multiple endocrine neoplasia syndrome type 1

Tatsiana Mokhort[1], Alena Khilko[2], Natalia Likharad[3] and Alena Atlivanchik[4]
[1]Endocrinology, Belarusian State Medical University, Minsk, Belarus; [2]Belarusian State Medical University, Minsk, Belarus; [3]1 Minsk City Hospital, Minsk, Belarus; [4]Minsk City Clinical Endocrinological Center, Minsk, Belarus

Introduction: Multiple endocrine neoplasia syndrome type 1 (MEN 1) is a group of heterogeneous inherited diseases, caused by hyperplasia or neoplastic transformation of several endocrine glands and characterized by variable combinations of endocrine disorders.

Results: Women, 45 y.o., was examined for newly registered episodes of hypoglycemia up to 1.9 mmol/L and hyperinsulinemia. According to imaging data, a mass measuring 43*52*48 mm was detected in the body of the pancreas, and a mass up to 1.7*1.1 cm with a density of up to 11 HU was detected in the left adrenal gland. Total gastro-pancreaticduodenal resection with splenectomy and cholecystectomy, left-sided adrenalectomy (morphologically—gastric and pancreatic NET's) was performed, after which malabsorption syndrome, pancreatogenic diabetes and hypercalcemia developed. Dominant parathyroid gland (left upper) and signs of activity of the remaining parathyroid glands were revealed after scintigraphy of the parathyroid gland (PTG) with pertechnetate (Tc-99m). After removal of the dominant parathyroid gland the patient continued to have malabsorption syndrome, despite the use of enzymatic drug. Genetic testing revealed a heterozygous variant (chr11: g.64804740dup, NM_001370259.2:c.1429dup, rs886041214) in exon 10 (out of 10) of the MEN1 gene, known in the literature as 1539insG. Hypercalcemia and elevated PTH levels persist. A family history includes the presence of NETs in 1st and 2nd degree relatives. Taking into account the patient's family history and the presence of genetically confirmed MEN 1 syndrome, surgical treatment with removal of active parathyroid glands and genetic testing of children are recommended.

Conclusions: One of the key issues in the management of MEN 1 is the choice of extent of surgery which is determined not only by the tumor size, invasion, and malignancy potential, but also by the presence of nonfunctioning gastroenteropancreatic NET's and manifestations of hyperparathyroidism.

Abstract citation ID: lvag096.871

EP336 - ECE_3735 - Hypopituitarism: a new risk factor for mineral and bone pathology

Miruna-Viorela Nacu[1], Oana Maria Teodora Georgescu[1], Sorina Martin[1,2], Anca Sirbu[1,2] and Carmen Barbu[1,2]
[1]Endocrinology, Diabetes Mellitus, Nutrition and Metabolic Diseases, Elias Emergency University Hospital, Bucharest, Romania; [2]Endocrinology, Diabetes Mellitus, Nutrition and Metabolic Diseases, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Neuroendocrinology of bone is an emerging domain exploring the direct impact of pituitary hormones on bone metabolism. Studies assessing bone health in patients with pituitary hyper or hypofunction are the cornerstone of understanding the in vivo effects of these hormonal disturbances. Data from clinical studies in patients with hypopituitarism are scarce and extremely heterogenous given the intricate complexities of this pathology and lack of objective biomarkers of adequate hormonal substitution. Herein we explore the relationship between hypopituitarism and bone metabolism.**Methods:** We performed a retrospective observational study between 2010-2024 in a tertiary endocrinology center with the aim of characterizing mineral and bone metabolism among patients with hypopituitarism (defined as deficiency in one or more pituitary axes).

Results: Sixty patients with hypopituitarism were included, mean age at diagnosis was 49.22 ± 17.11 years, 63.3% of them were women. In 36 cases, the etiology was a pituitary adenoma (83.34% macroadenomas). Using T-scores, 19 patients had osteopenia and 5 osteoporosis. In premenopausal women and men below 50 years, using Z-scores, 11 had low bone mineral density (BMD) for age and sex. Younger age at diagnosis was associated with lower BMD at lumbar spine ($P = .002$). 18 patients had low IGF1 levels matched for age and sex (median 76.73 ng/ml, IQR = 95.6) and these were positively correlated with serum levels of calcium ($P = .014$) and phosphate ($P = .033$), but not with BMD nor TBS (trabecular bone score). 80% of patients had central gonadal insufficiency. Testosterone levels were strongly significantly correlated with BMD at lumbar spine ($P = .008$). 60% of patients had central thyroid insufficiency (CTI), and 51.67% patients had central adrenal insufficiency (CAI). Patients with CTI were more likely to associate CAI ($P = .004$). FreeT4 levels had a median value of 1.09 ng/dl (IQR = 0.30) and were negatively correlated with BMD at lumbar spine ($P = .026$) and hip ($P = .003$) but not with TBS ($P = .355$). In our dataset, patients with thyroid insufficiency had lower levels of serum phosphate ($P = .004$) and alkaline phosphatase ($P = .021$), and higher levels of PTH ($P = .013$), BMD at lumbar spine and TBS, suggesting a possible low bone turnover state, with a possible compensatory rise in PTH. Patients with CAI also showed the same statistical significant associations but only for PTH levels and TBS.

Conclusions: More studies are needed to understand the mechanisms behind bone modeling and remodeling and their connection with pituitary hormones. First of all, awareness should be made among clinicians that hypopituitarism may be associated with disturbances in bone metabolism.

Abstract citation ID: lvag096.872

EP337 - ECE_1648 - Challenging hypoparathyroidism: two cases of poorly controlled disease

Carla Columbu, Alfredo Scillitani, Flavia Pugliese, Claudia Battista and Vito Guarnieri
Fondazione Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy

Background: Hypoparathyroidism is a rare endocrine disorder characterized by hypocalcemia and low parathyroid hormone (PTH) levels. Conventional therapy with oral calcium and active vitamin D is often biochemically effective; however, disease management can be challenging in specific clinical settings such as postsurgical hypoparathyroidism, long-standing idiopathic forms, and during pregnancy or lactation. In these contexts, calcium homeostasis may be highly unstable, resulting in recurrent

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

symptomatic hypo- or hypercalcemia along with a poor quality of life.

We report two cases of severe and poorly controlled hypoparathyroidism that required careful and individualized clinical management.

Case presentations: Case 1

A 63-year-old woman, with type 2 diabetes mellitus and arterial hypertension, developed severe postsurgical hypoparathyroidism following combined total thyroidectomy and parathyroidectomy performed for multinodular goiter and primary hyperparathyroidism. Her medical history was also notable for breast cancer, previously treated with quadrantectomy and she was still receiving aromatase inhibitor therapy. Two weeks after surgery, she presented to Emergency Department with symptomatic hypocalcemia (serum calcium albumin-adjusted 5.9 mg/dL), associated with neuromuscular irritability, dysphagia with progressive paresthesia, despite oral supplementation with calcium carbonate (1 g twice daily) and calcitriol (0.25 μg twice daily). Due to the persistence of severe hypocalcemia despite the progressive increase of conventional therapy, and despite patient's history of breast cancer, treatment with teriparatide 20 mcg/die started with complete resolution of symptom and progressive normalization of serum calcium levels.

Case 2

The second case involves a 29-year-old woman with long-standing idiopathic hypoparathyroidism, diagnosed in childhood following tetanic seizures that were misdiagnosed as epilepsy. Her clinical course was characterized by extreme variability of serum calcium levels, with recurrent episodes of symptomatic hypo- and hypercalcemia despite multiple adjustments of therapy with calcium, calcitriol and thiazides. She was referred to our Endocrinology Unit for severe hypercalcemia (serum calcium 16 mg/dL) occurring one month after delivery, during lactation. After withdrawal of therapy, eucalcemia was reached throughout the entire breastfeeding period. After cessation of lactation, the patient rapidly developed symptomatic hypocalcemia. Conventional therapy was reintroduced but for persistent serum calcium instability and increasing therapeutic requirements, treatment with recombinant human PTH (1-84) started, resulting in improved clinical and biochemical control.

Conclusions: These cases underscore the complexity of managing hypoparathyroidism in high-risk clinical scenarios. PTH analog therapy offers a valuable treatment option for patients with poorly controlled disease, improving biochemical picture and reducing symptom burden.

Abstract citation ID: lvag096.873

EP339 - ECE_2615 - Alternative treatment of hypercalcaemia caused by primary hyperparathyroidism: a clinical case of parathyroid cryoablation

Erika Bukelytė[1], Aurimas Mačionis[2], Aistė Kondrotienė[3], Diana Šimonienė[3], Rūta Dubeikaitė[2] and Birutė Žilaitienė[3]
[1]Faculty of Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Department of Radiology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [3]Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania

Introduction: The management of severe hypercalcaemia in patients with advanced chronic kidney disease and active malignancy is challenging, as standard pharmacological and surgical treatment options are often limited or contraindicated. In such cases, minimally invasive interventional techniques may represent an alternative therapeutic option; however, data on their use remain scarce.

Case presentation: An 80-year-old female with stage IV chronic kidney disease and active lung malignancy was hospitalised due to severe hypercalcaemia. Laboratory investigations revealed hypercalcaemia (3,19 mmol/L), hypokalaemia (3,37 mmol/L), hypomagnesaemia (0,67 mmol/L), hypophosphatemia (0,51 mmol/L), and agranulocytosis. The patient was immunosuppressed due to ongoing chemotherapy. Agranulocytosis was corrected with filgrastim, and hypercalcaemia was initially treated with intensive intravenous hydration and loop diuretics, alongside correction of electrolyte disturbances. Neck ultrasound demonstrated an enlarged left inferior parathyroid gland. Due to impaired renal function, zoledronic acid was contraindicated. After consultation with an interventional radiologist and fine-needle aspiration of the parathyroid lesion, markedly elevated parathyroid hormone (PTH) levels were detected in the aspirate (210,6 pmol/L), confirming the diagnosis of a parathyroid adenoma. Given the minimal cystic component and high vascularity of the lesion, ethanol ablation was considered unlikely to be effective. Parathyroid cryoablation was therefore performed under ultrasound guidance and general endotracheal anaesthesia. Post-procedural neck computed tomography revealed no acute complications. A rapid and pronounced biochemical response was observed, with PTH levels decreasing to 1,36 pmol/L on the first day and to 0,4 pmol/L on the second day after the procedure. Serum phosphate levels showed no significant change (0,89 mmol/L). Serum calcium levels gradually decreased to 2,7 mmol/L, and treatment with alfacalcidol (0,5 μg/day) and calcium carbonate (3 g/day) was initiated. The doses were subsequently increased to alfacalcidol 0,75 μg/day and calcium carbonate 4 g/day, achieving normocalcaemia and normophosphataemia. Following discontinuation of intensive hypercalcaemia treatment with intravenous fluids and diuretics, a transient deterioration in renal function was observed (serum creatinine 190 μmol/L). Renal function improved with renewed intensive hydration, with creatinine decreasing to 149 μmol/L. The patient continues follow-up under endocrinological care.

Conclusions: Parathyroid cryoablation may represent an effective and safe alternative for the treatment of severe hypercalcaemia in patients with primary hyperparathyroidism when surgical or standard pharmacological therapies are contraindicated. This case highlights the importance of individualised decision-making and a multidisciplinary approach in complex clinical scenarios

Abstract citation ID: lvag096.874

EP345 - ECE_3879 - Intrathyroidal parathyroid adenoma mimicking thyroid nodules: a diagnostic challenge

Elisabed Pkhaladze[1], Tea Khurodze[2,3], Vitali Vashakidze[1,4], Ana Pruidze[1], Basa Gegeshidze[1,5] and Mariam Tevzadze[6]
[1]David Tvildiani Medical University, Tbilisi, Georgia; [2]Endocrinology, David Tvildiani Medical University, Tbilisi, Georgia; [3]Endocrinology, Medical House, Tbilisi, Georgia; [4]OB/GYN, Gagua Clinic, Tbilisi, Georgia; [5]Radiology, Caucasus Medical Centre, Tbilisi, Georgia; [6]Tbilisi, Georgia

Background: The management of thyroid and parathyroid dysfunction in geriatric patients is associated with distinct clinical

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

challenges that require careful therapeutic consideration. Conditions like parathyroid disorders and multinodular goiter can contribute to osteoporosis, particularly in older adults, especially postmenopausal women, which increases the risk of skeletal fragility and fractures. The interplay between thyroid function, calcium metabolism, and bone health is crucial, necessitating comprehensive diagnostic evaluation, careful surgical intervention, and effective postoperative management.

Case presentation: A 78-year-old female was diagnosed with a multinodular goiter 2-3 years ago and was treated with 5 mg of methimazole daily for 12 months, achieving a euthyroid state. She also underwent a DEXA scan 1 year ago that revealed a high degree of osteoporosis, particularly in the left forearm, for which she was prescribed denosumab. The past medical history was significant for arrhythmia and arterial hypertension, which were managed by bisoprolol and captopril symptomatically. Surgical history includes tonsillectomy. Social history was notable for tobacco use and a sedentary lifestyle. The assessments showed the presence of negative TSH receptor antibodies, significantly elevated LDL cholesterol levels, and high calcium, which raised concerns about primary hyperparathyroidism in the context of severe osteoporosis. A SPECT/CT scan later confirmed the existence of bilateral intrathyroidal parathyroid adenomas. The patient underwent a total thyroidectomy and subtotal parathyroidectomy. Histopathological examination confirms the presence of both a follicular thyroid adenoma and an intrathyroidal parathyroid adenoma with hyperplastic features. Postoperative results initially showed a significant decrease in PTH levels, although a gradual increase has been observed over time. Throughout this period, electrolyte levels have remained stable, and TSH levels have been suppressed. Postoperative maintenance therapy included levothyroxine, calcitriol, and calcium supplements, along with a combination of statins for cholesterol and antiosteoporotic medication for bone health.

Conclusions: The concomitant occurrence of thyroid and parathyroid dysfunctions adds significant complexity to the diagnostic and therapeutic processes, particularly in geriatric patients. A thorough evaluation, followed by surgical intervention and diligent postoperative management, is crucial in this case for achieving hormonal balance and enhancing bone health. Multidisciplinary care is essential, as the dynamic nature of endocrine disorders requires adaptive management strategies. The challenges highlighted in this case underscore the importance of ongoing research and collaboration among healthcare professionals to enhance outcomes for patients with overlapping endocrine disorders.

Abstract citation ID: lvag096.875

EP347 - ECE_2474 - Severe chronic hypoparathyroidism—when convetional therapy fails

Pietro Locantore, Alessandro Romano, Erika Motolese, Gianluca Cera, Vincenzo Grasso and Alfredo Pontecorvi
Fondazione Policlinico Gemelli IRCCS—Università Cattolica del Sacro Cuore, Fondazione Policlinico Gemelli IRCCS, Translational Medicine and Surgery, Rome, Italy

Hypoparathyroidism consists in insufficient production of PTH, resulting in hypocalcemia. Its etiology is mainly post-surgical, following central neck surgery, whereas other causes (autoimmune and genetic parathyroid disorders) are less common.

Clinical manifestations include neuromuscular symptoms like paresthesias and cramps to overt tetanic crises. Chronic complications are nephrolithiasis, renal failure, bone fractures, extraskeletal calcifications, cognitive impairment and poor quality of life (QoL).

Conventional therapy is based on calcium and calcitriol. When conventional therapy fails, PTH analogues are recommended. Teriparatide improves calcium control and QoL, but requires multiple daily administrations because of its short half-life and its use is off-label in hypoparathyroidism, with inconstant control and long-term side effects.

TransCon-PTH is a long-acting PTH prodrug that allows stable PTH levels with a single daily subcutaneous administration.

We herein present three cases that may benefit from TransCon-PTH, which is not available in Italy at present.

V.I. is a 40-year-old woman affected by post-surgical hypoparathyroidism following total thyroidectomy (2018) for papillary thyroid cancer.

She initially achieved good calcium balance with a low dose calcitriol regimen; however, in 2019 she underwent duodeno–ileal bypass for severe obesity. Malabsorptive effects of bariatric surgery caused her to progressively increase oral calcium dose up to 6 gr and calcitriol dose up to 4 mcg daily. She subsequently started teriparatide bid; however, calcium control remains so poor that she needs frequent intravenous calcium administration.

N.T. is a 55-year-old woman affected by post-surgical hypoparathyroidism, following total thyroidectomy in 2016 for multinodular goiter.

Due to comorbidities that reduced her adherence to conventional therapy, she experienced significant fluctuations in serum calcium levels, ranging from severe hypocalcemia to symptomatic hypercalcemia. She therefore started teriparatide on a two daily dose regimen, which however did not completely improve serum calcium level control.

I.P. is a 35-years-old female who underwent total thyroidectomy in 2022 for papillary thyroid cancer.

She developed severe post-surgical hypoparathyroidism, requiring high doses of oral calcium and calcitriol. Management of treatment became complex, requiring frequent monitoring of serum calcium levels and corresponding dosage adjustments. She started teriparatide bis-in-die, which did not completely improve clinical management, given the persistence of hypocalcemic crises and episodes of hypercalcemia.

When conventional therapies fail to ensure adequate management of chronic hypoparathyroidism, TransCon-PTH can be a valid alternative to improve QoL and reduce risk of complications. New health policies are warranted to ensure access to TransCon-PTH for selected patients who could most benefit from it.

Abstract citation ID: lvag096.876

EP348 - ECE_3882 - Methotrexate osteopathy treated with teriparatide: a case report

Matej Rakusa
Department of Endocrinology, Diabetic and Metabolic Disease, University Medical Centre Ljubljana, University Medical Centre Ljubljana, Ljubljana, Slovenia

Introduction: Methotrexate osteopathy (MTXO) is a rare complication of methotrexate treatment characterized by low-energy stress fractures of the lower extremities. MTXO leads to chronic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

pain and subsequent immobility. Healing of fractures can be prolonged, with reports spanning over several years. Discontinued MTX treatment is associated with a greater chance of healing. The effectiveness of additional treatments to accelerate bone fracture healing is uncertain.

Case report: We present a case of a 66-year-old female with spontaneous, unhealed fractures of the lower limbs. She had a history of rheumatoid arthritis and leukopenia as part of Felty's syndrome. The patient was treated with methotrexate (20 mg weekly), folic acid, cholecalciferol (7000 IU weekly), and occasionally filgrastim. She experienced progressively worsening pain in both ankles and feet, left knee, without any evident injury. On the scale, pain was assessed as 8/10 and rendered the patient unable to walk. Magnetic resonance imaging (MRI) of the bones revealed stress fractures of both calcanei, the distal epiphysis of the right tibia, the second metatarsal of the right foot, the third metatarsal of the left foot, and the medial condyle of the left knee. Bone mineral density was decreased to osteoporotic levels, with the lowest T-score of −3.0 SD. Laboratory findings were in normal range as follows: corrected calcium 2.36 mmol/L, phosphate 1.02 mmol/L, alkaline phosphatase (AF) 1.89 µkat/L, creatinine 57 µmol/L, 25-hydroxyvitamin D 73.2 nmol/L, iPTH 29 ng/L, CTX 0.476 µg/L, and PINP 59.7 µg/L. Based on the fractures in typical locations and the absence of other causes, methotrexate osteopathy was confirmed. Methotrexate was discontinued, and treatment with teriparatide (20 µg daily) was initiated. One month after starting teriparatide therapy, the patient reported reduced pain, assessed on a scale of 2/10. After 1 year, PINP was 160.9 µg/L, CTX 0.144 µg/L. Only the fracture of the medial condyle of the left knee did not show signs of healing. All other healed at least partially.

Conclusions: Methotrexate osteopathy is a rare treatment complication. It is characterised by non-traumatic stress fractures of the distal and proximal tibia, calcaneus, talus, and metatarsals in patients treated with methotrexate. Discontinuation of methotrexate is critical for bone healing. Due to the rarity of methotrexate osteopathy, the optimal treatment approach is not entirely clear.

Abstract citation ID: lvag096.877

EP350 - ECE_2232 - Surgical treatment of primary hyperparathyroidism associated with MEN1 in children: report of 4 cases

Petr Libánský[1], Rami Katra[2], Magdalena Matejkova Behanova[3], Lukáš Plachý[4], Zdenek Sumnik[4], Josef Vcelak[5], Katerina Zajickova[5] and Vit Zikan[6,7]
[1], 3rd Department of Surgery, Motol and Homolka University Hospital, 1st Faculty of Medicine, Charles UniversityPrague, Czech Republic; [2]Department of Ear, Nose and Throat, Motol and Homolka University Hospital, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic; [3]Department of Nuclear Medicine and Endocrinology, Motol and Homolka University Hospital, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic; [4]Department of Pediatrics, Motol and Homolka University Hospital, Second Faculty of Medicine, Charles University, Prague, Czech Republic; [5]Clinical Endocrinology, Institute of Endocrinology Prague, Institute of Endocrinology, Prague, Czech Republic; [6]Third Department of Medicine-Department of Endocrinology and Metabolism, General University Hospital, Charles University, First Faculty of Medicine, Prague, Czech Republic; [7]Third Internal Clinic-Clinic of Endocrinology and Metabolism, General University Hospital, Charles University, First Faculty of Medicine 1, Prague, Czech Republic

Introduction: Primary hyperparathyroidism associated with multiple endocrine syndrom type 1 in children si very rare. It is caused by overproduction of parathormone by a pathologically changed parathyroid glands.

Methods: We carried out a retrospective study in 4 patients (age 8-17 years) who had surgical treatment between 2022-2025.

Results: All these patients had positive family history. Patients were examined using sonography, MIBI-scintigraphy and MRI. Calcium was measured before and after surgery: parathormone was monitored postoperative. First surgical operation was curative in three patients: reoperation was necessary in one patient. Other major complication were not observed.

Conclusions: Surgery offers definitive and safe treatment of primary hyperparathyroidism associated with MEN1 in children.

Abstract citation ID: lvag096.878

EP351 - ECE_3534 - When hydration masks diabetes insipidus: lithium toxicity with hypernatremia and hyperparathyroidism, a case report

Beatriz R. Pereira[1], Joana Vinhais[1], David Verissimo[1], Catarina Ivo[1], Ana Cláudia Martins[1], Luis Lopes[1], Ascension Lopez[2], Dolores Passos[1], Mafalda Marcelino[1], João Jácome de Castro[1] and João Nunes Silva[1]
[1]Endocrinology, Hospital Das Forças Armadas, Lisboa, Portugal; [2]Lisboa, Portugal

Introduction: Lithium has a narrow therapeutic window and can cause endocrine and renal complications, including lithium-associated hyperparathyroidism and impaired urinary concentration.

Case report: A 61-year-old woman presented to the emergency room with one-week of tremor and dizziness. Examination was positive for psychomotor retardation and fluctuating mental status. She had previous known history of bipolar disorder, treated with lithium (1200 mg/day), bupropion (150 mg/day), paliperidone (3 mg/day) and trazodone (150 mg/day).

Initial laboratory blood tests showed lithium 4.1 mmol/L (0.6-1.2), calcium 11.2 mg/dL (8.1-10.4), sodium 130 mmol/L (135-145) and mild acute kidney injury (eGFR 48 mL/min/1.73 m^2). Lithium was immediately discontinued and intravenous 0.9% sodium chloride initiated. Within 48 hours, lithium decreased to 1.5 mmol/L and calcium to 10.5 mg/dL, while sodium increased to 139 mmol/L. PTH was markedly elevated (331 pg/mL, 15-68.3), and thyroid function within normal range (TSH 3.29 uUI/mL, 0.27-4.2).

On day four of hospitalization, intravenous fluids were stopped, resulting in marked thirst and polyuria, as well as progressive hypernatremia (peak serum sodium 166 mmol/L on day five). Complementary evaluation evidenced dilute urine (urine osmolality 195 mOsm/kg) despite hyperosmolar plasma (serum osmolality 353 mOsm/kg) and elevated copeptin (26.5 pmol/L). A desmopressin trial (0.06 mg twice daily) lead to a mild clinical response, but persistent high urine output. Hypernatremia was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

corrected gradually with free-water replacement, normalizing by day 35.

On discharge (day forty-four), thirst and polyuria had resolved, sodium was 143 mmol/L, calcium 9.5 mg/dL, and PTH persisted elevated (189 pg/mL).

Two months after lithium discontinuation, renal function had normalized (eGFR 79 mL/min/1.73 m^2), calcium and sodium remained within the normal range (9.4 mg/dL and 144 mmol/L, respectively). However polyuria, polydipsia and elevated PTH (178 pg/mL) persisted, leading to desmopressin up-titration to 0.06 mg twice daily.

Discussion/Conclusions: Lithium suspension and intravenous fluids improved lithium toxicity and hypercalcemia. Subsequent reduction of free-water availability unmasked severe hypernatremia with inappropriately dilute urine and only partial response to desmopressin, consistent with nephrogenic diabetes insipidus.

Initial hyponatremia was most compatible with polydipsia in the setting of diabetes insipidus, with preserved thirst mechanisms. Concomitant psychotropic medications may have reduced free-water clearance, but the absence of urine volume and osmolality prior to fluid discontinuation limits confirmation of the underlying cause.

Lithium-associated endocrine complications show heterogenous reversibility timelines, ranging from normalization after cessation to persistence for weeks to months. In this patient, serum calcium normalized rapidly, while polyuria and PTH elevation persisted at two-month follow-up. This highlights the need for close monitoring and structured endocrine follow-up, even after lithium discontinuation.

Abstract citation ID: lvag096.879

EP352 - ECE_2801 - Densitometric vertebral morphometry in pseudohypoparathyroidism 1B and nonsurgical hypoparathyroidism: a case series study

Dana Michalska[1], Josef Vcelak[2,3], Dorota Baszczynska[4], Anna Kudlova[4] and Katerina Zajickova[1,2]
[1]. *Internal Clinic, Endocrinology and Metabolism, General University Hospital and First Faculty of Medicine, IIIPrague 2, Czech Republic;* [2]*Institute of Endocrinology, Prague, Czech Republic;* [3]*First Faculty of Medicine, Charles University, First Faculty of MedicinePrague 2, Czech Republic;* [4]*3rd Faculty of Medicine, Charles University, Prague 10, Czech Republic*

Pseudohypoparathyroidism (PHP) and nonsurgical hypoparathyroidism (Ns-HypoP) are rare diseases characterized by hypocalcemia. In PHP, parathyroid hormone (PTH) levels are elevated due to end-organ resistance, with variable tissue sensitivity. In PHP1B the skeletal system is believed to be spared.

Vertebral fracture assessment (VFA), bone densitometry, and bone biochemistry were evaluated in 5 patients with PHP1B and 5 patients with Ns-HypoP. There were no differences between the two groups in terms of age, body mass index, calcium and creatinine levels, 25-hydroxyvitamin D levels, lumbar spine bone mineral density, and trabecular bone score. However, individuals with PHP had significantly higher levels of parathyroid hormone (12.34 pmol/L vs 0.982 pmol/L, $P \leq .002$) and osteocalcin (34.56 vs 16.78 µg/L, $P \leq .021$). VFA detected one moderate biconcavity, one moderate wedge deformity, and two moderate compressions in patients with PHP. In contrast, only a single wedge vertebral deformity was observed in one elderly patient with Ns-HypoP.

VFA revealed morphometric changes predominantly in patients with PHP1B. Vertebral deformities have to be verified on spinal imaging. VFA may provide additional insights into trabecular bone involvement in PHP1B; however, larger studies are necessary to validate these preliminary findings.

Abstract citation ID: lvag096.880

EP353 - ECE_3703 - Pregnancy- and lactation-associated osteoporosis presenting with multiple vertebral fractures and marked bone density recovery: a case report

Ia Kavtiashvili, Ketevan Chanturishvili and Natia Shonia
Tbilisi Institute of Medicine, Tbilisi, Georgia

Background: Pregnancy- and lactation-associated osteoporosis (PLO) is a rare cause of fragility fractures in young women, most often presenting with thoracolumbar vertebral fractures in late pregnancy or early postpartum. Early recognition is critical to prevent prolonged disability and to guide future pregnancy planning.

Case presentation: A 28-year-old woman (G1P1) developed severe back pain with ~5 cm height loss during the third trimester. Delivery occurred at 37 weeks' gestation (06/2021). Postpartum spinal MRI demonstrated multiple vertebral compression fractures (Th11, Th12, L1, L2, L4). Past history included non-toxic nodular goiter (FNA Bethesda II) and vitamin D deficiency. BMI was 26.6 kg/m^2. Secondary causes of osteoporosis (including celiac disease, Cushing syndrome, hyperparathyroidism, and hyperthyroidism) were excluded, supporting the diagnosis of PLO.

Investigations (DXA): Baseline DXA (2021) showed severe osteoporosis: lumbar spine BMD 0.487 g/cm^2 with Z-score −5.1 (L4 Z-score −5.6). Hip measurements were also low (e.g., left femoral neck BMD 0.516 g/cm^2, T/Z −3.0; right femoral neck BMD 0.627 g/cm^2, T/Z −2.0).

Serial DXA demonstrated substantial improvement:

01/2023: Lumbar spine BMD 0.768 g/cm^2 (T-score −3.4), with reported gains vs baseline (lumbar + 57.7%; left femoral neck +46.5%; right femoral neck +30%).

09/2023: Lumbar spine BMD 0.784 g/cm^2 (T-score −3.3; Z-score −3.4).

03/2024: Lumbar spine BMD 0.786 g/cm^2 (T-score −3.3).

02/2025: Lumbar spine BMD 0.840 g/cm^2 (T-score −2.2; Z-score −2.2), with improved hip indices (left femoral neck BMD 0.807 g/cm^2; T/Z −1.0).

Treatment and Follow-up: Initial management included calcium 1200 mg/day and vitamin D 2000 IU/day plus denosumab 60 mg subcutaneously every 6 months. After three denosumab doses, an unplanned pregnancy was discovered. A multidisciplinary discussion addressed fetal risk and the implications of treatment interruption; ultimately, pregnancy was terminated and therapy was transitioned to annual zoledronic acid infusions with continued calcium/vitamin D supplementation. (Regulatory labeling warns denosumab may cause fetal harm and requires pregnancy exclusion prior to dosing.)

Conclusions: This case highlights severe PLO presenting antenatally with multiple thoracolumbar fractures and very low baseline lumbar BMD, followed by marked BMD recovery on

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

antiresorptive therapy with close DXA surveillance. It underscores the importance of (1) considering PLO in pregnant/postpartum women with acute back pain and height loss, (2) systematic exclusion of secondary osteoporosis, and (3) proactive counseling on medication choice and future pregnancy planning—particularly when denosumab exposure is possible.—check if it is correct for uploading?

Abstract citation ID: lvag096.881

EP354 - ECE_2745 - Atypical parathyroid adenomas—the borderline diagnosis in primary hyperparathyroidism

Mihaela Baranceanu[1], Nada Akad[2], Alexandru Florescu[1], Anca Matei[1] and Stefana Bilha[1]
[1]*Universitatea de Medicină și Farmacie 'Grigore T. Popa' Iași, Endocrinology, Iași, Romania;* [2]*Universitatea de Medicină și Farmacie 'Grigore T. Popa' Iași, Iași, Romania*

Introduction: Atypical parathyroid adenomas (APAs) represent a rare and diagnostically challenging cause of primary hyperparathyroidism (PHPT), classified as tumors of uncertain malignant potential and situated on the histopathological spectrum between benign parathyroid adenoma and parathyroid carcinoma. Their definitive diagnosis relies primarily on careful postoperative histopathological evaluation, as no preoperative clinical or biochemical features are pathognomonic.

Case presentation: We report two cases of APA in male patients presenting with severe manifestations of PHPT. The first case involved a 49-year-old man with a history of hypertension, recurrent nephrolithiasis, and a previous episode of urosepsis, who was found to have persistent hypercalcemia (serum calcium 13.2 mg/dL) and elevated parathyroid hormone (PTH 133 pg/mL), with preserved renal function. Screening for multiple endocrine neoplasia syndromes was negative. Parathyroid scintigraphy suggested a right inferior parathyroid adenoma, and surgical excision was performed. Histopathological examination revealed atypical features, including a thick fibrous capsule, trabecular growth pattern, and cellular atypia.

The second case involved a 74-year-old man with a history of prostate adenocarcinoma, who presented with markedly elevated PTH levels (1228 pg/mL), hypercalcemia (13.3 mg/dL), and hypercalciuria (367 mg/24 h). Skeletal evaluation demonstrated very low T-score of −5.9 at the forearm and multiple brown tumors on bone scintigraphy. Parathyroid scintigraphy identified a left-sided parathyroid adenoma, which was surgically removed. Histological analysis confirmed an atypical parathyroid adenoma composed predominantly of chief cells arranged in an insular and lobular pattern, with capsular adhesion, low mitotic activity, absence of vascular or perineural invasion, and a low Ki-67 proliferation index (<1%)

Conclusions:

1. APAs may present with moderate to severe biochemical abnormalities and significant renal and skeletal complications of PHPT, often overlapping clinically with parathyroid carcinoma.
2. Accurate diagnosis of atypical parathyroid adenomas relies on careful histopathological and immunohistochemical evaluation. Exclusion of absolute criteria of malignancy including-invasion of adjacent structures, vascular invasion, perineural invasion, and metastases is mandatory. Despite their limited specificity, immunohistochemical markers may provide supportive information in differentiating benign from malignant parathyroid lesions.
3. Surgical excision remains the treatment of choice, and long-term follow-up is essential due to the uncertain malignant potential and associated risk of recurrence.

Abstract citation ID: lvag096.882

EP355 - ECE_1932 - From suspected metastases to parathyroid disease: tertiary hyperparathyroidism mimicking metastatic bone disease in chronic kidney disease

Salome Kalandadze[1,2], Mariam Pailodze[1], Inga Shoshiashvili[1], Tedo Jokharidze[1], Ana Khoperia[1] and Ketevan Kankava[3]
[1]*New Hospitals, Tbilisi, Georgia;* [2]*Endocrinology, Caucasus Medical Center, Tbilisi, Georgia;* [3]*Megalab, Tbilisi, Georgia*

Introduction: A 65-year-old woman with a five-year history of advanced chronic kidney disease (serum creatinine 329 µmol/L) and type 2 diabetes presented with progressive left sacral pain over two months. Initial spine magnetic resonance imaging demonstrated infiltrative changes in the left sacrum, raising strong suspicion for metastatic bone disease. The patient was therefore referred to the oncology department with a presumed malignancy of unknown primary.

Investigations: Further imaging confirmed extensive skeletal involvement. MRI revealed multifocal infiltrative marrow changes involving S2-S3 and the left sacrum. Whole-body FDG PET/CT demonstrated multiple hypermetabolic lytic skeletal lesions, including the right scapula (SUVmax 9.2), left sacrum (SUVmax 6.6), pubic bone with an associated pathological fracture (SUVmax 16.4), left femoral shaft with cortical erosion (SUVmax 11.2), and right proximal tibia (SUVmax 9.3). Low-grade FDG uptake was noted in the cervical region (SUVmax 3.3).

Comprehensive oncologic evaluation, including gynecological assessment, failed to identify a primary tumor. Given the high metabolic activity and pathological fracture, a biopsy of the pubic bone lesion was performed. Histological and immunohistochemical analysis excluded malignancy, with differential diagnoses including giant cell tumor vs hyperparathyroidism-associated brown tumor.

In view of these findings, an endocrinologic evaluation was undertaken. Biochemical testing revealed markedly elevated parathyroid hormone levels (PTH 1139 ng/L; reference range 15-65) with concomitant borderline hypercalcemia (total calcium 11.0 mg/dL; ionized calcium 1.36 mmol/L), elevated alkaline phosphatase (211 U/L), severe vitamin D deficiency (25-hydroxy-vitamin D 9 ng/mL), low-normal phosphate (1.16 mmol/L), hypomagnesemia (0.60 mmol/L), and low 24-hour urinary calcium (1.2; reference 2.5-7.5). The patient was not receiving calcium supplements or active vitamin D at presentation.

The cervical FDG uptake observed on PET/CT was subsequently anatomically localized by targeted neck ultrasound to a 29 × 18 mm hypoechoic, hypervascular lesion in the expected anatomical location of a parathyroid gland.

Diagnosis: Based on the combination of long-standing CKD, markedly elevated PTH, hypercalcemia, extensive high-turnover

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

bone disease, and parathyroid imaging findings, a diagnosis of tertiary (autonomous) hyperparathyroidism in the context of CKD–mineral and bone disorder was established.

Management and Follow-up: Parathyroidectomy was recommended but declined. Medical therapy with cinacalcet resulted in early biochemical improvement, with reductions in both PTH and serum calcium.

Conclusions: This case highlights that severe CKD-related hyperparathyroidism may closely mimic metastatic malignancy on FDG PET/CT and underscores the critical importance of integrating histopathology, mineral metabolism, and targeted parathyroid imaging to avoid misdiagnosis and guide management.

Abstract citation ID: lvag096.883

EP360 - ECE_3562 - Tertiary hyperparathyroidism in advanced CKD: a case report

Cristina Contreras Pascual[1] and Paloma Gonzalez Lazaro[2]
[1]*Hospital Santa Bárbara, Soria, Spain;* [2]*Hospital General La Mancha Centro, Alcázar de San Juan, Spain*

Tertiary hyperparathyroidism (THPT) is an infrequent but clinically significant consequence of long-standing secondary hyperparathyroidism in patients with advanced chronic kidney disease (CKD). Persistent autonomous parathyroid hyperplasia may not resolve after kidney transplantation and can negatively impact graft function, making pre-transplant management particularly challenging.

We describe a 60-year-old male with end-stage renal disease (CKD G5) secondary to malignant hypertension and nephroangiosclerosis, on thrice-weekly hemodialysis since May 2023 and currently listed for kidney transplantation. His medical history included former heavy smoking, previous alcohol abuse, dyslipidemia, hypertensive cardiomyopathy, and grade 3 hypertensive retinopathy. The patient was referred to the Endocrinology Department for assessment of severe hyperparathyroidism prior to transplantation.

Biochemical evaluation revealed extremely elevated intact parathyroid hormone (PTH) concentrations (up to 1745 pg/mL), severe 25-hydroxyvitamin D deficiency (8.92 ng/mL), low–normal serum calcium (8.25 mg/dL), hyperphosphatemia (5.12 mg/dL), and an estimated glomerular filtration rate <15 mL/min/1.73 m^2. Cervical ultrasound suggested a small left parathyroid adenoma (7 mm), whereas parathyroid scintigraphy was negative. Choline PET imaging subsequently demonstrated hyperplasia of all four parathyroid glands, supporting the diagnosis of THPT due to prolonged uremic stimulation.

Considering the low likelihood of regression after kidney transplantation and the potential risk of post-transplant graft dysfunction, a subtotal parathyroidectomy with autotransplantation into the sternocleidomastoid muscle was performed. Within 24 hours postoperatively, the patient developed severe hypocalcemia (corrected calcium 6.79 mg/dL) associated with suppressed PTH levels (<2.4 pg/mL), consistent with postoperative hypoparathyroidism and hungry bone syndrome. One month after surgery, PTH levels normalized (31.5 pg/mL) and vitamin D status improved (34.2 ng/mL); however, persistent hypocalcemia required intensive calcium supplementation, including intravenous calcium during hemodialysis, oral calcium salts, and phosphate binders. Histopathological analysis confirmed diffuse parathyroid hyperplasia without evidence of malignancy.

This case highlights the complexity of managing tertiary hyperparathyroidism in patients with advanced CKD awaiting kidney transplantation. Although pre-transplant parathyroidectomy may reduce the risk of graft dysfunction, clinicians should anticipate severe postoperative hypocalcemia and hungry bone syndrome, even when parathyroid autotransplantation is performed.

Abstract citation ID: lvag096.884

EP361 - ECE_1723 - Screening for osteoporosis: to scan or not to scan both hips in dual energy absorptiometry (DXA)

Shahini Winson Gnanathayalan and Uditha Bulugahapitiya
Endocrinology and Diabetes, National Hospital of Sri Lanka, Colombo, Sri Lanka

Introduction: Controversy remains regarding the use of bilateral hip scanning when bone mineral density (BMD)is measured, and bilateral hip scanning is not mandatory in international guidelines for screening of osteoporosis. Scanning one hip is cost and time effective.

Objectives: This study aimed to compare the diagnostic ability of BMD assessment in one hip in comparison to both hips.

Methods: This cross-sectional study was performed in males and females (40-90 years of age), being screened for osteoporosis using DXA-scan at a tertiary hospital in Sri Lanka, in 2023. Scanning both hips in addition to lumbar spine is the usual practice in this center.

Results: In the preliminary analysis of 161 subjects screened for osteoporosis (88% females, mean age 62 years), 52% had lower BMD in the left, when comparing the femoral neck BMD in both sides. There was no significant difference in the mean femoral neck BMD of the left vs the right leg (0.685 vs 0.687 g/cm^2). Of the total 161 individuals, osteoporosis ($T \leq -2.5$) was detected in 62 (38.5%) using the lumbar spine and right hip, compared to 64 (39.8%) subjects using the lumbar spine and left hip. Using the lumbar spine and both hips identified 66 (41%) individuals with osteoporosis. Lowest T-score was detected in the lumbar spine in 68% (45/66) of osteoporotic patients. Therefore, diagnosis based on use of the lumbar spine and right hip BMD, or lumbar spine and left hip BMD failed to identify only 4 (6%) or 2 (3%) subjects with osteoporosis respectively. When FRAX (Fractur risk assessment tool) with BMD was applied to these 6 subjects in whom using lumbar spine and one hip BMD failed to detect osteoporosis, 5 were identified to have high fracture risk indicating treatment according to Sri Lankan specific intervention thresholds.

Conclusions: The results indicate that scanning only one hip in addition to lumbar spine is sufficient to screen for osteoporosis. Larger studies are required for more reliable results and to identify subgroups who would benefit from dual hip scanning.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.885

EP362 - ECE_2136 - Method for increasing the ultrasonic conductivity of skull bone tissue in patients who are planned to be treated with magnetic resonance imaging-guided focused ultrasonic imaging

Liliya Kuzina
Chystiakove, Ukraine

The invention relates to medicine, namely to endocrinology and neurosurgery, and can be used to treat patients with altered ultrasound conductivity of bone tissue who are planned to be treated with magnetic resonance imaging-guided focused ultrasound (MR-FUS) The MR-FUS method is most often used to treat movement disorders such as Parkinson's disease, dystonia, and essential tremor. The method is based on two technologies—high-intensity focused ultrasound (HIFU) and MRI. Using heating or cavitation at a variable distance from the sensor, HIFU can cause selective thermal coagulation in a clearly defined volume.The error in the destruction of brain tissue with this method is extremely small and averages 0.50-0.75 mm, varying depending on the technical characteristics of the selected equipment. The arsenal of solutions to the problem associated with low CUPT is very limited, which in turn leads to numerous refusals to perform operations using focused ultrasound. The objective of the invention is to develop a method for increasing the ultrasound conductivity of the bone tissue of the skull for further surgical interventions in patients using MR-FUS in a short time and with a safer method. The technical result of using the invention is a significant increase in the skull UCCT in patients with an initial UCCT of less than 0.35, achieving the threshold value necessary for thalamotomy with MR-FUS.The proposed method for increasing the ultrasound conductivity of the cranial bone tissue is carried out as follows. The patient for whom MR-FUS is planned undergoes CT of the cranial bones to determine the UPCCT, as well as laboratory tests for ionized calcium and vitamin D. If the coefficient is less than 0.35, the patient is administered Bonviva (Ibandronic acid) 3 mg intravenously by bolus over 15-30 seconds once every 3 months, Aquadetrim (Cholecalciferol) at a dose of 1500-5500 IU per day and Calcium D3 Nycomed (Calcium carbonate + Cholecalciferol) at a dose of 500 mg + 200 IU 2 times a day. The course of treatment is 3-6 months. After 3 months, the patient undergoes a repeat CT of the cranial bones on the same device and with the same program to assess the ultrasound conductivity coefficient of bone tissue, and laboratory tests for vitamin D and ionized calcium. If the cranial CUPCT increases by more than 0.35, the patient is referred for surgery using focused ultrasound. If there is no effect after 3 month.

Abstract citation ID: lvag096.886

EP363 - ECE_2684 - Cushing's hidden fragility: lessons from a case of severe skeletal impairment

Praveena Vankayalapati[1], Preeshila Behary[1,2], Jeremy Cox[1,2], Alexander Comninos[1,2], Karim Meeran[1,2], Niamh Martin[1,2], Nair Ramesh[1], Debbie Papadopoulou[1] and Jacques Abella[1]
[1]*Imperial College Healthcare NHS Trust, London, United Kingdom;* [2]*Imperial College, London, United Kingdom*

Introduction: Cushing's syndrome (CS) is associated with reduced bone density and increased risk of fragility fractures. Glucocorticoid-excess suppresses osteoblast function, enhances bone resorption, and disrupts calcium and vitamin D homeostasis, leading to skeletal fragility.

We present a case of pituitary CS, illustrating severe skeletal morbidity and response to targeted anabolic bone therapy.

Case presentation: A 35-year-old man with pituitary CS underwent a trans-sphenoidal surgery in March 2022 and started prednisolone 3 mg/day post-operatively. He reported ongoing disabling back pain and chest pain. MRI spine revealed bilateral rib fractures and multi-level vertebral compression fractures of various chronicity (T3-L1) and a severe kyphotic deformity. Dual-energy X-ray absorptiometry (DEXA) confirmed markedly reduced bone mineral density (BMD) with Z-scores of −3.1 and −3.3 at the lumbar spine (LS) and total hips respectively. Vitamin D levels were adequate and dietary calcium intake was optimised. Bone turnover markers were elevated, consistent with active fracture healing.

Severe pain caused significant functional impairment, requiring strong opioid analgesia and inability to work. After discussion in our Endocrinology Bone MDT treatment with teriparatide 20 µg daily mcg daily was initiated and kyphoplasty performed. Pain gradually improved, allowing opioid withdrawal. DEXA after 18 months of teriparatide demonstrated substantial improvement in BMD: +28.1% at the LS, +34% at the hip (Z-scores −1.1 and −1.6, respectively).

Discussion: Despite the well-recognised skeletal consequences of CS, bone health evaluation and management are often overlooked. Delays in CS diagnosis are common averaging 30.6 months (1), during which substantial skeletal impairment may occur.

We recently showed[1] that only 43% of patients presenting with CS had vitamin D measured and 39% received bone health management: calcium intake and/or vitamin D optimisation and/or initiation of bone-protective agents. Fracture risk persisted despite CS remission while early bone-protective therapy accelerated LS BMD recovery.

The choice of bone protective agent should be individualised. Concerns exist regarding prolonged suppression of bone turnover with antiresorptive agents, which may theoretically blunt osteoanabolic response in the post-remission skeletal recovery.[2] Anabolic therapy may therefore be preferred.[3,4]

Conclusions: This case highlights that in patients with CS, there is a need to

1. Assess bone health alongside definitive treatment of CS
2. Optimise calcium and vitamin D status early
3. Incorporate early fracture risk assessment, a low threshold for skeletal imaging and individualised bone-protective therapy, including anabolic agents, in selected high-risk individuals.

References

1. Behary P, Raveendran D, Nair R, et al. Clinical practice patterns in bone health assessment and management in endogenous Cushing's syndrome. *Clin Endocrinol (Oxf)*. 2026;104(4):302-311. https://doi.org/10.1111/cen.70085

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

2. Scillitani A, Mazziotti G, Di Somma C, et al. Treatment of skeletal impairment in patients with endogenous hypercortisolism: when and how? *Osteoporos Int*. 2014;25(2):441-446. https://doi.org/10.1007/s00198-013-2588-y
3. Scillitani A, Mazziotti G, Di Somma C, et al. Insights on accelerated skeletal repair in Cushing's disease. *Bone Rep*. 2015;2:32-35. https://doi.org/10.1016/j.bonr.2015.03.001
4. Scillitani A, Mazziotti G, Di Somma C, et al. A case of cushing syndrome diagnosed by recurrent pathologic fractures in a young woman. *J Bone Metab*. 2012;19(2):153-158. https://doi.org/10.11005/jbm.2012.19.2.153

Abstract citation ID: lvag096.887

EP364 - ECE_2791 - Primary hyperpathroidsm with negative 99mTc-sestamibi scintigraphy

Megi Lekbello[1], Dorina Ylli[2], Violeta Hoxha[2], Marjeta Kermaj[1] and Klodi Poshi[1]
[1]*Endocrinology, Internal Medicine, University Hospital Mother Tereza, Tirana, Albania;* [2]*Endocrinology, Internal Medicine, University of Medicine, Tirana, Albania*

Introduction: Primary hyperparathyroidism (PHPT) is caused by autonomous parathyroid hormone (PTH) secretion, most commonly from a single adenoma. Surgical treatment depends on accurate preoperative localization. Although 99mTc-sestamibi scintigraphy is widely used, false-negative results occur in up to 25% of cases, complicating management.

Case presentation: A 33-year-old male presented to the emergency department following a syncopal episode. On admission, he was bradycardic (heart rate 38 beats per minute) and reported fatigue and excessive sweating. Laboratory investigations revealed marked hypercalcemia (serum calcium 12.6 mg/dL). His medical history was significant for hypertension and nephrolithiasis. Biochemical evaluation demonstrated elevated serum PTH and calcium levels, low serum phosphate, and normal vitamin D levels, consistent with a diagnosis of primary hyperparathyroidism. Neck ultrasonography showed a normal thyroid gland, and the parathyroid glands were not visualized. Subsequent 99mTc-sestamibi scintigraphy was negative. Given the strong clinical and biochemical suspicion, a contrast-enhanced computed tomography (CT) scan of the neck was performed, revealing a suspected 7-mm parathyroid adenoma located in the posterior inferior cervical region. The patient's symptomatic bradycardia was attributed to severe hypercalcemia, and medical therapy with cinacalcet was initiated. He was referred for surgical evaluation; however, the patient expressed significant hesitation regarding parathyroidectomy.

Conclusions: Negative 99mTc-sestamibi scans significantly influence clinical decision-making for both endocrinologists and surgeons, often affecting referrals and recommendations for parathyroidectomy. Recognition of characteristic patterns in patients with negative MIBI scans, (such as small or single adenomas), may allow for more targeted diagnostic strategies. Discordant imaging findings are associated with lower cure rates, longer operative times, and delayed surgical referral, emphasizing the importance of integrating clinical, biochemical, and multimodal imaging data in the management of primary hyperparathyroidism.

Abstract citation ID: lvag096.888

EP365 - ECE_3692 - Rare case of Isolated Hypogonadotropic hypogonadism with concomitant osteoporosis

Tea Khurodze[1,2], Vitali Vashakidze[1], Ana Pruidze[1], Basa Gegeshidze[1] and Elisabed Pkhaladze[1]
[1]*Tbilisi, Georgia;* [2]*David Tvildiani Medical University, T'bilisi, Georgia*

Introduction: Isolated Hypogonadotropic hypogonadism(IHH) is a rare endocrine disorder with various clinical manifestations that results from impairment of the hypothalamic–pituitary–gonadal (HPG) axis and normal levels of remaining pituitary hormones. Although amenorrhea, infertility, and lack of secondary sexual characteristics are the main patient concerns, low estrogen levels enhance bone resorption, and late diagnoses can lead to irreversible bone loss and increased susceptibility to fractures.

Case report: A 21-year-old Caucasian female was referred to an endocrinologist with complaints of bone pain, weakness, hair loss, and brittle nails. At the age of 17, she was diagnosed with primary amenorrhea due to Isolated Hypogonadotropic Hypogonadism with decreased levels of LH, FSH, estrogen, hypoplastic ovaries, and uterus on ultrasound. Kallmann syndrome was excluded(no olfactory complaints). Patient did not report eating disorders, psychological stress, or strenuous physical activity during adolescence. Karyotyping revealed a normal female pattern 46. Sex hormone therapy was commenced, though the patient did not adhere to the prescribed regimen regularly. On physical examination, she had a normal habitus without congenital anatomical defects. Height:161 cm, Weight: 53 kg, BMI: 20.4. Lab tests revealed Hashimoto's hypothyroidism, normal phosphate-calcium metabolism. DEXA scan confirmed early onset osteoporosis. The patient was treated with levothyroxine, bisphosphonates, vitamin D, and calcium supplementation, resulting in both laboratory and clinical improvement. Hormone replacement therapy was restored by a gynecologist to optimize reproductive health outcomes.

Conclusions: This case illustrates the multisystemic and progressive nature of IHH. Diagnosis requires careful integration of clinical, biochemical, instrumental, and genetic investigations. Early treatment is crucial in preventing adverse endocrine, metabolic, and skeletal outcomes.

Abstract citation ID: lvag096.889

EP366 - ECE_3903 - When a fracture tells a hormonal story: unmasking primary hyperparathyroidism beyond imaging

Eni Celo[1] and Bariola Duro[2]
[1]*Trauma University Hospital, Tirana, Albania;* [2]*Poliklinika e Specialiteteve nr.4, Tirana, Albania*

Fragility fractures may be the first clinical manifestation of an underlying endocrine disorder. We report the case of a 61-year-old woman in whom evaluation following a left humeral fracture led to the diagnosis of primary hyperparathyroidism despite non-localizing imaging.

The patient presented with a traumatic fracture of the left proximal humerus. Osteoporotic changes were noted on plain radiographs, leading to subsequent assessment with dual-energy X-ray absorptiometry, which demonstrated reduced bone

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

density, with a T-score of −2.3 at the hip and −2.6 at the femoral neck. These findings led to further metabolic assessment, which revealed vitamin D deficiency (25-hydroxyvitamin D 16.6 ng/mL; reference >30 ng/mL), elevated ionized calcium (1.30 mmol/L; reference 1.12-1.30 mmol/L), and inappropriately increased parathyroid hormone (PTH) levels (86 pg/mL; reference range 10-65 pg/mL), with normal renal function. Neck ultrasonography showed a multinodular goitre without visualization of parathyroid enlargement.

Vitamin D supplementation with cholecalciferol 2000 IU daily was initiated. After one month, vitamin D levels improved to 27.8 ng/mL; however, hypercalcaemia persisted and became more pronounced (ionized calcium 1.35 mmol/L; reference 1.12-1.30 mmol/L; total calcium 11.5 mg/dL; reference 8.5-10.5 mg/dL), while PTH levels remained elevated (78 pg/mL). Technetium-99m sestamibi scintigraphy failed to localize hyperfunctioning parathyroid tissue, supporting a diagnosis of imaging-negative primary hyperparathyroidism.

Parathyroidectomy was discussed but declined by the patient. A conservative management strategy was therefore adopted, including optimization of vitamin D status, initiation of antiresorptive therapy for skeletal protection, and close biochemical and densitometric monitoring.

This case highlights the importance of considering primary hyperparathyroidism in patients presenting with fragility fractures and reduced bone density, even when localization studies are negative, and underscores the central role of biochemical assessment in guiding diagnosis and management.

Abstract citation ID: lvag096.890

EP368 - ECE_3787 - Postpartum osteoporosis as a diagnostic challenge: a case report

Marija Toshevska Stefanoska, Ivana Mladenovska, Argjent Mucha, Aleksandra Stevchevska, Elena Pavlevska and Sasha Jovanovska Mishevska
Clinic of Endocrinology, Diabetes and Metabolic Disease, Ss. Cyril and Methodius University in Skopje, Skopje, North Macedonia

Postpartum Osteoporosis as a Diagnostic Challenge: A Case ReportBackground: Postpartum osteoporosis, also referred to as pregnancy- and lactation-associated osteoporosis (PLO), is an uncommon condition characterized by substantial bone loss and an increased risk of fragility fractures in young women. As back pain is a frequent complaint in the postpartum period, the underlying diagnosis may be overlooked, contributing to delayed recognition of postpartum osteoporosis in clinical practice.

Case report: We describe the case of a 33-year-old woman, with a body mass index of 18.9 kg/m^2 who presented with acute, severe, non-traumatic back pain occurring six months after delivery**.** The patient was actively breastfeeding at the time of presentation. She had no prior fractures, chronic illnesses, or exposure to medications known to affect bone metabolism. Pregnancy and delivery were uncomplicated.

Physical examination revealed restricted spinal mobility with localized tenderness. Laboratory evaluation showed normal serum calcium, phosphate, parathyroid hormone, and 25 hydroxyvitamin D levels, with normal renal and thyroid function, excluding secondary causes of osteoporosis. Dual-energy X-ray absorptiometry demonstrated markedly reduced bone mineral density, predominantly at the lumbar spine (Z-score ≤ −2.5). Spinal magnetic resonance imaging revealed vertebral compression fractures.

Based on clinical presentation, imaging findings, prolonged lactation history, and exclusion of secondary etiologies, a diagnosis of postpartum osteoporosis was established. Discontinuation of lactation and initiation of supportive therapy with calcium and vitamin D supplementation resulted in significant clinical improvement within six months.

Conclusions: This case report underscores postpartum osteoporosis as a clinically relevant and frequently underestimated cause of severe back pain in young women.Increased clinician awareness is essential for early diagnosis, timely management, and prevention of long-term skeletal complications.

Keywords postpartum osteoporosis, pregnancy and lactation associated osteoporosis, case report, diagnostic challenge, severe back pain, vertebral fractures

Abstract citation ID: lvag096.891

EP369 - ECE_2300 - AI-based fractal and morphometric ultrasound analysis of peripheral nerves in diabetic neuropathy: a pilot study

Rostyslav Bubnov[1,2], Zbigniew Pilecki[3], Grzegorz Pilecki[3], Lev Kalika[4] and Karol Szyluk[5]
[1]*Ultrasound, Clinical hospital `Pheophania, Kyiv, Ukraine;* [2]*Zabolotny institute of microbiology and virology, Kyiv, Ukraine;* [3]*Orthopedics, Group of City Hospitals in Chorzow, Chorzow, Poland;* [4]*New York Dynamic Neuromuscular Rehabilitation & Physical Therapy, New York, United States;* [5]*Medical University Of Silesia, Katowice, Poland*

Background: Diabetic peripheral neuropathy (DPN) is a major chronic complication of diabetes mellitus, often diagnosed late due to limited sensitivity of conventional clinical and electrophysiological methods. Ultrasound (US) enables non-invasive visualization of peripheral nerves, but standard metrics such as cross-sectional area (CSA) provide incomplete information on microstructural damage. Fractal geometry allows quantitative assessment of tissue complexity and structural disorganization.

We **aimed** to evaluate an AI-assisted fractal–morphometric ultrasound approach for the assessment of diabetic neuropathy using the patented ultrasound-based framework, integrating ultrasound morphometry and fractal image analysis.[1-5]

Methods: Twenty patients with type 2 diabetes mellitus and clinically confirmed peripheral neuropathy were prospectively analyzed. High-frequency B-mode ultrasound of peripheral nerves (ulnar and median nerves) was performed. Morphometric parameters included CSA, fascicle diameters, and fascicular heterogeneity according to a patented ultrasound neuropathy method.[3-5] Fractal analysis of nerve images was conducted using a box-counting algorithm to calculate fractal dimension (FD) and lacunarity.[1,2] An AI-assisted pipeline integrated morphometric and fractal features to generate a composite neuropathy severity index. Findings were compared with reference values from healthy nerves.

Results: Diabetic neuropathy nerves demonstrated increased CSA, enlargement of selected fascicles, and loss of normal fascicular organization. Fractal analysis revealed significantly higher FD values (mean FD 1.74-1.82) and increased lacunarity compared to healthy

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

nerve patterns (FD ~1.40-1.45), indicating increased structural complexity and microarchitectural disorganization. Greater FD and fascicular heterogeneity correlated with clinical severity of neuropathy. AI-based feature integration improved differentiation between mild and advanced neuropathy patterns.

Conclusions: AI-assisted fractal–morphometric ultrasound analysis provides a novel, quantitative, and non-invasive approach for evaluating diabetic peripheral neuropathy. This method captures microstructural nerve alterations beyond conventional ultrasound metrics and may support early diagnosis, phenotyping, and monitoring of diabetic neuropathy for personalized and predictive endocrinology care.

Keywords diabetic neuropathy, ultrasound, fractal analysis, artificial intelligence, peripheral nerves, personalized medicine

References

1. Bubnov R, Spivak M. Fractal analysis of muscle ultrasound imaging to evaluate muscle health and spasticity. *Mov Disord*. 2020;35(Suppl 1):S58.
2. Bubnov R. Method for diagnosing peripheral neuropathy. UA 61290 U. Utility Model, Ukraine. Published 11.07.2011, Bulletin No. 13. https://iprop-ua.com/inv/oqgedaie/ https://iprop-ua.com/inv/pdf/oqgedaie-description.pdf
3. Bubnov RV. Ultrasonography diagnosis of peripheral neuropathy. The initial experience. *Ultrasound Med Biol*. 2011;37(8):S144-S145. https://doi.org/10.1016/j.ultrasmedbio.2011.05.773
4. Bubnov RV. Evidence-based pain management: is the concept of integrative medicine applicable? *EPMA J*. 2012;3(1):13. https://doi.org/10.1186/1878-5085-3-13

Abstract citation ID: lvag096.892

EP370 - ECE_2737 - Combination therapy with SGLT2i and polyethylene glycol loxenatide vs SGLT2i monotherapy for cardiovascular events in Chinese patients with type 2 diabetes: a multicenter retrospective study

Yaqian Duan[1], Peiyun Chen[1], Ke Li[1], Shengbing Li[1], Mengliu Yang[1], Shaowei Duan[2], Yale Duan[2], Zhizhen Hu[2] and Dongfang Liu[1]

[1]*The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China;* [2]*Jiangsu Hansoh Pharmaceutical Group Co., Ltd., Shanghai, China*

Background: In real-world Chinese patients with type 2 diabetes (T2D), whether combining sodium-glucose co-transporter 2 inhibitors (SGLT2i) with Glucagon-like peptide-1 receptor agonists (GLP-1RAs) further reduces the risk of major adverse cardiovascular events (MACE) compared with SGLT2i monotherapy remains unclear. Therefore, this study aimed to evaluate the comparative cardiovascular effectiveness of SGLT2i plus the specific GLP-1 RA Polyethylene Glycol (PEG)-loxenatide vs SGLT2i monotherapy in this population.

Methodology: This multicenter retrospective cohort analysis used data from the Tianjin Health Care Data Platform, covering 82 hospitals in China. Adult patients with T2D and cardiovascular disease (CVD) or CVD risk factors who initiated treatment with either SGLT2i plus PEG-loxenatide or SGLT2i monotherapy for >3 months between Jan 2016 and Dec 2024 were identified. Propensity score matching (PSM, caliper = 0.1) was performed based on age, sex, diabetes duration, CVD, dyslipidemia, renal disease, and the use of antihypertensive and lipid-lowering medications. The index date was defined as the date of the first prescription of the respective treatment regimen. All analyses followed the intention-to-treat principle, from the index date until the occurrence of an outcome event, death, or last observation. The primary endpoint was 3P-MACE (all-cause mortality, nonfatal myocardial infarction, and nonfatal stroke). The Cox proportional hazards regression models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs).

Results: After 1:1 PSM, 4020 patients were included in each group. The median duration of medication use was 228 days (combination) and 333 days (SGLT2i monotherapy). Combination therapy was associated with a 28% lower risk of 3P-MACE (HR, 0.72; 95% CI, 0.60-0.88; $P < .001$; Table 1), including significant reductions in nonfatal myocardial infarction (HR, 0.42; 95% CI, 0.24-0.74; $P = .002$) and non-fatal stroke (HR, 0.77; 95% CI, 0.63-0.94; $P = .012$). The risks of coronary revascularization (HR, 0.52; 95% CI, 0.36-0.76; $P < .001$) and hospitalization for unstable angina (HR, 0.73; 95% CI, 0.56-0.95; $P = .021$) were also significantly lower in the combination therapy group.

Conclusions: In this real-world cohort study involving Chinese patients with T2D, combination therapy with SGLT2i and PEG-loxenatide was associated with a significant lower risk of MACE compared with SGLT2i monotherapy.

Keywords type 2 diabetes, major adverse cardiovascular events, GLP-1 receptor agonists, loxenatide, SGLT2 inhibitors, propensity score matching

Abstract citation ID: lvag096.893

EP371 - ECE_3158 - Genetically predicted HbA1c and the risk of acute pancreatitis in a mendelian randomization study

Silvano da Silva[1], Vasiliki Lagou[2], Vinicius Ribeiro[1] and Camilly de Paiva[1]

[1]*Faculty of Medical Sciences of Santos (FCMS)—UNILUS—Lusíada University Center, Santos, Brazil;* [2]*Bioinformatics Multidisciplinary Environment, Federal University of Rio Grande do Norte, Natal, Brazil*

Introduction: Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are widely used for the treatment of type 2 diabetes and obesity, but their potential association with acute pancreatitis, largely based on observational evidence, remains an area of concern. Glycated hemoglobin A1c (HbA1c) reflects long-term glycemic exposure and represents a key metabolic pathway modulated by GLP-1 receptor activation. Mendelian randomization (MR) enables causal inference between an exposure and an outcome using genetic variants as instrumental variables (IVs). In this study, we applied a two-sample MR approach to evaluate whether genetic liability to higher HbA1c levels is causally associated with acute pancreatitis risk using data from FinnGen and the UK Biobank for independent replication.

Aim: To determine whether genetically predicted HbA1c levels have a causal effect on the risk of acute pancreatitis.

Methods: Genome-wide significant variants ($P < 5 \times 10^{-8}$) for HbA1c were selected from a large European-ancestry genome-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

wide association study (GWAS) (ieu-b-4841) and clumping was performed ($r^2 < 0.001$) to obtain independent variants as IVs. For acute pancreatitis, GWAS data from FinnGen (finn-b-K11_ACUTPANC) and UK Biobank (ukb-b-19388) were used. Exposure and outcome datasets were harmonized to align effect alleles, excluding ambiguous palindromic variants. Causal estimates were obtained using the inverse variance weighted (IVW) method, with MR-Egger, weighted median, and mode-based approaches as sensitivity analyses. Heterogeneity and directional pleiotropy were assessed using Cochran's Q statistic and MR-Egger intercept, respectively.

Results: Genetic instruments for HbA1c comprised 12 independent variants, of which nine were retained after harmonization with the FinnGen acute pancreatitis dataset. In the primary analysis, genetically predicted HbA1c levels were not causally associated with acute pancreatitis risk ($\beta_{IWV} = -0.091$, $P = .45$). Results were consistent across other MR methods, with no evidence of heterogeneity or directional pleiotropy, and leave-one-out analyses showed no influential single variant.

Similarly, in UK Biobank, no causal association between HbA1c and acute pancreatitis was observed (inverse variance weighted $\beta = -7.3 \times 10^{-4}$, $P = .36$, IVs = 5), with concordant findings across other MR methods and no evidence of heterogeneity or pleiotropy.

Conclusions: This MR study found no causal association between genetically predicted HbA1c levels and acute pancreatitis risk. From a clinical endocrinology perspective, these results indicate that glycemic dysregulation alone does not seem to contribute to pancreatitis development. Therefore, potential pancreatic adverse events related to GLP-1RAs are unlikely to be mediated by glucose-lowering mechanisms.

Abstract citation ID: lvag096.894

EP372 - ECE_2269 - Masld metabolomic staging association to atherosclerotic plaque burden beyond traditional risk factors

Belén García Izquierdo[1], Sonsoles Guadalix[2], Rebeca Mayo[3], Delia D'ávola[4], Janire Allende[3], Manuel García de Yébenes[5], Marta Mediero Benítez[2], Gorka Bastarrika Alemañ[6], Javier Escalada[7], Ainara Martínez-López[3], Carolina M. Perdomo[7], Ana Huerta[4], Fernando Hernández-Terciado[5], Sonsoles Gutierrez-Medina[2], Juan Carlos Pastrana[4] and Diego Martínez-Urbistondo[4]

[1]Endocrinology and Nutrition, Clínica Universidad de Navarra, Madrid, Spain; [2]Endocrinology and Nutrition, Clínica universidad de Navarra, Madrid, Spain; [3]Derio, Rubió Metabolomics, Vizcaya, Spain; [4]Internal Medicine, Clínica universidad de Navarra, Madrid, Spain; [5]Cardiology, Clínica universidad de Navarra, Madrid, Spain; [6]Radiology, Clínica universidad de Navarra, Pamplona, Spain; [7]Endocrinology and Nutrition, Clínica universidad de Navarra, Pamplona, Spain

Aims: Although cardiovascular prevention strategies based on traditional risk factors are effective, they may not fully capture subclinical atherosclerosis. Metabolic dysfunction–associated steatotic liver disease (MASLD) has emerged as a potential contributor to cardiovascular risk, yet its independent role in clinical risk stratification remains controversial. This study aimed to evaluate the ability of metabolomic-defined MASLD to predict coronary atherosclerotic burden beyond traditional risk factors.

Materials and Methods: A cross-sectional study was conducted in asymptomatic adults aged 40-80 years undergoing a comprehensive cardiovascular evaluation, including coronary computed tomography angiography. Patients with previous cardiovascular disease, excessive alcohol intake, or body mass index <25 kg/m^2 were excluded. Cardiovascular risk was categorized according to ESC guidelines. Hepatic status was assessed using the OWLiver® serum metabolomic test, classifying participants as healthy liver, metabolic dysfunction–associated steatotic liver (MASL), metabolic dysfunction–associated steatohepatitis (MASH), or MASH at risk (MASH with fibrosis stage ≥ 2). Coronary artery disease severity was classified using CAD-RADS.

"Cardiovascular risk excess" was defined as coronary disease exceeding that expected for each ESC risk category: CAD-RAD S ≥ 2 in low-to-moderate risk, CAD-RADS ≥ 3 in high risk, and CAD-RADS ≥ 4 in very high risk).

Results: A total of 144 participants were included (mean age 58.7 ± 8.6 years; 12.5% women). MASLD stratification showed healthy liver in 13.2%, MASL in 68.1%, MASH in 11.8%, and MASH at risk in 6.9% patients. CAD-RADS ≥2 was detected in 36.1% of individuals, and cardiovascular risk excess in 19.4%.

Advanced MASLD phenotypes (MASH and MASH at risk) were associated with a higher prevalence of cardiovascular risk excess across ESC categories, with a significant interaction between hepatic stage and baseline risk ($P < .05$). This enabled the definition of a composite phenotype termed "MASH at cardiovascular risk," representing 9% of the cohort and characterized by a markedly higher prevalence of both CAD-RADS ≥ 2 and cardiovascular risk excess, independently of age, sex, ESC risk category and coronary calcium score ($P < .01$). Inclusion of this phenotype improved discrimination and risk reclassification beyond traditional clinical models and coronary calcium. Clinically, this subgroup had substantially higher absolute risk, with an estimated number needed to screen of 2-3 to detect one case with CAD-RADS ≥ 2, and 3 to identify one individual with cardiovascular risk excess.

Conclusions: Metabolomic evaluation of MASLD using OWLiver is a potential tool to identify patients at higher risk of coronary artery disease, with potential clinical implications.

Abstract citation ID: lvag096.895

EP374 - ECE_1795 - RBC distribution width predicts progression of coronary artery calcification

Jong Suk Park[1], Jeong Kyu Kim[2] and Min Kyung Kim[3]

[1]Seoul, South Korea; [2]Yonsei University College of Medicine, Seoul, South Korea; [3]Hallym University College of Medicine, Seoul, South Korea

Background: Recent studies have reported that red blood cell distribution width (RDW) is a risk factor for cardiovascular disease; however, the relationship between RDW and coronary artery calcification (CAC) progression remains unclear. This study aimed to examine the association between RDW and CAC progression in asymptomatic Korean adults.

Methods: A total of 1166 subjects who underwent at least two CAC evaluations in a healthcare center were selected. The subjects were stratified into three groups based on RDW. CAC progression was defined as either the presence of incident CAC in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

CAC-free subjects at the baseline or an increase of ≥2.5 units between the square root of the baseline and follow-up CAC scores (CACSs) in subjects with detectable CAC at baseline.

Results: CAC progression was observed in 305 subjects (26.2%) during the 4.2-year follow-up period. The subjects were categorized into three groups based on their RDW, the baseline CACS and prevalence of CAC (CACS > 0) increased significantly with a gradual increase in the order of the RDW tertile. The follow-up CACS and the incidence of CAC progression increased significantly in the order of increasing RDW tertiles, the $\Delta\sqrt{}$transformed CACS values ((T1, 1.19 ± 1.96; T2, 1.39 ± 2.84; T3, 1.75 ± 3.74; $P < .05$) were found to be higher in individuals with higher baseline RDW. In addition, individuals with higher baseline RDW exhibited greater increases in $\Delta\sqrt{}$transformed CACS values. The results of the multivariate logistic regression analysis indicated that age, male, BMI, LDL-C level, presence of diabetes and hypertension, and observation time were independent predictors of CAC progression. Furthermore, RDW was also identified as an independent predictor of CAC progression (AOR = 1.298, 95% CI = 1.028-1.639, $P < .01$).

Conclusions: RDW is significantly associated with CAC progression; therefore, RDW has been identified as a potential predictor of CAC progression. Further prospective large-scale studies are required to clarify the mechanism of this relationship.

Abstract citation ID: lvag096.896

EP376 - ECE_3160 - Genetically predicted expression of the SGLT2 gene (SLC5A2) and risk of diabetic ketoacidosis

Silvano Da Silva[1], Vasiliki Lagou[2], Gabriel Mendieta[1], Maria Eduarda de Santana[1] and Maria Fernanda Gonçalves[1]
[1]Faculty of Medical Sciences of Santos (FCMS)—UNILUS—Lusíada University Center, Santos, Brazil; [2]Bioinformatics Multidisciplinary Environment, Federal University of Rio Grande do Norte, Natal, Brazil

Introduction: Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are widely used in type 2 diabetes treatment due to their metabolic, cardiovascular, and renal benefits. However, rare cases of diabetic ketoacidosis, including euglycemic presentations, have been reported, posing diagnostic and safety challenges in clinical practice. The mechanisms underlying individual susceptibility to ketoacidosis during SGLT2 inhibition are not fully understood. Mendelian randomization (MR) enables causal inference between an exposure and an outcome providing insights into biological mechanisms involved in disease risk in this approach, expression quantitative trait loci (eQTLs) can be used as instrumental variables (IVs) to estimate the causal effect of the expression of *SLC5A2*, which encodes the renal SGLT2, on the risk of diabetic ketoacidosis.

Aim: To evaluate the causal association between genetically predicted *SLC5A2* expression and diabetic ketoacidosis risk.

Methods: A two-sample MR study was conducted using summary-level genome-wide association data. Genetic instruments for *SLC5A2* expression were obtained from a publicly available cis-eQTL dataset of European ancestry ($N = 31\,306$) selecting genome-wide significant variants ($P < 5 \times 10^{-8}$) and performing clumping ($r^2 < 0.001$). Diabetic ketoacidosis was used as the primary outcome, with summary statistics derived from the FinnGen consortium (345 cases/183 185 controls). Causal estimates were calculated using the Wald ratio, with results expressed as odds ratios (OR) and 95% confidence intervals.

Results: After clumping, only one independent genome-wide significant eQTL (rs6565236) remained and was used as an IV in MR. Two-sample MR using this variant showed no evidence of a causal association between genetically predicted *SLC5A2* expression and diabetic ketoacidosis risk (OR 0.46, 95% CI 0.06-3.52; $P = .46$).

Conclusions: Genetically predicted *SLC5A2* expression was not causally associated with the risk of diabetic ketoacidosis. These findings suggest that the increased risk of ketoacidosis reported with SGLT2i is unlikely to be driven by inherited variation in the *SGLT2* pathway, highlighting the importance of clinical and pharmacodynamic factors in patient susceptibility.

Abstract citation ID: lvag096.897

EP377 - ECE_3691 - FABP4 and fatty liver index in obesity: insights across metabolic health categories

Barbara Bromińska, Aleksandra Krygier, Ewa Milewska-Kobos, Ewelina Szczepanek-Parulska and Marek Ruchala
Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznan, Poland

Introduction: Fatty Acid Binding Protein 4 (FABP4) is an intracellular lipid-binding protein involved in the regulation of fatty acid transport, lipid signalling, and cholesterol homeostasis. Elevated circulating FABP4 levels have been proposed as a potential biomarker for the detection and progression of liver steatosis. It represents the initial stage of non-alcoholic fatty liver disease (NAFDL), a condition strongly linked to metabolic dysregulation. Moreover, metabolic syndrome (MetS) is frequently associated with the development and severity of liver steatosis.

Objective: The goal of this study is to examine the association of FAB4 with liver steatosis in metabolic healthy obese (MHO), pre-metabolic syndrome(pre—MetS) and metabolic syndrome (MetS) patient.

Materials and Methods: We conducted a cross-sectional study including 103 treatment-naive obese patients (body mass index, BMI ≥ 30 kg/m^2). Participants were divided into three groups: MHO ($n = 18$), who did not meet any MetS criteria and were not using antihypertensive, glucose-lowering, or lipid-lowering medications; pre-MetS ($n = 32$), who met at least one MetS criterion (excluding waist circumference), but did not fulfil the full MetS definition; and MetS ($n = 53$). Multiple biochemical parameters were analysed. BMI and waist circumference (WC) were assessed. The fatty liver index (FLI) was calculated using a validated logistic regression formula. An FLI ≥ 60 was considered indicative of a high risk of liver steatosis.

Results: FABP4 levels differed significantly between the three groups ($P < .001$). Further analysis showed lower FABP4 in the MHO group compared with both METS ($P = .001$) and pre-METs ($P = .032$), while MetS and pre-METs did not differ ($P = .354$). FLI also differed significantly between groups ($P < .001$), with all pairwise comparisons showing significance. FLI was higher in the MetS group than in the other groups, and higher in the pre-MetS group than in the MHO group. FABP4 correlated with FLI ($r = 0.430$), GGTP ($r = 0.264$) and ALT ($r = 0.212$). In binary logistic regression, FABP4 was positively associated with liver steatosis (FLI ≥ 60) in both crude ($P < .001$; OR 42.530 95% CI 6.12-295.58) and adjusted models ($P < .001$; OR 1.22, 95% CI 1.078-1.378). FABP4 levels were

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

higher in patients with FLI ≥ 60 than in those with FLI < 60 ($P <$ .001).

Conclusions: Overall, our findings support FABP4 as a potential biomarker reflecting both metabolic phenotype and liver steatosis in obesity. Further studies are needed to clarify the role of FABP4 as a non-invasive indicator of NAFDL.

Abstract citation ID: lvag096.898

EP378 - ECE_2268 - Early setmelanotide treatment in a child with Bardet–Biedl syndrome type 5

Dimitrios Papadimitriou, Stavroula Kontogianni, Aspasia Michoula, Eleni Dermitzaki and Ioanna Grivea
Pediatric Endocrinology, Pediatrics, University of Thessaly, Larisa, Greece

Background: Bardet Biedl syndrome (BBS) is a rare genetic disorder classified among primary ciliopathies, characterized by multisystem involvement. Its estimated prevalence is 1 in100.000-160.000 live births. It is inherited in an autosomal recessive manner. Over 20 BBS genes have been identified. It is clinically diagnosed based on Beales criteria (>4 primary features or 3 primary and >2 secondary).

Case report: We present the case of a 4-year and 10-month-old girl with genetically confirmed Bardet-Biedl syndrome type 5 (BBS5), carrying a homozygous c.619-1G > C mutation in the BBS5 gene. The clinical phenotype included severe early-onset obesity (BMI SDS: +6.94), hypothyroidism, postaxial polydactyly of the right foot, intellectual RRoutine cardiac, renal, and ophthalmologic assessments (including echocardiogram, renal ultrasound, and fundus examination) were all normal. Marked hypothyroidism with TSH 24.5 IU/L but normal FT4 1.3 ng/dl was treated with levothyroxine 100 mcg/day to optimize thyroid function together with life style modification as possible and metformin suspension 500 mg × 2 p.o. Within 7 months BMI reduced from +6.94 to +5.81 SDS. Given the severity of obesity and the persistent hyperphagic behavior, following genetic confirmation of BBS5, the patient was considered for targeted therapy with setmelanotide, the melanocortin-4 receptor (MC4R) agonist approved for the treatment of obesity due to POMC, LEPR, and BBS-related deficiencies. BMI SDS further reduced from +5.81 to +4.64 within 5 months with marked resolution of hyperphagic behavior. This was the first pediatric case in Greece for which approval for setmelanotide treatment was granted by the National Health Organization (EOPYY). Treatment with setmelanotide was initiated under close clinical monitoring. The response was remarkable, with rapid and sustained reduction in appetite, improved satiety, and a significant decrease in body weight. After six months of therapy, the patient's BMI SDS decreased from +6.94 to +4.64, marking a clinically meaningful improvement. The only reported side effect was skin hyperpigmentation, a known class effect of MC4R agonists. However, this was well tolerated by the patient and family, particularly as the child had a naturally darker skin tone, and the change was not considered cosmetically distressing.

Conclusions: This case underscores the importance of early genetic diagnosis in syndromic obesity, as it allows for personalized therapeutic strategies. It also highlights the clinical efficacy and tolerability of setmelanotide in a young child with BBS5, contributing to the limited but growing body of real-world evidence supporting its use.

Abstract citation ID: lvag096.899

EP379 - ECE_2907 - Triglyceride-to–HDL cholesterol ratio as an independent predictor of incident diabetes in obese individuals: a KoGES-based analysis

Soo Jin Yun
Kyung Hee University, Seoul Campus, Seoul, South Korea

Background: The triglyceride-to–HDL cholesterol (TG/HDL) ratio has been proposed as a surrogate marker of insulin resistance and metabolic risk. However, its predictive value for incident diabetes mellitus (DM) among obese individuals remains unclear, particularly after accounting for baseline glycemic indices.

Methods: We analyzed data from the Korean Genome and Epidemiology Study (KoGES). Obesity was defined as a body mass index (BMI) ≥ 25 kg/m^2. Baseline TG/HDL ratio was calculated as triglycerides divided by HDL cholesterol. Incident DM was defined as the first occurrence of physician-diagnosed diabetes or use of antidiabetic medication during follow-up. Participants with diabetes at baseline were excluded. The association between log-transformed TG/HDL ratio and incident DM was evaluated using multivariable models adjusted for age, sex, fasting glucose, and HbA1c. Kaplan–Meier curves were constructed according to quartiles of TG/HDL ratio to compare cumulative DM incidence. Predictive performance was assessed using receiver operating characteristic (ROC) curve analysis by comparing the area under the curve (AUC) of a basic model (age, sex, fasting glucose, and HbA1c) with that of an extended model including TG/HDL ratio.

Results: Among obese participants without diabetes at baseline (n = 3956), 780 individuals developed DM during follow-up. Baseline log-transformed TG/HDL ratio was independently associated with incident DM after adjustment for age, sex, fasting glucose, and HbA1c (odds ratio per 1–standard deviation increase, approximately 1.32). Kaplan–Meier analyses demonstrated stepwise increases in cumulative DM incidence across increasing quartiles of TG/HDL ratio. The addition of log(TG/HDL) to a basic model including age, sex, fasting glucose, and HbA1c improved discrimination for incident DM, with the AUC increasing from 0.814 to 0.821 (ΔAUC = 0.0067).

Conclusions: In obese individuals, the TG/HDL ratio was independently associated with the risk of incident DM, even after adjustment for baseline glycemic indices. Furthermore, incorporation of TG/HDL ratio into a conventional risk model significantly improved the prediction of future DM. These findings suggest that the TG/HDL ratio may serve as a simple and clinically useful marker for diabetes risk stratification in obese populations.

Abstract citation ID: lvag096.900

EP382 - ECE_3302 - Clinical impact and long-term sustainability of advanced hybrid closed-loop systems therapy in type 1 diabetes patients in real-world settings

Ana Rocío Martínez Hartmann, Cristian Jesús Lucena Morales, Carlos López-Pereira, María Ángeles Cutilla Muñoz and Isabel Torres-Barea
Endocrinology and Nutrition Department, Endocrinology and Nutrition, Puerta del Mar Hospital, Puerta del Mar Hospital, Cadiz, Spain

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Objectives: To evaluate the real-world efficacy and safety of Advanced Hybrid Closed-Loop (AHCL) systems therapy by analyzing the evolution of glycemic parameters and insulin requirements before treatment initiation and during the first year of follow-up.

Material and Methods: An observational study was conducted on a cohort of 83 adult patients with T1D (mean age 32.7 ± 15.7 years; 66.3% female) treated at a specialized unit of Puerta del Mar Hospital. 86.7% who initiated treatment with the Minimed 780G system. 70% transitioned from multiple daily injections (MDI) therapy and 30% from open-loop therapy.

Glycemic variables and insulin doses were analyzed, comparing prior data against 1, 6, and 12 months of treatment. The Wilcoxon test was used for continuous variables and McNemar's test for analyzing changes in the proportion of patients achieving targets.

Results: Use of the AHCL system was associated with an early and significant improvement in metabolic control. Time in Range (TIR 70-180 mg/dL) increased significantly at all visits compared to baseline ($P < .001$). This improvement was achieved through a drastic reduction in Time Above Range (TAR > 180 mg/dL) and Time Below Range (TBR < 70 mg/dL) ($P < .001$).

The proportion of patients achieving the composite target (TIR ≥ 70% + TBR < 4% + CV < 36%) increased significantly from 11% at baseline to 56.6% at one year ($P < .001$).

Regarding insulin therapy, although the Total Daily Dose showed a non-significant reduction ($P = .07$), the decrease in basal insulin dose was significant ($P < .01$) compared to prior treatment. The system retention rate at one year was 87.8%.

Table 1 Evolution of metabolic parameters: Prior vs 1 year (Data expressed as Mean ± SD. *P*-value according to Wilcoxon test).

Parameter	Pre-AHCL	1 Year (AHCL)	*P*-value
HbA1c (%)	7.61 ± 1.15	6.95 ± 0.60	<.001
TIR (% 70-180)	55.9 ± 16.0	77.3 ± 10.3	<.001
TAR (% >180)	40.6 ± 17.5	20.2 ± 10.6	<.001
TBR (% <70)	4.22 ± 4.62	2.42 ± 2.12	.01
CV (% Variability)	37.0 ± 6.93	32.2 ± 4.79	<.001

Conclusions: Treatment with AHCL systems in patients with T1D proves to be highly effective and safe in real clinical practice, with early and sustained results. It optimizes glucometrics by halving time in hyperglycemia and minimizing time in hypoglycemia, alongside a reduction in glycemic variability. It notably optimizes the insulin profile, achieving these goals with a reduced need for insulin, primarily basal insulin.

Abstract citation ID: lvag096.901

EP383 - ECE_2964 - Comparison of the clinical effectiveness of three different dietary patterns in overweight and obese adults

Christina Balamoti and Alexandra Bargiota
Department of Endocrinology and Metabolic Diseases, University Hospital of Larissa, Larissa, Greece

Introduction: A large proportion of adults are overweight or obese. Digital health strategies are increasingly used for obesity management.

Objective: We studied the effectiveness of three different hypocaloric dietary interventions in overweight and obese adults, their weight-loss sustainability, adherence to the Mediterranean diet and satisfaction levels.

Methods: Randomized 5-month trial. 158 adults (mean age 49.5 ± 10.6 years) were stratified by BMI and age and allocated to a Fixed-Daily Diet (FDD), Multiple-Choice Diet (MCD), or App-Based Diet (ABD) with an energy deficit of 563 kcal/day. Effectiveness was assessed by changes in body weight (BW), percentage body weight (%BW), body fat percentage (BF%), waist circumference (WC), hip circumference (HC), and waist-to-hip ratio (WHR). Adherence to Mediterranean diet was assessed by MedDiet Score (low ≤20, moderate 21-35, high 35-55). Post-intervention dietary satisfaction assessed by the Diet Satisfaction Questionnaire (DSat-28).

Results: Baseline characteristics were similar across groups. At 5 months, the ABD group achieved greater absolute BW loss compared with the FDD and MCD groups (−8.0 ± 4.0 kg vs −4.8 ± 5.3 in FDD and −4.7 ± 3.7 in MCD; $P = .003$) and greater %BW loss (−8.3 ± 4.5% vs −5.4 ± 5.3% in FDD and −5.0 ± 3.7% in MCD; $P = .006$). ABD showed greater reductions in %BF (−4.9 ± 2.8% vs −2.8 ± 2.5% in FDD and −3.0 ± 2.0% in MCD; $P = .001$), in minimum WC (−7.6 ± 4.2 cm vs −4.5 ± 5.0 and −3.4 ± 3.4; $P < .001$), in umbilical WC (−7.1 ± 3.4 cm vs −5.3 ± 5.1 and −4.0 ± 4.4; $P = .009$), in HC (−6.4 ± 3.0 cm vs −4.1 ± 3.8 and −3.5 ± 3.5; $P = .002$), and in WHR (−0.028 ± 0.024 vs −0.012 ± 0.034 in FDD and −0.008 ± 0.026 in MCD; $P = .010$). Adherence to Mediterranean diet was moderate and comparable across groups (FDD: 26.1 ± 6.2; MCD: 27.7 ± 5.3; ABD: 28.2 ± 5.8; $P = .145$). Dietary satisfaction was higher in the ABD group compared with the FDD and MCD groups (113.0 ± 12.5 vs 100.9 ± 18.3 in FDD and 100.7 ± 20.4 in MCD; $P = .006$).

Conclusions: The ABD found to be the most effective intervention for improving the assessed anthropometric parameters with the highest satisfaction score, suggesting that mobile nutrition applications may serve as valuable tools to support dietary management and weight control.

Abstract citation ID: lvag096.902

EP385 - ECE_1876 - Dual activation of PPARα and PPARγ by Liquiritigenin attenuates hepatic lipid accumulation and insulin resistance through AMPK signaling

Hae Jin Kim, Yu Jung Heo, Jieun Park, Nami Lee, Sung-E Choi, Ja Young Jeon, Seung Jin Han, Dae Jung Kim and Kwan-Woo Lee
Ajou University School of Medicine, Institute of Medical Science, Suwon, South Korea

Metabolic dysfunction-associated steatotic liver disease (MASLD) is characterized by excessive triglyceride accumulation and chronic inflammation in the liver, driven largely by impaired fatty acid oxidation and disrupted metabolic signaling. Liquiritigenin (LQ), a flavonoid derived from licorice root, exhibits various biological properties. However, its specific role in mitigating MASLD and its associated metabolic disorders has not yet been clearly

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

elucidated. In this study, we evaluated the effects of LQ in both a high-fat diet (HFD)-induced mouse model of MASLD and HepG2 cells. C57BL/6J mice were fed a HFD for 14 weeks, and LQ (20 or 40 mg/kg) was administered daily for the final 2 weeks before sacrifice. LQ treatment significantly reduced the elevated levels of triglycerides, aspartate aminotransferase, and alanine aminotransferase observed in HFD-fed mice. Moreover, LQ alleviated the HFD-induced glucose intolerance and insulin resistance, as evidenced by intraperitoneal glucose and insulin tolerance tests. Following LQ treatment, phosphorylation of AMPK and the protein expression levels of SIRT1, PGC-1α, PPARα, and PPARγ were markedly increased. The expression of SREBP1 was significantly decreased, while the expression of fatty acid oxidation-related genes was upregulated. In FFA-treated HepG2 cells, LQ activated AMPK signaling, enhanced fatty acid oxidation gene expression, improved insulin sensitivity (p-AKT, p-IRS1), and suppressed inflammatory cytokines (IL-6, IL-1β, TNF-α). Notably, pharmacological inhibition of AMPK abolished LQ-induced enhancements in fatty acid oxidation. Collectively, these findings demonstrate that LQ ameliorates MASLD by activating the AMPK-SIRT1-PGC-1α-PPARα/γ axis to promote hepatic fatty acid oxidation, suppress lipogenesis, enhance insulin sensitivity, and attenuate inflammation, positioning LQ as a promising therapeutic candidate for MASLD.

Abstract citation ID: lvag096.903

EP386 - ECE_2716 - Perceived stigma and the impact of healthcare professionals' language on people with type 1 diabetes: a single-center study

Patrícia Brito[1], Carlos Lucas Calheno[2], Rita Ribeiro[1], Nuno Faria[1], Olinda Marques[1] and Diana Borges Duarte[1]
[1]*Endocrinology Department, Unidade Local de Saúde de Braga, Braga, Portugal;* [2]*Escola de Medicina da Universidade do Minho, Braga, Portugal*

Introduction: Type 1 diabetes mellitus (T1DM) requires intensive daily management and can generate significant emotional burden, influenced both by the stigma associated with the disease and by the language used during clinical consultations. This study evaluated the perception of stigma and the impact of clinical communication in adults with T1DM followed at our department.

Methods: This was a cross-sectional observational study involving 134 adults with T1DM. Data collection included sociodemographic and clinical variables, supplemented by a questionnaire composed of the "Guilt and judgement" and "Identity concerns" subscales from the Type 1 Diabetes Stigma Assessment Scale, the Problem Areas in Diabetes—5 scale and questions about communication experiences and linguistic perception.

Results: Despite generally good metabolic control and widespread use of technology, high levels of stigma and emotional distress were observed. "Guilt and judgement" stigma was more prevalent among women, younger individuals, those with higher education levels and those with shorter disease duration. The "Identity concerns" subscale scored higher among participants who perceived their economic situation as unfavorable and among those not native to Portugal. Distress associated with T1DM was higher among women, those in a relationship, individuals diagnosed at older ages, and participants with chronic complications, and was significantly associated with the stigma subscales evaluated. The absence of close contacts with T1DM was linked to higher stigma, while experiences of rejection or bullying due to the disease were consistently associated with higher levels of both stigma and distress. Additionally, 52.2% of participants reported a negative impact of clinical communication, and 90.3% attributed high importance to the language used during consultations.

Conclusions: Stigma and emotional distress are central elements in the experience of living with T1DM. These results reinforce the need to integrate psychosocial dimensions and person-centered communication strategies into T1DM management.

Abstract citation ID: lvag096.904

EP388 - ECE_3156 - Genetic evaluation of glycemic pathways targeted by GLP-1 receptor agonists and the risk of anterior ischemic optic neuropathy

Silvano Da Silva[1], Vasiliki Lagou[2], Vinicius Ribeiro[1] and Camilly de Paiva[1]
[1]*Faculty of Medical Sciences of Santos (FCMS)—UNILUS—Lusíada University Center, Santos, Brazil;* [2]*Bioinformatics Multidisciplinary Environment, Federal University of Rio Grande do Norte, Natal, Brazil*

Introduction: Anterior ischemic optic neuropathy (AION) is a rare but vision-threatening condition associated with vascular and metabolic risk factors. Although recent pharmacovigilance reports have suggested a possible link between glucagon-like peptide-1 receptor agonists (GLP-1RAs) and non-arthritic AION, the causal mechanisms remain unclear. GLP-1RAs exert broad metabolic effects, particularly on glycemic regulation. Mendelian randomization (MR) is a method that allows causal inference between an exposure and an outcome using genetic variants as instrumental variables (IVs).

Aim: To assess whether genetic liability to glycemic traits is causally associated with the risk of AION using a two-sample Mendelian randomization approach.

Methods: A two-sample MR study was conducted using summary-level genome-wide association data. Genetic instruments for glycemic traits (HbA1c) were obtained from two independent GWAS datasets (ieu-b-4841 and ieu-b-103) at genome-wide significance ($P < 5 \times 10^{-8}$) and clumped for clumped to obtain approximately independent signals based on linkage disequilibrium ($r^2 < 0.001$, 10 000 kb). The outcome was anterior ischemic optic neuropathy (AION) from the FinnGen consortium (finn-b-DM_AION). Causal estimates were derived primarily using the inverse variance-weighted (IVW) method, with weighted median, MR-Egger, and mode-based as additional MR methods for checking consistency. Heterogeneity and directional pleiotropy were assessed using Cochran's Q statistics and the MR-Egger intercept.

Results: Genome-wide significant instruments for HbA1c were obtained from two independent GWAS. For the first MR analysis (ieu-b-4841), nine variants were used as IVs; IVW showed no causal effects of HbA1c on AION (OR 1.53, 95% CI 0.74-3.16, $P =$ .25), with consistent null findings across other MR methods

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and no evidence of heterogeneity (Q $P = .55$) or pleiotropy (Egger $P = .38$). Similarly, the second MR analysis (ieu-b-103) on 11 IVs revealed no significant causal estimates (IVW: OR 1.88, 95% CI 0.26-13.77, $P = .54$), with no evidence of heterogeneity (Q $P = .52$) or directional pleiotropy (Egger $P = .85$).

Conclusions: Our analyses do not support a causal effect of genetic liability to glycemic traits on the risk of AION, suggesting that a potential association between GLP-1 receptor agonists and AION might be primarily mediated by other, non-glycemic pathways.

Abstract citation ID: lvag096.905

EP389 - ECE_2263 - Comparative analysis of corneal and epithelial thickness in patients with type 2 diabetes mellitus

Iryna Havryliak[1] and Natalia Greben[2]
[1]*Ophtalmology, Bogomolets National Medical University, Kyiv, Ukraine;* [2]*Bogomolets National Medical University, Kyiv, Ukraine*

Diabetes mellitus can affect all ocular structures, from the retina to the cornea. Corneal alterations collectively referred to as diabetic keratopathy include recurrent corneal erosions, persistent corneal ulcers, severe dry eye disease, reduced corneal sensitivity, impairment of epithelial and endothelial barrier functions, and stromal edema. Central corneal thickness is an important clinical parameter used to assess the condition of the cornea prior to refractive surgery, detect corneal dystrophies and ectasias, and serve as an indicator of endothelial function, which plays a key role in maintaining the structure and function of the cornea.**Materials and Methods:** The study included 44 patients with type 2 diabetes, divided into groups with a history of more than 10 years and less than 10 years, and a control group of 10 people (healthy patients). Visometry, biomicroscopy, Schirmer's test, tear break-up time, and central corneal thickness were performed.

Results: Patients with DM were divided into two groups according to disease duration: less than 10 years (Group 1) and more than 10 years (Group 2).

Central corneal thickness (CCT) was significantly higher in patients with DM compared to the control group. The mean CCT was 556.0 ± 23.1 μm in Group 1 and 581.1 ± 24.4 μм in Group 2, compared to 534.1 ± 18.8 μм in the control group ($P < .05$). Patients with disease duration longer than 10 years demonstrated a statistically significant increase in CCT compared to those with a shorter duration ($P < .05$).

Schirmer's test values were significantly reduced in both diabetic groups compared to controls ($4{,}5 \pm 0.4$ mm and $4{,}3 \pm 0.6$ mm and $11{,}2 \pm 2{,}2$ mm, respectively; $P < .05$), with the lowest values observed in patients with longer disease duration.

Tear break-up time (TBUT) was also significantly decreased in patients with DM, particularly in Group 2 ($4{,}2 \pm 0{,}12$ s) compared to Group 1 ($3{,}8 \pm 0{,}06$ s) and the control group ($2{,}6 \pm 0{,}04$ s, $P < .05$).

Conclusions: Patients with type 2 diabetes mellitus have structural and functional changes in the cornea, including increased CCT and changes in the surface of the eye, compared to healthy individuals. The severity of these changes increases with the duration of the disease, suggesting a progression of the diabetic corneal pathology. Assessment of central corneal thickness and ocular surface parameters may be useful for early detection and monitoring of diabetic keratopathy.

Abstract citation ID: lvag096.906

EP390 - ECE_3121 - Role of FIB-4 in predicting TOAST and recurrence in diabetics with acute ischemic stroke

Pilar Pérez Reyes[1], Jerónimo Cruces Párraga[2], Pablo Doblas Ráez[2], Francisco Javier Serrano García[2], Julia Silva Fernandez[1] and Mª Rosa Alhambra Expósito[1,3]
[1]*Unidad de Gestión Clínica de Endocrinología y Nutrición, Hospital Universitario Reina Sofía, Córdoba, Spain;* [2]*Unidad de Gestión Clínica de Neurología, Hospital Universitario Reina Sofía., Córdoba, Spain;* [3]*Endocrinología y Nutrición, Hospital Universitario Reina Sofía, Córdoba, Spain*

Background and Aims: FIB-4 has been associated with a higher prevalence of atrial fibrillation (AF), increased stroke recurrence and type of stroke according to TOAST (Trial of Org 10172 in Acute Stroke Treatment). The aim of this study was to determine the prevalence of type 2 diabetes mellitus (T2DM) in patients with ischemic stroke, as well as to assess if FIB-4 levels in patients with T2DM are linked to these factors.

Materials and Methods: Prospective study of patients admitted in 2024 with acute ischemic stroke. Presence of AF and previous infarcts according to HbA1c and FIB-4 levels in diabetic and non-diabetic patients were evaluated. SPSS v.29 was used.

Results: 265 patients (64.5% men, 35.5% women) with ischemic stroke. Mean age of 68.68 ± 13.04 years. T2DM was present in 25.6% ($n = 68$), 0.75% ($n = 2$) had previously been diagnosed with type 1 diabetes (T1DM). Overall mean HbA1c level was $6.19\% \pm 1.01$, and $7.11\% \pm 1.25$ among patients with T2DM. Overall mean FIB-4 was 1.86 ± 1.07 and 1.83 ± 0.91 in patients with T2DM, with no significant differences in FIB-4 between patients with and without T2DM ($P = .201$).

In patients with T2DM, atherosclerosis stroke was the most frequent (46.6%), followed by cardioembolic stroke (27.6%). Higher FIB-4 values were significative associated with cardioembolic stroke overall ($P < .001$) and in patients without T2DM ($P = .006$). We found no significative differences between TOAST and FIB-4 in patients with T2DM ($P = .103$). No statistically significative differences were found between HbA1c and TOAST overall ($P = .105$) and in patients with T2DM ($P = .700$).

Presence of old infarcts at the diagnosis was significative higher in patients with T2DM (51.4% vs 34.71%, $P = .014$). Higher FIB-4 values were significative associated with presence of old infarcts in patients with T2DM ($P = .017$) but it was not in patients without T2DM ($P = .808$). AF was present at hospital admission in 29.95% of patients overall and 27.1% in patients with T2DM. Higher FIB-4 scores were statistically significative associated with the presence of AF at admission, regardless of T2DM status ($P = .010$ T2DM patients; $P < .001$ non-T2DM patients).

Conclusions: T2DM has a considerable prevalence among admissions due to ischemic stroke at our hospital. No significant associations were found between FIB-4 and TOAST classification in T2DM patients in this sample. Higher FIB-4 scores were associated with AF and old infarcts presence in T2DM patients, suggesting that follow-up care for T2DM patients

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

should consider AF and elevated FIB-4 scores. Further studies with larger sample sizes are warranted.

Abstract citation ID: lvag096.907

EP391 - ECE_3647 - Early endothelial dysfunction in type 1 diabetes mellitus: a multimodal assessment using flow-mediated dilation, carotid intima-media thickness, and inflammatory biomarkers

D. Amulya Reddy[1,2], Vijay Sheker Danda[1], Vivek Kyatham[1], Ann Elias[1], Venu Gopal Reddy K.[1] and Bhanusree Kalava[1]
[1]*Hyderabad, India;* [2]*Department of Endocrinology, Gandhi Medical College, Hyderabad, India*

Background: Individuals with type 1 diabetes mellitus (T1DM) are at increased risk of premature cardiovascular disease, with endothelial dysfunction representing an early and potentially reversible stage of vascular injury. Indian data integrating functional, structural, and inflammatory markers of vascular health in youth with T1DM remain limited.

Objective: To assess endothelial dysfunction in children and adolescents with T1DM and examine its association with glycemic control and duration of diabetes using flow-mediated dilation (FMD), carotid intima-media thickness (CIMT), and inflammatory biomarkers.

Methods: In this single-centre cross-sectional study, 41 patients with T1DM (median age 15 years) and 41 age- and sex-matched healthy controls were evaluated. Endothelial function was assessed using brachial artery FMD, including time-to-peak dilation and percentage peak FMD. Structural vascular changes were assessed using CIMT. Serum high-sensitivity C-reactive protein (hsCRP) and endothelin-1 (ET-1) were measured using ELISA. Correlations with HbA1c and duration of diabetes were analysed.

Results: Compared to controls, patients with T1DM demonstrated significantly reduced percentage peak FMD [6.55% (IQR 5.83-7.17) vs 8.21% (7.50-8.74); $P < .001$] and markedly delayed time-to-peak FMD [240 s (120-240) vs 30 s (30-60); $P < .001$], despite comparable baseline and peak brachial artery diameters. CIMT did not differ significantly between groups. Both hsCRP and ET-1 levels were significantly elevated in the T1DM group ($P = .003$ and $P < .001$ respectively). Percentage peak FMD correlated negatively with HbA1c ($\rho = -0.52$, $P < .001$) and duration of diabetes ($\rho = -0.33$, $P = .033$), while CIMT correlated positively with diabetes duration but not HbA1c.

Conclusions: Children and adolescents with T1DM exhibit early endothelial dysfunction characterized by impaired and delayed FMD responses, preceding structural vascular changes. Elevated hsCRP and ET-1 levels indicate early inflammatory and endothelial activation. Non-invasive vascular functional assessment may improve early cardiovascular risk stratification in youth with T1DM.

Abstract citation ID: lvag096.908

EP392 - ECE_3710 - Evaluation of diabetes related distress in adolescents with type 1 diabetes during the transition to adult care

Soukaina Lahlou, Nassim Essabah Haraj, Malak Iggar, Siham El Aziz and Asma Chadli
Clinical Neuroscience and Mental Health Laboratory, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Ibn Rochd University Hospital, Casablanca, Morocco

Introduction: The transition from adolescence to adulthood is a sensitive period characterized by major physical, psychological, and social changes. For adolescents living with type 1 diabetes (T1D), this phase involves a heavy daily treatment burden and complex self-management demands, which can lead to emotional distress and reduced adherence to care.

The aim of this study was to assess diabetes-related distress in adolescents with T1D and to evaluate its impact on glycemic control.

Materials and Methods: This was a descriptive cross-sectional study including adolescents aged 15 to 18 years with type 1 diabetes, followed in the Endocrinology Department between January 2021 and December 2024. Diabetes-related emotional distress was assessed using the Problem Areas in Diabetes (PAID) questionnaire. Clinical, biological, and therapeutic data were collected from medical records. Statistical analysis was performed using SPSS software.

Results: A total of 100 patients were included, with a female-to-male ratio of 1.5. The mean age was 16 years, and the mean duration of diabetes was 5 years. The mean HbA1c was 10.6%, reflecting poor glycemic control.

The mean PAID score was 27%, with moderate to high distress observed in 91% of patients. A significant positive correlation was found between PAID score and HbA1c ($P < .001$), indicating that higher emotional distress was associated with poorer glycemic control.

Conclusions: Diabetes-related emotional distress is common among adolescents with T1D and is associated with suboptimal glycemic control. These findings highlight the importance of integrating psychological assessment and support into routine diabetes care.

Abstract citation ID: lvag096.909

EP393 - ECE_1290 - Modulation of mitochondrial function and Ca^{2+} dynamics by semaglutide in pancreatic beta cells

Éverton Vogt[1], Eloisa Vilas-Boas[2], Debora Rocha[1], Camille Caldeira[1] and Alicia Kowaltowski[1]
[1]*Departamento de Bioquímica, Instituto de Química and Centro de Metabolismo CoMeta, São Paulo, Brazil;* [2]*Faculdade de Ciências Farmacêuticas, São Paulo, Brazil*

GLP-1 receptor agonists such as semaglutide regulate multiple stimulus–secretion coupling components in pancreatic beta cells, integrating metabolic, ionic, and secretory pathways. These agents influence mitochondrial ATP production, membrane excitability, and Ca^{2+} handling, all of which are essential for insulin secretion. Despite their clinical relevance, the mechanistic links between GLP-1 signaling, mitochondrial remodeling, and intracellular Ca^{2+} dynamics remain incompletely defined. This study aimed to determine whether semaglutide alters mitochondrial morphology and function, oxygen consumption, Ca^{2+} dynamics, and the immunocontent of ion-transport proteins in INS-1E beta cells. Cells were treated with 0-200 nM semaglutide for 24–72 h and evaluated using fluorescence microscopy for

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

mitochondrial morphology, Seahorse extracellular flux analysis for respiratory parameters, FURA-2 imaging for Ca^{2+} dynamics (in the presence or absence of extracellular Ca^{2+} and in the presence of specific inhibitors), Amplex Red assays for extracellular H_2O_2 production, and automated Western protein detection. Semaglutide did not affect cell viability. Basal and ATP-linked oxygen consumption decreased over time, whereas non-mitochondrial oxygen consumption increased in a dose-dependent manner, with no differences in glucose-stimulated H_2O_2 formation. Mitochondrial volume decreased over time, whereas sphericity and branching parameters increased independently of semaglutide concentration. Semaglutide increased cytosolic Ca^{2+} in a dose-dependent manner in the presence of extracellular Ca^{2+}; this response was abolished under Ca^{2+}-free conditions and by verapamil or glibenclamide, indicating dependence on VDCCs and upstream modulation of KATP channels. Inhibitors of mitochondrial Ca^{2+} transport (CGP and ruthenium red) eliminated the effect, and thapsigargin suppressed the signal, indicating contributions from both mitochondrial uptake and ER store mobilization. Store-operated calcium entry was reduced only at 200 nM semaglutide. MCU protein content increased exclusively at 200 nM, whereas NCLX remained unchanged. Together, these preliminary findings indicate that semaglutide integrates bioenergetic and Ca^{2+}-signaling responses in beta cells through combined modulation of mitochondrial remodeling, respiratory activity, and organelle-dependent Ca^{2+} handling.

Abstract citation ID: lvag096.910

EP394 - ECE_3560 - Effect of a 6-months culturally tailored lifestyle intervention on weight, waist circumference and HbA1c in multi-ethnic patients with type 2 diabetes

Sabrina Berti[1,2], Vania Campanella[1,2], Silvia Ricci Bitti[1], Michele Baldari[1,2], Valentina Lo Preiato[2], Flaminia Fanelli[1,2], Emmanuele Capobianco[1,2], Cristiana Cantone[1,2], Guido Di Dalmazi[1,2] and Uberto Pagotto[1,2]

[1]Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna, Italy; [2]Endocrinology and Diabetes Prevention and Care Unit, IRCCS Policlinico di S. Orsola, Bologna, Italy

Background and Aims: In type 2 diabetes, ethnic background can influence dietary habits and response to standard nutritional interventions. This study, part of the ongoing PLANEAT Horizon Europe Project, aims to evaluate the effectiveness of a simple culturally tailored, sustainability-oriented lifestyle intervention on body weight, waist circumference, and HbA1c in patients living in Italy with different cultural backgrounds.

Methods: All patients had Type 2 diabetes. At baseline, patients chose between a lifestyle intervention that could integrate, at their request, culturally tailored dietary advice, plus supervised weekly physical activity ("intervention group"), or general Mediterranean dietary recommendations alone ("control group"). At baseline, 3 months, and 6 months, all patients underwent medical visits with antidiabetic therapy adjustment if needed and received dietary counselling.

Results: A total of 101 patients were enrolled (South Asia $n = 27$; North Africa $n = 25$; Eastern Europe $n = 23$; Italy $n = 26$). South Asians and North Africans were younger than Italians (48 ± 7 and 51 ± 9 vs 64 ± 6 years; $P < .001$ and $P = .02$). Waist circumference was lower in South Asians than in all other groups (91 ± 9 vs 106 ± 11 cm; $P < .001$). BMI was lower in South Asians compared with Italians and Eastern Europeans (27.0 ± 4.4 vs 31.6 ± 4.6 and 31.9 ± 5.0 kg/m^2; $P = .01$ for both). HbA1c was similar across groups.

Overall, 42 (41.6%) patients chose the intervention group and 59 (58.4%) the control group. Compared with Italians (reference group), Eastern Europeans were less likely to choose the lifestyle intervention (OR 0.26, 95% CI 0.08-0.87; $P = .03$), while the other groups showed similar probabilities. In the intervention group, all patients requested culturally tailored dietary advice.

At 3 ($n = 89$) and 6 months ($n = 69$), a significant weight loss was observed (6 months: -1.7 ± 5.3% of body weight vs baseline, $P = .019$). However, the intervention was not superior to general dietary recommendations in terms of weight loss (6-month percentage weight change from baseline: -1.3 ± 4.2% in the intervention group vs -1.8 ± 6.1% in the control group; $P = .70$). No significant interaction between ethnic origin and intervention group on weight loss was found (p for interaction = 0.095).

HbA1c significantly improved from baseline to 6 months (57.1 ± 18.8 vs 50.5 ± 8.3 mmol/mol; $P = .02$), with no differences among cultural groups ($P = .106$) or between intervention or control ($P = .132$, P for interaction = 0.899). Waist circumference did not improve significantly over time or within specific ethnic groups.

Conclusions: So far, culturally tailored lifestyle intervention did not show to be superior to general dietary recommendations on weight, waist circumference, or HbA1c reduction.

Abstract citation ID: lvag096.911

EP395 - ECE_1221 - Linking stress-related behavior to adipose tissue function in vulnerable and resilient mice

Adrian Segev, Saumya Kishor Mehta, Suparna Sen, Ayala Wollman, Albert Pinhasov and Tovit Rosenzweig

Department of Molecular Biology, and The Adelson School of Medicine, Ariel University, Ariel, Israel

Chronic stress contributes to multiple morbidities, including metabolic disorders. Our previous work demonstrated that stress-coping phenotypes are closely associated with obesity-related metabolic dysfunction and white adipose tissue (WAT) impairment in mouse models of stress vulnerability and stress resilience. When challenged with a high-fat diet (HFD), stress-vulnerable mice developed obesity-associated metabolic alterations, whereas stress-resilient mice were largely protected.

Although WAT is well recognized as a central regulator of metabolic health, the bidirectional relationship between behavioral regulation and adipose tissue function remains poorly understood. The present study aimed to investigate the interplay between WAT function and mood-related behaviors, with a particular focus on stress-coping characteristics. Specifically, we examined whether pharmacological interventions targeting either mood regulation (paroxetine, an SSRI) or adipose tissue function (pioglitazone, a PPARγ agonist) exert reciprocal effects on behavioral outcomes and WAT functionality in stress-vulnerable mice. In parallel, we assessed the impact of chronic stress exposure on WAT function in stress-vulnerable and stress-resilient mice.

The study was conducted using a unique, selectively-bred mouse model. Animals were classified as dominant (Dom) or

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

submissive (Sub) based on a dominance–submissiveness relationship test, in which mice compete for access to sweetened milk. Stress-vulnerable (Sub) mice were treated for four weeks with paroxetine or pioglitazone while maintained on a standard diet (STD). Both treatments improved social behavior in the three-chamber test. Anxiety-like behavior in the open-field test was reduced only by pioglitazone, whereas exploratory activity in the hole-board test and active coping strategies in the forced swim test were enhanced by both drugs.

To assess adipose tissue responses, stromal vascular cells were isolated from WAT. Both treatments enhanced preadipocyte proliferation and adipogenic differentiation in subcutaneous depots, while impairments persisted in visceral depots.

To further examine the effects of stress on adipose tissue function, mice were subjected to an unpredictable chronic mild stress (UCMS) paradigm for three weeks. Preadipocyte proliferation and adipogenesis in subcutanous WAT were higher in Dom than in Sub mice, accompanied by a greater abundance of preadipocytes as revealed by FACS analysis. UCMS further enhanced proliferation and differentiation in Dom mice, while suppressing these processes in Sub mice.

In summary, pharmacological targeting of either mood or adipose tissue induced parallel behavioral and adipose cellular changes. Moreover, chronic stress differentially modulated adipose tissue function in stress-vulnerable vs stress-resilient mice, supporting a bidirectional link between stress-related behavior and adipose tissue plasticity.

Abstract citation ID: lvag096.912

EP396 - ECE_1460 - Impact of subclinical hypothyroidism on postprandial triglycerides and MASLD in obese individuals with and without type 2 diabetes mellitus

Lavina Patnaik[1], Sv Madhu[1], Nishant Raizada[1] and Shuchi Bhatt[2]
[1]*Endocrinology, University College of Medical Sciences, New Delhi, India;* [2]*Radiology, University College of Medical Sciences, New Delhi, India*

Introduction: Diabetes and obesity are associated with increased cardiometabolic risk, largely due to dyslipidemia, particularly postprandial hypertriglyceridemia. Postprandial hypertriglyceridemia has been associated with increased risk of Metabolic dysfunction–associated Steatotic Liver Disease (MASLD) and cardiovascular complications. Subclinical hypothyroidism (SCH) is also linked to increased postprandial triglyceride (PPTG) levels and its adverse consequences. Thus, SCH could further exaggerate the cardiometabolic risk in individuals with obesity and type 2 diabetes mellitus. Extrathyroidal effects of thyroid stimulating hormone (TSH), such as effects in adipose tissue and hepatocytes, along with modulation of bile acid metabolism and fibroblast growth factor-21 (FGF-21) levels, may be important links in this enhanced cardiometabolic risk in such patients. Hence, we conducted this study to look at the association of SCH with PPTG, total bile acid and FGF-21 levels and MASLD in obese individuals with and without type 2 diabetes mellitus.

Methodology: This cross-sectional analytical study included 212 overweight/obese participants divided into four groups: obese type 2 diabetes with and without SCH, obese non-diabetic with and without SCH. Postprandial triglyceride levels were assessed by oral fat challenge at 0, 2, 4, 6, and 8 hours. Total bile acids and FGF-21 were measured using enzymatic and ELISA methods, respectively. MASLD was graded by ultrasonography. Data were analyzed using ANOVA, Mann–Whitney and chi-square tests (SPSS v29).

Results: Participants with coexistent type 2 diabetes and SCH had the highest PPTG area under curve (AUC) and peak PPTG levels compared to other groups ($P < .05$). Individuals with SCH without diabetes had significantly lower PPTG-AUC and peak PPTG than their euthyroid counterparts. No significant differences in total bile acids or FGF-21 were observed between groups. PPTG-AUC and baseline and 2-hour post-fat challenge triglyceride levels were significantly associated with MASLD severity ($P < .05$), but bile acid and TSH levels were not.

Discussion and Conclusions: This study highlights the impact of coexistence of type 2 diabetes and SCH in obese individuals who showed highest postprandial hypertriglyceridemia, compared to obese with diabetes only, thereby indicating increased cardiometabolic risk as a result of SCH. Obese individuals without diabetes or SCH showed higher PPTG AUC and peak triglycerides than obese with SCH alone, suggesting a differential effect of TSH on lipid metabolism in individuals with and without type 2 diabetes mellitus. Thus, SCH modifies PPTG and metabolic risk in those with both obesity and type 2 diabetes, supporting consideration of treatment of SCH to reduce risk.

Abstract citation ID: lvag096.913

EP397 - ECE_1506 - Beyond BMI: obesity phenotype with sarcopenia

Sadaf Ali[1,2,3], Gabriela Da Silva Xavier[1] and Tarekegn Hiwot[4]
[1]*University of Birmingham, Birmingham, United Kingdom;* [2]*Metabolism and Systems Science, University of Birmingham, Birmingham, United Kingdom;* [3]*Institute of Metabolism & Systems Sciences, Birmingham, United Kingdom;* [4]*University Hospitals Birmingham, Birmingham, United Kingdom*

Background: Obesity is typically associated with preserved or increased lean mass; however, certain monogenic forms present with a contrasting and clinically significant phenotype characterised by **marked reductions in muscle mass alongside excess adiposity**. This **sarcopenic obesity phenotype** is recognised as one of the most dangerous body-composition profiles, conferring **higher mortality, greater functional decline and accelerated metabolic deterioration** in middle-aged and older adults. Monogenic obesity syndromes offer a unique model for understanding these mechanisms, as metabolic dysfunction arises independently of overall adiposity. Emerging evidence suggests that defects in skeletal muscle oxidative capacity and mitochondrial structure may underlie the profound insulin resistance observed in these individuals. Defining how altered body composition and muscle bioenergetics interact is therefore critical to understanding disease pathophysiology and guiding targeted treatment.

Methods: Ten adults with monogenic obesity of Alstrom syndrome were compared with ten BMI-matched obese controls. Body composition (fat-free mass [FFM], total body water [TBW], and predicted regional muscle mass) was assessed by bioimpedance. Metabolic profiling included fasting glucose, insulin, c-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

peptide, HbA1c, lipid panels, HOMA-IR, and liver enzymes. High-resolution respirometry on freshly isolated skeletal muscle fibres quantified oxidative phosphorylation capacity. Electron microscopy (EM) assessed mitochondrial area, number, aspect ratio and form factor. Statistical significance was set at $P \leq .05$.

Results: Despite comparable BMI, participants with monogenic obesity exhibited a pronounced **sarcopenic phenotype**, with significantly lower FFM, TBW and muscle mass across trunk and limbs (all $P \leq .01$). Metabolic evaluation revealed markedly elevated fasting glucose ($P = .003$), hyperinsulinaemia and increased c-peptide ($P \leq .05$), alongside higher HbA1c and HOMA-IR ($P \leq .05$), indicating **severe insulin resistance**. Liver enzymes, including ALT and alkaline phosphatase, were significantly raised ($P \leq .05$), suggesting hepatic involvement.

High-resolution respirometry demonstrated a **global reduction in mitochondrial oxidative phosphorylation**, with significantly lower oxygen flux across all substrates. Overall mitochondrial capacity decreased **1.49 ± 0.03-fold** compared with controls. EM analyses showed no change in mitochondrial area or number; however, mitochondrial **aspect ratio** (-0.127 ± 0.0449) and **form factor** (-0.0106 ± 0.0273) were significantly reduced, indicating impaired mitochondrial shape, branching and network complexity.

Conclusions: This study identifies a **high-risk sarcopenic obesity phenotype** in monogenic obesity, characterised by low lean mass, severe insulin resistance, impaired mitochondrial oxidative capacity and altered mitochondrial structure. These findings emphasise the need to move **beyond BMI** when defining obesity phenotypes and highlight skeletal muscle mitochondrial dysfunction as a key driver of metabolic disease in this population.

Abstract citation ID: lvag096.914

EP398 - ECE_1825 - Early childhood adiposity assessed by waist-to-height ratio and its impact on later obesity

Markéta Vaňková[1], Tereza Svobodová[1], Josef Vcelak[1], Radka Taxová Braunerová[2] and Tereza Metelcová[2]
[1]*Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic;* [2]*Obesity Management Centre, Institute of Endocrinology, Prague, Czech Republic*

Rapid weight gain and changes in body composition during early childhood are strongly associated with an increased risk of obesity and cardiometabolic diseases later in life. Early-life exposures play a critical role in obesity development. Although body mass index (BMI) is widely used to assess normal body weight, alternative indices such as waist-to-height ratio (WHtR) may better reflect cardiometabolic risk by capturing central adiposity.

This study investigated the risk of increased adiposity in early childhood and its association with excess weight in adolescence and young adulthood.**Methods:** Three study populations were analyzed: (1) 11 307 children aged 6.5-7.9 years from the WHO Childhood Obesity Surveillance Initiative (COSI) collected between 2008 and 2025; (2) a longitudinal subsample of 613 children assessed at ages 6.5-7.9 years in the 5th round of COSI (2019) and re-evaluated at ages 11-13 years (2022-2024); and (3) 253 young adults (mean age 23.3 ± 2.04 years) with available WHtR data from adolescence (mean age 15.3 ± 1.88 years). In children, waist circumference, height, weight, and BMI were measured, and overweight and obesity were classified according to WHO criteria. In adults, BMI and waist circumference were assessed. Abdominal obesity was defined as WHtR ≥ 0.5 in all participants. Statistical analyses included chi-square tests (NCSS 2019) and multivariate regression using O2PLS (SIMCA).

Results: Adiposity risk was identified in 94% of children with severe obesity, 72% with obesity, 26% with overweight, and 2.7% of normal-weight children. Modifiable factors associated with higher adiposity risk included parental underestimation of child weight, shorter breastfeeding duration, insufficient sleep, low physical activity, sedentary behavior, unhealthy diet, family history of metabolic disease, and lower parental education. While overweight and obesity were more prevalent in boys, sex was not associated with adiposity risk. During the 4-year follow-up, 78.7% of children maintained a healthy WHtR, whereas 6.4% exhibited persistently elevated WHtR. In young adulthood, 63% of individuals with elevated WHtR had already shown increased adiposity in childhood.

Conclusions: Early identification of children at high risk of adiposity and targeted intervention on modifiable factors may be more effective than treating obesity at later stages. While BMI remains useful for population surveillance, direct assessment of adiposity provides a clearer link to obesity-related risk factors and long-term outcomes.

Funding: Supported by the Ministry of Health of the Czech Republic in cooperation with the Czech Health Research Council under project No. AZV NU23-09-00252 and project MH-CZ-DRO (EU00023761).

Abstract citation ID: lvag096.915

EP399 - ECE_1918 - A/J male mice resist obesity-driven bone loss through increased antioxidant enzyme capacity compared to obesity-prone C57Bl/6J male mice

Michaela Ferencakova[1], Martina Dzubanova[1], Andrea Benova[1], Dung Nguyen[1], Jan Prochazka[2], Frantisek Spoutil[2], Tomas Cajka[1], Marek Vrbacky[1], Kristina Bardova[1], Martin Rossmeisl[1], Jan Kopecky[1] and Michaela Tencerova[1]
[1]*Prague, Czech Republic;* [2]*Czech Centre for Phenogenomics & Laboratory of Transgenic Models of Diseases, Institute of Molecular Genetics of the Czech Academy of Sciences, Prague, Czech Republic*

Background: Obesity-associated bone fractures are not manifested in all obese individuals. However, the underlying mechanism behind this phenomenon has not been well described. Thus, we investigated the effect of obesity on bone and bone marrow stromal cell (BMSCs) metabolism in obesity-prone C57BL/6J (B6) mice and obesity-resistant A/J mice under obesogenic condition.

Methods: Eight-week-old B6 and A/J male mice were either fed with normal diet (ND) or high-fat-diet (HFD) (60% kcal from fat) ($n = 10$/group) for 3 months and examined for metabolic and bone parameters. Primary BMSCs were obtained from treated mice for cellular analyses. Proteomic and metabolomic analysis of bone marrow (BM) was performed using LC-MS. siRNA transfection of selected targets from proteomics in primary B6 and A/J BMSC was performed followed by measurements of osteogenic and adipogenic potential and cellular metabolism.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: After 3 months of HFD, B6 mice gained body weight (+1.5-fold, $P < .001$) and impaired glucose tolerance (+1.3-fold, $P < .05$) comparing to A/J mice. HFD impaired trabecular and cortical bone in B6 mice, while HFD A/J mice did not manifest trabecular bone loss ($P > .10$) and increased cortical thickness and decreased porosity ($P < .001$). These obesity-induced changes were accompanied by lower bone marrow adiposity in A/J vs B6 mice ($P < .01$). Further, primary BMSCs isolated from A/J mice manifested higher glycolytic profile compared to respiratory profile in B6 BMSCs ($P < .001$) correlating with higher osteogenic potential of A/J BMSCs under HFD. Proteomic analysis revealed increased levels of antioxidant enzymes (e.g. GLO1, DPP7) in A/J compared to B6 mice. siGlo and siDpp7 BMSCs showed lower osteogenic capacity suggesting its important role for bone homeostasis.

Conclusions: Our data show that obesity induced worse impact on bone and fat metabolism in B6 compared to A/J mice associated with lower BMSC glycolytic capacity in B6 mice. These changes were accompanied by increased levels of antioxidative enzymes in A/J HFD BM suggesting protection from HFD-induced oxidative stress.

Abstract citation ID: lvag096.916

EP400 - ECE_2249 - Benefits of a short-term Mediterranean Diet (MD) intervention on circadian expression profile of the clock gene BMAL1 and of TLR4 in Peripheral Blood Mononuclear Cells (PBMC) of patients with obesity

Claudia Pivonello[1], Nunzia Magnacca[2], Chiara Graziadio[1], Mariarosaria Negri[3], Feliciana Amatrudo[4], Elisabetta Vozza[5], Guendalina Del Vecchio[1], Claudia Vetrani[3], Sabrina Tini[6], Flavia Prodam[6], Rosario Pivonello[2] and Annamaria Colao[2]
[1]Department of Public Health, Federico II University, Naples 80131, Italy; [2]Department of Clinical Medicine and Surgery, Federico II University, Naples 80131, Italy; [3]Department of Psychology and Health Sciences, Pegaso Telematic University, Napoli, Italy; [4]Pegaso Telematic University, Napoli, Italy; [5]Department of Experimental Medicine, La Sapienza University of Rome, Rome, Italy; [6]Department of Health Sciences, University of Piemonte Orientale, Novara, Italy

A low-grade chronic inflammatory condition characterises obesity, with a dominant infiltration in adipose tissue of activated macrophages expressing high levels of Toll-like receptor 4 (TLR4), whose exaggerated and uncontrolled pro-inflammatory signalling induced by infection can lead to septic shock and death. Circadian rhythm-related gene expression patterns in PBMC exhibited marked variation in subjects with obesity compared to controls, often associated with the upregulation of certain clock genes, such as BMAL1, contributing to metabolic comorbidities. Moreover, BMAL1 regulates time-dependent inflammatory responses following TLR4 activation by modulating enhancer activity.

The current study investigated the effect of a short-term MD intervention (STMD) on the circadian gene and TLR4 profiles in PBMC of 38 obese patients (24 F (63%), 14 M (37%)) and 7 obese diabetic patients (2 F (29%), 5 M (71%)), enrolled at AOU Federico II of Naples and University of Piemonte Orientale, respectively. Anthropometric and biochemical parameters were assessed before (T0) and after six weeks of MD intervention (T1). Blood samples for PBMC extraction were collected in the morning (8AM) and in the afternoon (4PM) in fasting conditions, both at T0 and T1. Clock genes (BMAL1, PER1, PER2, CRY1, CRY2) and TLR4 were evaluated in PBMC by RT-qPCR. At T0, only BMAL1($P = .036$) and TLR4 ($P = .0004$) expression at 4PM were significantly higher than 8AM. After normalization on weight and BMI, BMAL1 and TLR4 expression significantly correlated in both the morning ($r = 0.530$, $P < .001$) and the afternoon ($r = 0.579$, $P < .001$).

Although STMD only a slight but non-significant improvement of the anthropometric and biochemical parameters, it was sufficient to modulate the expression of some clock genes (PER1 $P = .002$, PER2 $P = .012$ and CRY1 $P = .027$) that resulted in significantly lower in the afternoon (T1 4PM) compared with the morning (T1 8AM). However, compared to T0 4PM, STMD significantly decreased the clock genes (BMAL1 $P = .03$, PER1 $P = .002$, CRY1 $P = .001$, CRY2 $P = .017$) and TLR4 ($P < .0001$) expression at T1 4PM, thus restoring gene levels to normal values at T1 compared to T0. After normalization on weight and BMI, BMAL1 and TLR4 expression significantly correlated both the morning ($r = 0.384$, $P = .036$) and the afternoon ($r = 0.936$, $P < .001$) at T1. In conclusion, patients with obesity display higher expression of BMAL1 and TLR4 in PBMC during the afternoon, increasing inflammation susceptibility. STMD restores a more physiological BMAL1 gene profile in PBMC and consequently reduces the expression and activation of TLR4 and thus macrophages' immune activity and inflammatory response.

Abstract citation ID: lvag096.917

EP401 - ECE_2274 - Prevalence and impact of first-trimester obesity on maternal and fetal outcomes in a South Asian population

Minuri Fernando[1], Indunil Piyadigama[2,3], Dulani Samaranayake[4,5] and Prasad Katulanda[6,7]
[1]National Hospital—Sri Lanka, University Medical Unit, Colombo, Sri Lanka; [2]Faculty of Medicine, University of Colombo, Sri Lanka; [3]Gynaecology and Obstetric Department, De Soysa Maternity Hospital- University Gynaecology and Obstetric Clinic, Colombo, Sri Lanka; [4]Faculty of Medicine, University of Colombo, Sri Lanka; [5]Community Medicine Department, Colmbo, Sri Lanka; [6]Faculty of Medicine, University of Colombo, Sri Lanka; [7]University Medical Unit-Endocrine Clinic, University Medical Unit, Colombo, Sri Lanka

Background: Obesity is an epidemic that has now invaded the low and middle-income countries. This is common among females of the reproductive age group, which paves the way to obesity in pregnancy, resulting in increased risk of pregnancy-related adverse outcomes, even at a lower pre-pregnancy BMI among Asians, due to their differences in body fat compositions compared to the non-Asian population. South Asian data is limited.

Methods: This is a retrospective descriptive cross-sectional study, among postpartum mothers aged ≥16 years, with a singleton pregnancy, having a first-trimester BMI on records, and delivered at De Soyza Maternity Hospital, Colombo, Sri Lanka, during July 2024 to September 2024. An interviewer-administered questionnaire was used for data collection. Data analysis was done using SPSS 26 software. Asian BMI cut-offs were used. Overweight and obesity were combined to assess the risk of complications. Bivariate analysis using the chi-square test was done

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

to determine the significance of maternal and fetal/neonatal outcomes with the combination of overweight-obesity.

Results: Four hundred mothers participated in the study. According to Asian cut-offs, the prevalence of first-trimester obesity was 41.8% (95%CI 36.92-46.58), overweight was 17.5% (95%CI 13.78-21.22), and underweight was 11.8% (95%CI 8.59-14.91). The first-trimester overweight-obesity combination was significantly associated with maternal complications: gestational diabetes mellitus [OR = 1.66 (95% CI 1.06—2.60; $P = .025$)], pregnancy-induced hypertension [OR = 3.73 (95% CI 1.40—9.95; $P = .005$)], premature labor [OR = 2.2 (95% CI 1.01—4.81; $P = .044$)], emergency cesarean section [OR = 1.71 (95% CI 1.06—2.77; $P = .028$)], and the presence of one or more maternal complication [OR = 1.80 (95% CI 1.18—2.72; $P = .006$)]. None of the fetal/neonatal complications had any significant association with the overweight-obesity combination.

Conclusions: According to Asian BMI cut-offs, South Asians have a higher prevalence of obesity in pregnancy, which is significantly associated with maternal adverse outcomes. This highlights the importance of using Asian BMI cut-offs for Asian patients and the importance of preconception BMI optimization to prevent maternal morbidity.

Keywords first-trimester obesity, Asian, adverse maternal outcomes

Abstract citation ID: lvag096.918

EP402 - ECE_2635 - Circulating humanin is inversely associated with obesity in patients with acromegaly

Dorota Filipowicz[1], Daniela Dadej[1], Marianna Cemel[1] and Marek Ruchala[1]

[1]*Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznań, Poland*

Introduction: Cardiovascular complications are the leading cause of premature mortality in patients with acromegaly and are linked to metabolic disturbances driven by prolonged exposure to elevated IGF-1 levels. Humanin, a mitochondria-derived peptide with protective properties against cellular stress and regulatory effects on insulin and IGF signalling, may influence pathways underlying metabolic and cardiovascular risk; however, its role in acromegaly remains unclear. The aim of this study was to evaluate circulating humanin concentrations in patients with acromegaly and to assess their associations with disease activity, anthropometric, and inflammatory parameters.

Materials and Methods: This cross-sectional study included 130 participants (55% women): patients with active ($n = 52$) and inactive acromegaly ($n = 37$), and a control group without acromegaly ($n = 41$). Serum humanin concentrations were measured using a commercial Human Putative Humanin Peptide (MT-RNR2) ELISA kit (Cusabio). Anthropometric (body weight, BMI), hormonal (IGF-1, GH, SAGIT score), and inflammatory parameters (CBC, CRP, Fe, TIBC, ferritin) were collected. Statistical analyses were performed using Statistica 13 (TIBCO Software Inc.), with $P < .05$ considered statistically significant.

Results: Serum humanin concentrations did not differ between patients with active acromegaly, inactive acromegaly, and controls (Kruskal–Wallis: $H(2) = 1.69$, $P = .43$). In patients with acromegaly, humanin levels were inversely correlated with BMI (Spearman's $\rho = -0.21$, $P < .05$). Acromegaly patients with BMI $\geq$ 30 kg/m^2 (62%) had significantly lower humanin concentrations than patients with BMI < 30 kg/m^2 (median 1046 [IQR 750-1680] vs 1498 [998-2446] pg/mL; Mann–Whitney $P = .011$). In multivariable linear regression adjusted for age and sex, obesity remained independently associated with lower log-transformed humanin concentrations ($b = -0.38$, $P = .038$), corresponding to around 30% lower levels. Results were consistent in sensitivity analyses excluding values above the 95th percentile ($b = -0.33$, $P = .045$).

Conclusions: Circulating humanin concentrations are not associated with acromegaly presence or activity but decline with increasing obesity in this high cardiometabolic risk population. This finding may suggest attenuation of humanin's mitochondrial-related protective effects with excess adiposity and highlights the potential importance of weight-reduction strategies in acromegaly. These findings support further evaluation of humanin as a potential biomarker of metabolic risk in acromegaly; further studies are warranted to clarify its role in obesity.

Abstract citation ID: lvag096.919

EP403 - ECE_3269 - Efficacy and safety of semaglutide injection in weight management: a subgroup analysis in patients based on Waist circumference

Unnikrishnan Gopalkrishnan[1], Ameya Joshi[2], Harish Kumar[3], Richa Giri[4], Sanjiv Maheshswari[5], Valluri Prasad[6], Jitendra Shukla[7], M.C. Rekha[8], Nutankumar Agrawal[9], Yogesh Rasal[10], Banshidhar Sahoo[11], Shweta Bhandari[12], Ambana Gowda[13], Phadke Keshav[14], Pravin Supe[15], Niranjan Pathak[16], C. Ambrish[17], Ashutosh Sonawane[18], Yash Bahulikar[19], Amit Bhaskar[20], R. Arunkumar[21], Priyanka Yadav[22], Supriya Sonowal[22], Dipak Patil[22], Sucheta Pandit[22], Pravin Ghadge[22] and Suyog Mehta[22]

[1]*Chellaram Diabetes Institute, Pune, India;* [2]*Bhaktivedanta Hospital and Research Institute, Thane, India;* [3]*Amrita institute of Medical Sciences and Research Centre, Kochi, India;* [4]*G.S.V.M medical College, Kanpur, India;* [5]*Jawahar Lal Nehru Medical College, Ajmer, India;* [6]*King George Hospital, Visakhapatnam, India;* [7]*Moti Lal Nehru Medical College, Prayagraj, India;* [8]*Mandya Institute of Medical Science, Mandya, India;* [9]*M.L.B Medical College, Jhansi, India;* [10]*Pulse Multispecialty Hospital, Pune, India;* [11]*KIDS Hospital, Bhubaneswar, India;* [12]*Vincare Hospital, Bathinda, India;* [13]*Citizen Hospital, Bangalore, India;* [14]*Sahyadri Super Speciality Hospital, Pune, India;* [15]*Supe Heart and Diabetes Hospital and Research Centre, Nashik, India;* [16]*OJAS Multispeciality Hospital, Pune, India;* [17]*Medstar Speciality Hospital, Bangalore, India;* [18]*Panacea Hospital, Nashik, India;* [19]*MMFHA Joshi Hospital, Pune, India;* [20]*Janta Hospital and Maternity Center, Varanasi, India;* [21]*Chettinad Hospital & Research Institute, Chengalpattu, India;* [22]*Sun Pharma Laboratories Limited, Medical affairs and Clinical Research, Mumbai, India*

Objectives: To evaluate the efficacy and safety of synthetic semaglutide injection (Test drug) compared with Wegovy® (Reference drug) 2.4 mg subcutaneously for weight management in patients with waist circumference <112 cm (Subgroup 1[S1]) and ≥112 cm (Subgroup 2 [S2]).

Materials and Methods: A phase III, multicentre, randomized, open-label, active-controlled clinical study (CTRI/2025/04/085487) was conducted across 22 study sites in India after

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

receiving regulatory and ethics committee approvals. In this study, 267 adult patients with (BMI) ≥ 30 kg/m^2 or ≥27 kg/m^2 with the presence of at least one co-morbidity of hypertension, dyslipidaemia and/or type 2 diabetes mellitus were included. Patients were randomized to receive either test drug or reference drug weekly for 24 weeks. Secondary endpoints included change in BMI, waist circumference, SF-36, and glycaemic measures in diabetic and non-diabetic patients. Safety assessments included incidence of TEAEs and anti-drug/neutralizing antibody.

Results: At baseline, 132 patients were included in S1 and 135 patients were included in S2. Mean (±SD) percentage reduction in weight from baseline to week 24 was −14.0 (±3.97) with test drug and −13.6 (±3.80) with reference drug in S1 ($P = .4116$) and −13.7 (±4.59) with test drug and −14.5 (±4.36) with reference drug in S2 ($P = .3244$) respectively. Proportion of patient achieving ≥ 5% and ≥10% body weight reduction was comparable between test and the reference drug in both S1 and S2 ($P = .3217$ and $P = .1152$ for S1 and $P = .4703$ and $P = .3423$ for S2 respectively). Mean (±SD) change in waist circumference with test and the reference drug was −9.62(±3.53) cm and −8.81 (±4.03) cm respectively in S1 ($P = .0790$) and −11.8 (±7.17) cm and −14.1(±11.66) cm respectively in S2 ($P = .1483$) at week 24. In diabetic patients there was decrease in glycaemic parameters (HbA1c, FBG and PPBG) from baseline to week 24 in both S1 and S2 and was comparable between arms ($P > .05$). In non-diabetic patients decrease in glycaemic parameters (HbA1c, FBG and PPBG) from baseline to week 24 was not clinically relevant compared to diabetic patients and was comparable between arms ($P > .05$). Study medications were well tolerated.

Conclusions: Semaglutide injection is effective in weight management irrespective of baseline waist circumference and can be a treatment of choice in weight management with or without co-morbidities

Abstract citation ID: lvag096.920

EP404 - ECE_3547 - Effect of CPAP and testosterone replacement on serum testosterone in obese men with obstructive sleep apnea and varying degrees of glucose metabolism disorders

Violetta Yuzvenko, Tetiana Yuzvenko, Oleksandr Tovkai, Volodymyr Pankiv, Olena Tretyak, Dmytro Kogut and Vadym Ischuk
Kiev, Ukraine

Background/Objectives: Obstructive sleep apnea (OSA) is associated with hypogonadism in obese men and is frequently accompanied by disorders of glucose metabolism. In men with prediabetes and type 2 diabetes mellitus, OSA may further aggravate insulinresistance and glycemic control, contributing to hormonal imbalance. This study aimed to evaluate the impact of continuous positive airway pressure (CPAP) and testosterone replacement therapy (TRT) on serum total testosterone and metabolic parameters in obese men with OSA and impaired glucose metabolism.

Methods: Seventy-seven men aged 24-72 years (mean 47.8 ± 11.4) with overweight or obesity were studied. Patients were categorized as having type 2 diabetes ($n = 37$), prediabetes ($n = 16$), or insulin resistance without glucose impairment ($n = 24$). All participants underwent anthropometric assessment and measurement of fasting plasma glucose, insulin, HbA1c, lipid profile, and total testosterone. Baseline HbA1c levels were 8.1 ± 2.2% in patients with type 2 diabetes, 6.6 ± 1.3% in those with prediabetes, and 6.9 ± 1.5% in patients with insulin resistance. Obstructive sleep apnea was diagnosed using SOMNOtouch RESP eco monitoring. Patients were stratified by apnea-hypopnea index (AHI): ?15 ($n = 11$), 15-29.9 ($n = 23$), and ≥30 events/hour ($n = 43$). After 6 months of treatment, HbA1c significantly decreased in all groups, with the greatest improvement in patients receiving combined CPAP and TRT ($P < .05$). Treatment groups were: Group 1—CPAP ($n = 26$); Group 2—TRT ($n = 25$); Group 3—CPAP + TRT ($n = 17$). Statistical analysis was performed using Kruskal-Wallis ANOVA; $P < .05$.

Results: Baseline testosterone and anthropometric parameters were similar across groups. Post-treatment, all groups showed significant BMI reduction and increased serum testosterone ($P < .001$). Group 3 exhibited the largest increase, with most patients experiencing more than a twofold rise.

Conclusions: OSA significantly reduces serum testosterone in obese men. CPAP therapy increases testosterone levels, and combination with TRT provides the greatest effect. OSA should be considered a factor affecting hormonal balance and male reproductive health, beyond sleep-related breathing disturbances.

Keywords obstructive sleep apnea, CPAP, testosterone, obesity, hypogonadism

Abstract citation ID: lvag096.921

EP405 - ECE_3803 - Muscle mass, cellular integrity, and physical function after bariatric surgery: a Longitudinal Study in Severe Obesity

María Garcia Olivares[1], Rocío Fernández Jiménez[1], Cristina Navas-Moreno[1], Nerea Ruiz-Campos[1], Ángela Martínez-Martínez[1], José Ignacio Martínez Montoro[1], Carolina Gutiérrez-Repiso[1], Ángela Núñez-Morales[1], Rocío Soler-Humanes[2], Luís Ocaña-Wilhelmi[2], Diéter Morales-García[1], Francisco J. Tinahones[3], Jose Manuel Garcia-Almeida[1,4] and Lourdes Garrido-Sánchez[1]
[1]Instituto de Investigación Biomédica de Málaga-Plataforma en Nanomedicina (IBIMA Plataforma BIONAND), Málaga, Spain; [2]Instituto de Investigación Biomédica de Málaga-Plataforma en Nanomedicina (IBIMA Plataforma BIONAND), Virgen de la Victoria University Hospital, Surgery, Málaga, Spain; [3]Instituto de Investigación Biomédica de Málaga-Plataforma en Nanomedicina (IBIMA Plataforma BIONAND), Virgen de la Victoria University Hospital, Endocrinology and nutrition, Málaga, Spain; [4]Málaga, Spain

Introduction: Bariatric surgery in patients with severe obesity leads to substantial weight loss and marked metabolic improvements. However, its effects on muscle mass, cellular integrity, and physical function remain a matter of debate.

Objectives: To evaluate longitudinal changes in muscle mass, cellular integrity, and physical function in patients with severe obesity before and one year after bariatric surgery.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Materials and Methods: This longitudinal study included patients with severe obesity assessed preoperatively and at 12 months after bariatric surgery. Anthropometric and biochemical parameters were collected. Body composition was evaluated using bioelectrical impedance vector analysis (BIVA) and thigh nutritional ultrasound. Physical function was assessed by handgrip dynamometry and the Timed Up and Go test.

Results and Conclusions: At 12 months post-surgery, significant reductions were observed in body weight (−29.0%), BMI (−28.9%), and fat mass (−43.1%) ($P < .001$). These changes were accompanied by marked metabolic improvements, including significant decreases in glucose, insulin, HOMA-IR, and triglyceride levels (all $P < .001$).

Concurrently, significant reductions in fat-free mass (−12.4%), body cell mass (BCM; −16.6%), and body cell mass index (BCMI; −16.9%) were observed. Phase angle declined significantly (−8.4%; $P < .001$), suggesting impaired cellular integrity. In multivariate analysis, higher baseline BCM was independently associated with lower relative muscle mass loss ($\beta = 1.06$; $P < .001$), whereas older age and female sex were associated with greater muscle loss. Regarding physical performance, baseline phase angle ($\beta = .36$; $P = .026$) and baseline BCM ($\beta = .54$; $P = .033$) independently predicted improvement in Timed Up and Go performance.

Conclusions: Despite significant metabolic benefits and improvements in functional performance, bariatric surgery is associated with substantial loss of muscle mass and deterioration in muscle quality. Baseline BCM and phase angle emerge as key markers to identify patients at higher risk of muscle loss and may help guide targeted preoperative nutritional and exercise interventions.

Acknowledgements: This work was partially supported by ISCIII (PI23-01724).CIBEROBN is an initiative of ISCIII and co-funded by FEDER.

Abstract citation ID: lvag096.922

EP406 - ECE_1369 - Impact of ethnicity and antihyperglycemic medications on dementia incidence in older adults with type 2 diabetes

Elena Chertok Shacham[1,2], Sireen Sharif[1], Muhammad Kadah[1] and Snait Ayalon[3]
[1]*Emek Medical Center, Internal Medicine B, Afula, Israel;* [2]*Technion, Israel institute of Technology, Medical Faculty, Haifa, Israel;* [3]*Emek Medical Center, Research Authority, Afula, Israel*

Background: Type 2 diabetes increases the risk of cognitive decline and dementia. Data on ethnic differences in dementia prevalence among patients with diabetes remain limited.

Methods: We conducted a retrospective matched case–control study of Clalit Health Services members aged 60 or older. Matching (1:3) was based on age, sex, language, and socioeconomic status. Ethnicity was determined by spoken language or place of birth. Prescriptions and refills for antidiabetic medications were recorded for the two years preceding the index date. Clinical, anthropometric, and comorbidity data were analysed.

Results: Our final cohort consisted of data from 150 237 patients. During up to 20 years of follow-up, 39% of participants developed dementia (crude proportion); however, when accounting for death as a competing risk, the 10-year cumulative incidence was approximately 9-10%, and ethnic differences were attenuated after multivariable adjustment. The use of SGLT-2 and DPP-4 inhibitors was associated with a lower probability of dementia. Specifically, SGLT-2 inhibitors (HR, 0.40; 95% CI, 0.38-0.41), GLP-1 agonists (HR, 0.64; 95% CI, 0.62-0.67), and DPP-4 inhibitors (HR, 0.67; 95% CI, 0.65-0.68 were associated with a reduced risk of dementia-related mortality.

Conclusions: SGLT-2 inhibitors, DPP-4 inhibitors, and GLP-1 receptor agonists were associated with reduced dementia-related mortality in older adults with type 2 diabetes. The effect was robust across ethnic groups, supporting their potential role in mitigating neurodegenerative outcomes.

Table 1 Demographic and anthropomorphic characteristics of patients.

	Total	A	E	H	R	*P*-value
Number of Patients	$N = 150\,237$	$N = 18\,137$	$N = 2208$	$N = 99\,998$	$N = 29\,894$	
Dementia *N* (%)	$N = 58\,728$(39%)	$N = 5854$(32%)	$N = 693$(31%)	$N = 39\,559$ (40%)	$N = 12\,590$(42%)	.001
Age at event (M)	73 ± 8.3	70.4 ± 7.5	76 ± 9.7	72.2 ± 8	74.3 ± 8.3	.001
Age et event (F)	73 ± 8.1	70.2 ± 7.4	75 ± 9	73 ± 8	75 ± 8	.001
Gender: Male *N* (%)	70 287(47%)	7530(41%)	1080(49%)	49 529(49%)	12 148(40%)	.001
Gender: Female *N* (%)	79 950(53%)	10 607(59%)	1128(51%)	50 469(51%)	17 746(60%)	.001
Socioeconomic (high)	46 352 (31%)	366 (1.6%)	144(6%)	44 037(37%)	7473 (25%)	.001
Medium	56 740 (38%)	2405(13%)	754(34%)	40 707 (41%)	12 874 (43%)	.001
Low	47 145 (31%)	15 432 (85%)	1318 (60%)	20 848(21%)	9547 (32%)	.001
Smoking (current)	13 853 (11%)	2546 (16%)	40 (2%)	9370 (12%)	1897 (8%)	.001
BMI [kg/m^2]	29 ± 5.3	30.5 ± 5.9	25.7 ± 4.3	28.5 ± 5.3	29.5 ± 5.6	.001
HbA1C (%)	7.1 ± 1.4	7.4 ± 1.6	7.5 ± 1.8	7.1 ± 1.4	7.0 ± 1.3	.001
GFR mll/min	66 ± 23	68 ± 23	81 ± 20	66 ± 22	62 ± 22	.001
Cardiovascular *n* (%)	108 669(72.3%)	12 321(67%)	1116(51%)	73 018(73%)	22 214(74%)	.001
Congestive heart *n*(%)	57 477(38%)	6850(38%)	512(23%)	38 118(38%)	11 997(40%)	.001
Kidney disease	74 959 (50%)	8436 (47%)	552 (25%)	50 012 (50%)	15 959 (53%)	.001

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.923

EP408 - ECE_2828 - In vivo overexposure to non-esterified fatty acids increases circulating basal and postprandial androgen levels in normal female mongrel dogs

Christophe Richer dit Laflèche[1], Joanie Faubert[1], Foued Naimi[1], Sylvain Bellanger[1], Marie-Claude Battista[1], Ouhida Benrezzak[2], André Carpentier[1,2] and Jean-Patrice Baillargeon[1,2]
[1]*Sherbrooke, Canada;* [2]*Centre de recherche du Centre hospitalier universitaire de Sherbrooke, Sherbrooke, Canada*

Background: The etiology of the polycystic ovary syndrome is poorly understood, but studies suggest that lipotoxicity may be an important contributor.

Aim: To evaluate the effects of an in vivo overexposure to non-esterified fatty acids (NEFA) on changes in circulating androgen levels.

Methods: Female mongrel dogs underwent a 17.5-hour metabolic protocol. During the first 8 hours (night period), dogs ($n = 6$/group) received either a Intralipid-heparin 20% (IH; 0.02 ml/kg/min + 0.5 U/kg/min) or a saline infusion (control group), followed by a standard meal at 08h30. Blood samples were drawn every 60 minutes during the night period (8h) and for 9 hours post-meal (day period). Only 2 dogs (1/group) were in estrus. Changes from baseline were calculated as the incremental area under the curve (iAUC) of the fold increase from baseline and were compared between groups using t tests, unadjusted or adjusted for potential confounders or mediators. Correlations between parameters were done using linear regressions.

Results: In the 12 dogs studied (27.6 ± 2.9 kg), baseline androgen levels were comparable between experimental groups. NEFA levels more than doubled within one hour of infusion in the IH group. NEFA iAUC was significantly higher in response to the nocturnal IH infusion compared to the saline group (461 vs −47.7, $P = .001$) and rapidly returned to normal after discontinuation. The 17-hydroxyprogesterone (17-OHP) iAUCs were significantly higher in the IH group than in the saline group both at night (−73.0 vs −255, $P = .024$) and during the day (−49.6 vs −329, $P = .015$). No statistically significant changes in other androgens were detected. In multivariate analyses, the effects of IH on 17-OHP iAUCs were independent from night or day iAUCs of insulin, ACTH, and cortisol, and of day NEFA iAUC. Nocturnal NEFA, and cortisol iAUCs correlated with both the nocturnal and diurnal 17-OHP iAUCs ($R^2 = 0.49$, $P = .011$, and $R^2 = 0.35$, $P = .044$ for NEFA; and $R^2 = 0.42$, $P = .022$, and $R^2 = 0.33$, $P = .049$ for cortisol). Interaction analyses suggested a modifying effect of NEFA iAUC on the association between night 17-OHP, and insulin iAUC. The slope of the association tended to be more pronounced with higher NEFA exposure, though subgroup analyses underpowered.

Conclusions: An acute in vivo elevation of circulating NEFA using an IH protocol induces a significant increase in fasting and insulin-stimulated, postprandial androgen precursor production in normal female dogs.

Abstract citation ID: lvag096.924

EP411 - ECE_1500 - Non-invasive blood glucose measurement using visible light photoplethysmography signals in subjects with diabetes

Hyeong-Kyu Park[1] and Chul Sik Kim[2]
[1]*Soonchunhyang University, Seoul, South Korea;* [2]*Yonsei University, Yongin, South Korea*

The global diabetic population is expected to reach 800 million by 2035, increasing the need for continuous blood glucose monitoring. Conventional methods, like finger-prick glucometers and invasive continuous glucose monitors, are burdensome due to pain, infection risks, and consumable costs. Several non-invasive devices measuring glucose via fingertip tissue have been developed but lack the required accuracy for commercialization. This study was aimed to investigate a non-invasive optical glucose meter that accounts for fingertip thickness, skin condition, and body mass index. Blood glucose was measured by analyzing photoplethysmography signals from 660 nm light irradiated onto the fingertip, with venous blood glucose levels used for calibration. Individual characteristics were incorporated during calibration by determining baseline values and applying an appropriate feature extraction algorithm to derive the final formula. A total of 28 subjects with diabetes (13 males, 15 females; 3 with type 1 and 25 with type 2 diabetes) had their fasting and postprandial glucose levels measured using both the non-invasive device and venous blood sampling. The device's accuracy was evaluated with the mean absolute relative deviation (MARD), which was 8.8%, showing superior accuracy compared to previous studies. Consensus Error Grid (Type 1) analysis revealed 100% of data in zones A and B, confirming clinical reliability. ISO 15197 requires 99% of glucose values to fall within these zones, and this clinical trial confirmed 100% compliance. In summary, our results have demonstrated the feasibility of non-invasive glucose measurement with accuracy comparable to venous blood glucose levels in subjects with diabetes. To commercialize our novel device, further studies to address the wider ranges of blood glucose levels in various subjects, such as individuals with anemia, chronic kidney or liver diseases will be needed.

Abstract citation ID: lvag096.925

EP413 - ECE_2894 - Development of a rabbit model for type 2 diabetes mellitus

Denis Visotskii[1,2], Dmitrii Popov[2], Kseniya Vysotskaya[1] and Gleb Kosovsky[2]
[1]*Endocrinology Research Centre, Moscow, Russia;* [2]*Afanas'ev Institute of Fur-bearing Animal Breeding and Rabbit Breeding, Rodniki, Russia*

Introduction: The domestic rabbit (*Oryctolagus cuniculus*) is a classic model in biomedical research. However, all existing diabetic models in this species rely on beta-cytotoxic agents to induce a state of absolute insulin deficiency, mimicking type 1 diabetes mellitus (T1DM). A model capturing the pathogenesis of type 2 diabetes mellitus (T2DM), with its characteristic insulin resistance and compensatory hyperinsulinemia, has yet to be developed in rabbits.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Aim: To develop and validate a reproducible model of T2DM in rabbits that replicates its characteristic metabolic disturbances

Materials and Methods: The experiment was performed on eight female soviet chinchilla rabbits aged 6 weeks, which were divided into an experimental group ($n = 4$) and a control group ($n = 4$). The T2DM model was induced through a two-stage protocol: a 12-week high-fat diet (HFD, 17% fat) followed by a 2-week course of intramuscular dexamethasone injections (0.5 mg/kg) to simulate glucocorticoid-induced insulin resistance. Weekly monitoring included body weight, morphometry (body length and waist circumference), and fasting blood glucose. Metabolic assessments was performed via intravenous glucose tolerance tests (IVGTT) and comprehensive biochemical profiling (lipid panel, insulin).

Results: The combined HFD and dexamethasone protocol successfully induced a sustained metabolic syndrome consistent with T2DM. Key features included: persistent hyperglycemia (IVGTT: 0 min: 8.1 ± 0.4 vs control 6.97 ± 0.83 mmol/L; 120 min: 9.1 ± 0.9 vs 7.93 ± 0.77 mmol/L), hyperinsulinemia (1.06 ± 0.5 vs 0.61 ± 0.3 μU/mL), abdominal obesity, and atherogenic dyslipidemia (elevated triglycerides, LDL, VLDL, and atherogenic index). These metabolic alterations persisted for at least two weeks after dexamethasone withdrawal. Notably, traditional markers of chronic hyperglycemia (HbA1c, fructosamine) did not show significant elevation.

Conclusions: We have developed the first easily reproducible rabbit model that reflects fundamental pathophysiological features of of T2DM: abdominal obesity, insulin resistance, chronic hyperglycemia, and atherogenic dyslipidemia. However, the absence of significant differences in chronic hyperglycemia markers (glycated hemoglobin A1c and fructosamine) in animals from the diabetes model group highlights the importance of species-specific considerations in preclinical research and the necessity of identifying adequate species-specific markers for assessing chronic hyperglycemia in rabbits.

Funding: This study was supported by the Ministry of Science and Higher Education of the Russian Federation (state grant № 075-00504-26-00).

Abstract citation ID: lvag096.926

EP414 - ECE_3498 - Variants in the NME7 gene contribute to impaired fasting glucose in adolescents

Tereza Svobodová[1,2], Daniela Vejrazkova[1], Josef Vcelak[1], Tereza Metelcová[3] and Markéta Vaňková[1]

[1]Institute of Endocrinology, Molecular Endocrinology, Prague, Czech Republic; [2]Faculty of Science, Charles University, Anthropology and Human Genetics, Prague, Czech Republic; [3]Institute of Endocrinology, Obesitology, Prague, Czech Republic

Background: Genetic susceptibility to impaired glucose metabolism is shaped by complex metabolic pathways that may act differently across developmental stages. While many diabetes-associated genetic variants exert their effects through obesity and insulin resistance, alternative adiposity-independent mechanisms remain insufficiently explored, particularly in paediatric populations. Impaired fasting glucose (IFG) in adolescence may represent an early manifestation of dysregulated glucose homeostasis and a precursor of later metabolic disease. Variability in the *NME7* gene, encoding nucleoside diphosphate kinase 7, has previously been linked to glucose tolerance dynamics, including oral glucose tolerance test curve shape in adults, suggesting a potential role in glucose regulation. This study aimed to investigate whether selected variants in the *NME7* gene are associated with IFG in adolescents and whether these associations are related to adiposity.

Methods: Selected single-nucleotide polymorphisms within the *NME7* genomic region were analysed in a case–control study including 2129 adolescents (mean age 15.4 ± 1.73 years). Cases ($n = 159$) were defined by impaired fasting glucose (fasting plasma glucose > 5.6 mmol/L), while controls had normal fasting glucose levels. Associations with IFG were assessed using logistic regression under dominant genetic models adjusted for sex. To evaluate adiposity, linear regression analyses were performed for SDS BMI and waist-to-height ratio. In addition, categorical obesity phenotypes were analysed using three definitions: (i) overweight + obesity + severe obesity vs normal weight, (ii) obesity + severe obesity vs normal weight, and (iii) severe obesity vs normal weight. Obesity categories were defined using SDS BMI thresholds: overweight (≥1 to <2), obesity (≥2), and severe obesity (≥3 SDS BMI).

Results: Two *NME7* variants (rs4656659 and rs2157597) were associated with increased risk of IFG in adolescents (OR = 1.53 [1.08-2.15] and OR = 1.47 [1.06-2.05], respectively). These associations were not accompanied by differences in general or central adiposity, as no significant relationships were observed with SDS BMI, waist-to-height ratio, or categorical obesity phenotypes.

Conclusions: Genetic variability in the *NME7* region is associated with impaired fasting glucose in adolescents independently of adiposity. These findings suggest that *NME7* may influence early glucose dysregulation through non-obesity-mediated mechanisms and highlight the importance of paediatric genetic studies for identifying pathways relevant to early metabolic disease development.

Funding: Supported by the Ministry of Health of the Czech Republic in cooperation with the Czech Health Research Council under project No. AZV NU23-09-00252 and project MH-CZ-DRO (EU00023761).

Abstract citation ID: lvag096.927

EP415 - ECE_1409 - LETM-domain containing 1 (LETMD1) as a key player in adipocyte energy dissipation

Hannah Hui

Hong Kong, Hong Kong

Obesity is characterized by excessive accumulation of body fat and is now becoming a major public health issue. Beige adipocyte is a special type of adipocyte that is capable of burning energy in the form of heat and therefore has been a new therapeutic target for weight control and metabolic diseases. By Tandem Mass Tag-based quantitative proteomics analysis of the purified mitochondria from inguinal white adipose tissue (iWAT), we previously identified LETMD1 protein as a potential candidate contributing to energy dissipation in mouse beige adipocyte. However, the function of LETMD1 in human beige adipocytes as well as how the expression of LETMD1 is regulated

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

remain to be elucidated. In this project, we cultured the human induced pluopotent stem cell (hiPSC)-derived beige adipocyte, and demonstrated that overexpression of LETMD1 enhanced mitochondrial respiration. Furthermore, such an effect was still present when uncoupling protein 1 (UCP1), the classical thermogenic gene was knocked-out, demonstrating that LETMD1 engages a non-classical energy dissipation pathway. Further, we established a fluorescence-based LETMD1 reporter hiPSC line, which can reflect endogenous LETMD1 expression in a high-throughput manner. This LETMD1 reporter cell line enabled us to screen a preclinical compound library in which several potential hits have been identified. An unbiased CRISPR-Cas9-based transcription factor knockout library screening will also be performed to identify key regulators and pathways controlling LETMD1 expression in human beige adipocytes. Meanwhile we are currently also examining the anti-obese, anti-diabetes function of LETMD1 in the animal model, where we will transfer the LETMD1 overexpressing beige adipocytes to immune-deficient mice and examine whether enhancing the expression of LETMD1 in beige adipocytes could improve the whole-body metabolism of the recipient mice. Collectively, the work of the current project will provide valuable insight into LETMD1-targeted approaches for the management of obesity, diabetes, and metabolic diseases.

Funding: This work is supported by General Research Fund (14109622) of General Grant Council.

Abstract citation ID: lvag096.928

EP416 - ECE_1411 - Risk of incident chronic obstructive pulmonary disease in type 2 diabetes treated with SGLT2 inhibitors or GLP-1 receptor agonists vs DPP-4 inhibitors: a Real-World Cohort Study

Wei-Chuan Chang[1], Alice Yi-Yun Chan[2], Wan-Ting Huang[3], Ching-Hui Loh[2,4] and Huei-Kai Huang[2,3,5]
[1]Hualien County, Taiwan; [2]School of Medicine, Tzu Chi University, Hualien, Taiwan; [3]Center for Clinical Epidemiology and Biostatistics, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan; [4]Center for Aging and Health, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan; [5]Department of Family Medicine, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan

Background: Patients with type 2 diabetes (T2D) have a higher risk of developing chronic obstructive pulmonary disease (COPD), which is associated with substantial morbidity and mortality. Although sodium–glucose cotransporter-2 inhibitors (SGLT2is) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have demonstrated pleiotropic cardiometabolic effects and potential pulmonary benefits, their associations with incident COPD risk remain unclear.

Objective: To evaluate the associations of SGLT2is and GLP-1 RAs, using dipeptidyl peptidase-4 inhibitors (DPP4is) as an active comparator, with the risk of incident COPD in patients with T2D.

Method: We conducted a retrospective cohort study using the TriNetX Global Collaborative Network (2015-2024), emulating a target trial with a new-user, active-comparator approach. Adults with T2D initiating SGLT2is or GLP-1 RAs were compared with DPP4i users. Propensity score matching was used to balance baseline demographics, comorbidities, medication use, and laboratory data. Cox proportional hazards models were used to estimate hazard ratios for incident COPD.

Results: After propensity score matching, 329,987 matched pairs were included in the SGLT2is vs DPP4is comparison, and 303,020 matched pairs were included in the GLP-1 RAs vs DPP4is comparison. Compared with DPP4is, SGLT2i use was associated with a lower risk of incident COPD (HR, 0.86; 95% CI, 0.84-0.87), and GLP-1 RA use was associated with a similar risk reduction (HR, 0.86; 95% CI, 0.85-0.88). These associations were consistent across age and sex subgroups. In the direct comparison between GLP-1 RAs and SGLT2is (301 664 matched pairs), no significant difference in incident COPD risk was observed (HR, 0.98; 95% CI, 0.96-1.01).

Conclusions: SGLT2is and GLP-1 RAs were associated with a significantly lower risk of incident COPD compared with DPP4is in patients with T2D. These findings support the potential respiratory-protective pleiotropic effects of these agents and may inform treatment selection for patients with T2D at risk for chronic lung disease.

Abstract citation ID: lvag096.929

EP417 - ECE_2075 - Hepatoprotective benefits of gliflozins in patients with type 2 diabetes and nonalcoholic steatohepatitis

Iryna Kostitska[1], Nadiia Protas[2], Yurii Protas[1], Daryna Hrychyniuk[1] and Myroslav Lehun[1]
[1]Ivano-Frankivsk National Medical University, Endocrinology, Ivano-Frankivsk, Ukraine; [2]Ivano-Frankivsk National Medical University, Endocrinology, Ivano-Frankivska miska hromada, Ukraine

Background and Aims: Type 2 diabetes mellitus (T2D) is frequently associated with metabolic comorbidities that substantially increase the risk of nonalcoholic steatohepatitis (NASH). Fetuin-A, a liver-derived hepatokine, plays a pivotal role in the pathogenesis of insulin resistance (IR), dyslipidemia and hepatic fibrogenesis in patients with NASH. Despite growing evidence of pleiotropic metabolic benefits, the effects of sodium–glucose cotransporter-2 inhibitors (SGLT2i, gliflozins) on hepatokine regulation and liver fibrosis remain controversial. This study aimed to compare the hepatoprotective effects of dapagliflozin and empagliflozin in patients with T2D and NASH.

Materials and Methods: 42 patients with T2D and NASH were enrolled (60.2% males; mean age 59.2 ± 8.5 years; T2D duration 15.2 ± 4.3 years; body mass index (BMI) 38.1 ± 6.6 kg/m^2; waist circumference 121.4 ± 4.6 cm; glycated hemoglobin (HbA1c)- 8.23 ± 0.16%; index HOMA 6.32 ± 1.25; FIB-4 index 1.39 ± 0.28; METAVIR score at liver elastography—8.59 ± 0.58 kPa). Clinical, laboratory and instrumental assessments were performed at baseline and after 12 weeks. Serum fetuin-A and insulin were measured by ELISA. Patients were allocated into three groups (Grs): Gr 1 ($n = 14$) received basic medical therapy (BMT), including metformin (MET-2000 mg/day), alpha-lipoic acid (600 mg/day), rosuvastatin (10 mg/day); Gr 2 ($n = 14$) received dapagliflozin (DAPA-10 mg/day) in addition to BMT; Gr 3 ($n = 14$) received empagliflozin (EMPA 10-25 mg/day) plus BMT.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: After 12 weeks of treatment the greater reduction in WC were observed in Gr 2 (−3.08 ± 0.02 cm, $P < .01$) and Gr 3 (−2.99 ± 0.04 cm, $P < .01$) vs compared to Gr 1 (−0.69 ± 0.08 cm), concurrently BMI decreased significantly in the subjects receiving DAPA (−1.96 ± 2.58 kg/m^2, $P < .05$) and EMPA (−1.74 ± 2.72 kg/m^2, $P < .05$). HbA1C level was lowered by 0.48% (Gr 1); 0.96% (Gr 2) and 0.94% (Gr 3). Index HOMA was lowered by 0.25% (Gr 1); 1.02% (Gr 2) and 0.99% (Gr 3). FIB-4 decreased significantly in patints of Gr 2 (1.29 ± 0.14 to 0.59 ± 0.04, $P < .01$) and Gr 3 (1.28 ± 0.15 to 0.60 ± 0.08, $P < .01$) that in the Gr 1 (1.21 ± 0.11-1.16 ± 0.09). Due to the positive result of METAVIR score was higher in subjects of Gr 2 (8,58 ± 1,31 vs 5.43 ± 0.25 kPa, $P < .01$) and Gr 3 (8.54 ± 1.62 vs 5.22 ± 0.62 kPa; $P < .01$) compared with Gr 1 (8.51 ± 1.64 vs 7.76 ± 1.06 kPa). As regards to effect gliflozins on fetuin-A positive effect (0.6 time) in both groups. SGLT2i therapy resulted in a greater reduction of hepatic fibrosis and serum fetuin-A levels compared with Gr1.

Conclusions: Gliflozins exert hepatoprotective and metabolic benefits, supporting their potential as an innovative therapy for patients with NASH.

Abstract citation ID: lvag096.930

EP418 - ECE_2665 - Epigenetic inhibition of class I histone deacetylases by MS-275 attenuates diabetic skeletal muscle atrophy via Akt/ARK5–FoxO and myostatin–Smad signaling

Tae Ho Kim[1], Youngho Son[2,3], Suji Choi[2,3], Sung-E Choi[2], Youngha Kim[2], Seung Jin Han[2], Ja Young Jeon[2], Hae Jin Kim[2], Dae Jung Kim[2], Nami Lee[2] and Kwan-Woo Lee[2]
[1]*Division of Endocrinology and Metabolism, Seoul Medical Center, Seoul, South Korea;* [2]*Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon, South Korea;* [3]*Department of Biomedical Sciences, Graduate School of Ajou University, Suwon, South Korea*

Background: Sarcopenia is highly prevalent in individuals with diabetes and is associated with impaired physical function and increased mortality. Diabetes-associated skeletal muscle atrophy is driven by chronic inflammation, dysregulated anabolic–catabolic signaling, and activation of ubiquitin–proteasome–mediated protein degradation. Emerging evidence suggests that histone deacetylases (HDACs) act as epigenetic regulators of metabolic and inflammatory pathways; however, their role in diabetic sarcopenia remains incompletely understood.

Methods: Male *db/db* mice were used as a model of diabetes-associated muscle atrophy and treated with MS-275 (entinostat), a selective class I HDAC inhibitor, for 4 weeks. Skeletal muscle mass and fiber cross-sectional area were assessed by magnetic resonance imaging and histological analysis. Inflammatory responses, myostatin signaling, and Akt/ARK5–FoxO–mediated catabolic pathways were evaluated using immunohistochemistry, quantitative PCR, ELISA, and western blotting.

Results: MS-275 treatment significantly restored skeletal muscle mass and myofiber size in *db/db* mice. These effects were accompanied by marked reductions in macrophage infiltration, pro-inflammatory cytokine expression, and NF-κB activation. MS-275 also suppressed circulating myostatin levels and attenuated downstream Smad2/3 signaling. Furthermore, MS-275 restored Akt and ARK5 phosphorylation and promoted FoxO1/3 phosphorylation, resulting in decreased expression of the muscle-specific E3 ubiquitin ligases MuRF1 and atrogin-1.

Conclusions: Our findings demonstrate that epigenetic inhibition of class I HDACs by MS-275 attenuates diabetes-associated skeletal muscle atrophy by coordinately suppressing inflammatory signaling and myostatin-driven catabolic pathways while restoring Akt/ARK5–FoxO signaling. Targeting HDAC-mediated epigenetic regulation may represent a promising therapeutic strategy for preserving skeletal muscle mass in diabetic sarcopenia.

Abstract citation ID: lvag096.931

EP419 - ECE_2284 - Real-world glycaemic outcomes of advanced hybrid closed-loop insulin pump therapy in adults with Type 1 diabetes in a regional centre in Ireland

Hafiz Muhammad Sohail[1,2], Nehan Shakeel[1,2], Georgina Doyle[1], Lorraine Kelly[1], Michelle McCormack[1], Catherine McGarry[1], Ciara O'brien[1], Meadhbh Ní Ghallchóir[1], Jayant Sharma[1] and M.A. Pyeh Kyithar[1,3]
[1]*Diabetes & Endocrinology Department, Midland Regional Hospital, Portlaoise, Ireland;* [2]*College of Physicians and Surgeons of Pakistan, Karachi, Pakistan;* [3]*Dublin, Ireland*

Background: Advanced hybrid closed-loop (AHCL) insulin pump systems combine continuous glucose monitoring with automated insulin delivery and are increasingly used in management of Type 1 diabetes(T1D). While randomised trials demonstrate improved glycaemic outcomes, real-world audit data are essential to assess whether these benefits are sustained in routine practice and whether internationally recommended targets are achieved.

Methods: We conducted a retrospective analysis of adults (≥18 years) with T1D commenced on AHCL insulin pump therapy at a regional diabetes centre, with a median age of 37.3 years (IQR 25.8-48.1), comprising 56 females and 32 males. Continuous glucose monitoring (CGM) and clinical data were collected from Dexcom Clarity platform, Medtronic CareLink system and medical records. Pre-AHCL data were compared with the most recent available post-AHCL data. Outcomes included time-in-range (TIR), time-above-range (TAR), time-below-range (TBR), glucose management indicator (GMI), glycaemic variability expressed as coefficient of variation (CV), HbA1c and sensor utilisation. Results are presented as medians and interquartile ranges (IQR). Paired t-tests were used for matched pre- and post-AHCL comparisons, with $P < .05$ considered statistically significant.

Results: 88 adults with T1D were included, all of whom used the MiniMed™ 780G AHCL system. The median duration of AHCL use at the time of study was 9.6 months (IQR 5.6-17.7). Median TIR improved from 46.0% (IQR 30.5-63.0) prior to AHCL initiation to 74.5% (IQR 66.0-82.3) on AHCL. In paired analyses ($n = 53$), median TIR increased by 27.8% ($P < .001$), with a significant reduction in TAR (−28.3%, $P < .001$). Importantly TBR remained low and did not change significantly (median TBR pre-AHCL 0.4% vs on AHCL 0.47% ($P = .64$) indicating that improvements in glycaemic control were not achieved at the expense of increased hypoglycaemia. Median GMI improved from 7.9% (IQR 7.35-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

8.70) pre-AHCL to 6.9% (IQR 6.7-7.2) on AHCL. Among individuals on AHCL, 65% achieved the recommended target of TIR ≥70%.There was also a significant improvement in HbA1c after initiation of AHCL system 61(IQR 52.8-71.3) mmol/mol vs 54 mmol/mol (IQR 52.8-71.3) ($P = .0097$). 32% of the cohort did not consistently share or upload their AHCL data. No pump-related hospital admissions or emergency department attendances were recorded.

Conclusions: AHCL insulin pump therapy is associated with clinically meaningful improvements in glycaemic ranges and variability in adults with T1D without an increase in hypoglycaemia. While median glycaemic outcomes exceeded international guideline targets, a proportion of patients remained below target highlighting the need for ongoing optimisation and structured follow-up.

Abstract citation ID: lvag096.932

EP420 - ECE_3669 - Pancreatic transplantation in monogenic vs type 1 diabetes: insights from a Spanish Referral Center

Mariana Jesús Gomes Porras[1,2,3], Virginia Morillas Jiménez[1], Carmen Bautista Recio[1], Marta Elena Domínguez-López[1], Raquel Niddam Sanchez[4], José Antonio Pérez Daga[5], Verónica López Jiménez[6], Elena Gutierrez Vilchez[6] and María Soledad Ruiz de Adana Navas[1,2]

[1]Endocrinology and Nutrition, Regional University Hospital of Málaga, Malaga, Spain; [2]Institute of Biomedical Research of Málaga (IIBIMA), BIONAND Platform, Málaga, Spain; [3]Biomedical Research Networking Center for Diabetes and Associated Metabolic Diseases (CIBERDEM), group CB07/08/0019, Málaga, Spain; [4]Endocrinology and Nutrition, Príncipe de Asturias University Hospital, Madrid, Spain; [5]General Surgery, Regional University Hospital of Málaga, Málaga, Spain; [6]Nephrology, Regional University Hospital of Málaga, Málaga, Spain

Objective: To compare the sociodemographic characteristics and post-transplant outcomes of patients with type 1 diabetes mellitus (T1D) and monogenic diabetes (MoD) who underwent pancreas transplantation at a Spanish national referral center.

Materials and Methods: This retrospective descriptive study included 224 patients with T1D and 8 with MoD who underwent pancreatic transplantation since 1992 at a single Spanish referral center. A comprehensive, specialized multidisciplinary clinical follow-up was conducted both pre- and post-transplantation.

Results: Of 248 pancreatic transplants, 217 (87.5%) were simultaneous pancreas–kidney (SPK) procedures, including 209 in T1D (84.3%) and 8 in MoD (3.2%); 13 (5.2%) were pancreas-after-kidney (PAK) transplants, all in T1D; 2 (0.8%) were pancreas transplant alone (PTA), all in T1D; and 16 (6.4%) were pancreatic retransplants, including 15 in T1D (6.0%) and 1 in MoD (0.4%). Of the patients with MoD, seven (87.5%) had MODY, including HNF1A-MODY ($n = 4$), HNF4A-MODY ($n = 1$), and two digenic forms (GCK+HNF1A-MODY and HNF4A+HNF1A-MODY), while one patient (12.5%) had mitochondrial diabetes (m.3243A>G variant in the *MT-TL1* gene). The median delay to genetic diagnosis was 27 years (P25-P75: 15.5-34). Male predominance was observed in both groups (MoD 62.5% vs T1D 65%). Patients with MoD were slightly older at transplantation than those with T1D (mean age 44.6 vs 41 years) and had a longer duration of diabetes prior to transplantation (median 30.5 vs 25 years). All patients had microvascular complications, particularly advanced chronic kidney disease (ACKD). At the time of pancreatic transplantation, a similar proportion of patients were on dialysis in both groups (MoD 75% vs T1D 78%). Most patients also had macrovascular complications of diabetes (MoD 62.5% vs T1D 57%), especially peripheral arterial disease and ischemic heart disease. Pancreatic graft survival was higher in T1D than in MoD patients (70% vs 55.5%), with graft loss mainly due to early postoperative complications (MoD 44.5% vs T1D 30%). Graft vascular thrombosis was the most common complication, and one MoD patient developed peripancreatic necrosis secondary to a pancreatic fistula. Ninety-day perioperative mortality was higher in MoD than in T1D (12.5% vs 2.6%).

Conclusions: Pancreatic trasplantation may be an effective therapeutic option for selected patients with T1D and MoD, particularly when endocrinological evaluation is performed promptly before the initiation of dialysis. Delayed genetic diagnosis (median of 27 years) and lack of personalized treatment may contribute to higher perioperative risk, increased mortality, and lower pancreatic graft survival in MoD, highlighting the importance of applying precision medicine.

Abstract citation ID: lvag096.933

EP423 - ECE_1970 - Anti-inflammatory & anti-fibrotic effects of semaglutide in a rat model for metabolic kidney disease

Felix Wiegand[1], Simon Kloock[1], Palina Zytner[1], Thorsten Bischler[2], Panagiota Arampatzi[2], Max Kurlbaum[3], Elion Hoxha[4], Martin Fassnacht[1], Kerstin Amann[5], Christoph Daniel[5] and Ulrich Dischinger[1]

[1]Department for Internal Medicine, Division of Endocrinology and Diabetes, University of Wuerzburg, University Hospital of Wuerzburg, Wuerzburg, Germany; [2]Core Unit Systems Medicine, University of Wuerzburg, Wuerzburg, Germany; [3]Core Unit Clinical Mass Spectrometry, University of Wuerzburg, University Hospital Wuerzburg, Wuerzburg, Germany; [4]Department of Internal Medicine, Division of Nephrology, University of Wuerzburg, University Hospital Wuerzburg, Wuerzburg, Germany; [5]Department of Nephropathology, Friedrich-Alexander University Erlangen-Nuremberg, University Hospital Erlangen, Institute of Pathology, Erlangen, Germany

Introduction: The metabolic syndrome is a major risk factor for chronic kidney disease (CKD). Clinical trials show nephroprotective effects of Glucagon-like peptide (GLP)-1 receptor agonists, eg, semaglutide. In order to elucidate the mechanism of action of semaglutide in CKD, we investigate molecular kidney effects of semaglutide in a “two-hit” rat model for metabolic-induced CKD.

Methods: Renal impairment was induced by high-fat/fructose “Western” diet and chronic NO-synthase inhibition (L-NAME) in male Wistar rats. After 8 weeks, rats were randomized to either semaglutide injections ([sema], $n = 6$) or to saline sham intervention (kidney damage [KD], $n = 6$). A healthy control group received standard chow ([ctrl], $n = 6$) for 16 weeks. After 8 weeks on treatment, blood biomarkers, steroid hormone profiling (LC/MS), urinary protein/creatinine ratio quantification (UPCR, mg/mg), histology, qPCR and RNA-seq of the kidneys were performed.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: Kidney damage was confirmed by elevated blood creatinine levels (ctrl 28.2 ± 6.2 µmol/L, KD 55.8 ± 32.4 µmol/L, n.s.), urea (ctrl 8.4 ± 0.6 mmol/L, KD 10.2 ± 2.3 mmol/L, $P = .065$) & UPCR (ctrl 1.9 ± 1.2 g/g; KD 19.1 ± 11.1 g/g, $P < .01$). Compared with ctrl, KD showed significantly elevated aldosterone concentrations (ctrl 1.55 ± 0.1 ng/L, KD 2.54 ± 0.7 ng/L, $P < .01$). In sema, aldosterone concentrations showed a trend toward lower levels compared with KD, although statistical significance was not reached (sema 1.9 ± 0.2 ng/L, $P = .093$). Histology showed tubulo-interstitial damage with tubular dilatation, tubular atrophy & interstitial inflammation in KD. qPCR revealed significantly elevated gene expression of KIM-1, OPN, Tgfb and PAI-1 in KD vs ctrl. Sema contributed to favorable kidney function, as indicated by reduced urea (sema 6.0 ± 0.4 mmol/L, $P < .01$) and UPCR (sema 2.2 ± 2.4, $P < .01$). Sema exhibited lower expression of KIM-1, OPN, Tgfb, PAI-1 (all $P < .5$). RNA-seq showed upregulation of TNF-, PI3K/Akt- and NFκB signaling in KD compared to ctrl (adj.$P < .001$), which was reversed by sema treatment (all adj.$P < .001$).

Conclusions: The reduction of proteinuria and serum urea confirms nephroprotection under semaglutide. Semaglutide exerts anti-inflammatory & anti-fibrotic effects in this model of metabolic CKD. The PI3K/Akt axis may serve as a central integrator of inflammatory, fibrotic, and structural pathways, potentially mediating nephroprotection and warranting further investigation.

Abstract citation ID: lvag096.934

EP424 - ECE_1984 - Reversal of metabolic dysfunction-associated steatohepatitis by galectin-3 inhibition

Anne Raissa Melo Santos[1], Alessandra Gonçalves Da Cruz[1], Felipe Nunes de Camargo[1], Jessica Denielle Matos Dos Santos[1], Helena Gaspar Monteiro[1], Sandro Leão Matos[1], Jorge Felipe Argenta Model[1], Layanne Cabral Da Cunha Araujo[2] and João Paulo Camporez[1]

[1]Department of Phisiology, Faculdade de Medicina de Ribeirão Preto, Clinic, Ribeirão Preto, Brazil; [2]Superior Institute of Biomedical Sciences, State University of Ceara, Biomedical Sciences, Fortaleza, Brazil

Metabolic dysfunction–associated fatty liver disease (MAFLD) is characterized by excessive accumulation of triglycerides in the liver and is strongly associated with hepatic insulin resistance and type 2 diabetes mellitus. MAFLD may progress to metabolic dysfunction–associated steatohepatitis (MASH), a severe condition marked by hepatic inflammation and fibrosis, which can lead to hepatocellular carcinoma. Galectin-3 (Gal-3), a β-galactoside–binding lectin, has been implicated in inflammatory and fibrotic diseases and has emerged as a mediator in liver injury. Thus, strategies targeting Gal-3 inhibition represent a promising therapeutic approach for MASH. This study evaluated the effects of oral treatment with modified citrus pectin (MCP), a potential Gal-3 inhibitor, on metabolic and hepatic alterations associated with MASH. Male ApoE knockout mice ($n = 15$) were divided into four experimental groups: control diet (CTL), control diet supplemented with MCP (CTL+MCP), Western diet (WD), and Western diet with MCP (WD+MCP) (CEUA 1376/2024R2). After 11 weeks of dietary intervention, glucose metabolism was assessed by glucose tolerance test (GTT), and body composition was evaluated by magnetic resonance imaging. Hepatic triglyceride content and lipid droplet accumulation were determined using colorimetric assays and Oil Red O staining. Inflammatory signaling pathways were assessed by quantifying JNK protein levels, and insulin sensitivity was evaluated by Western blotting for total and phosphorylated AKT2. Total Gal-3 protein levels were quantified, and macrophage infiltration was assessed by F4/80 immunohistochemistry. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were measured using kinetic kits. The WD and WD+MCP groups exhibited a significant increase in fat and lean mass compared to the CTL group. In the GTT, CTL, and WD+MCP mice, a significant reduction in the area under the glucose curve was observed compared to the WD mice. Hepatic triglyceride content and lipid droplet accumulation were increased in the WD group relative to CTL and reduced in the WD +MCP group. Also, the WD+MCP group showed a significant reduction in JNK phosphorylation compared with the WD group, accompanied by decreased F4/80 staining, indicating lower macrophage infiltration. Insulin signaling was improved in WD +MCP mice, as evidenced by increased AKT2 phosphorylation. ALT and AST levels were elevated in WD mice and reduced by MCP treatment. Furthermore, collagen deposition and Gal-3 protein levels were increased in the WD group and reduced in WD +MCP mice. Overall, our data suggest that Gal-3 inhibition shows promise as a potential therapeutic approach to partially reverse MASH.

Abstract citation ID: lvag096.935

EP425 - ECE_2237 - Molecular and functional characterization of aminoacyl-tRNA synthetases in hepatocellular carcinoma

María Serrano-Jiménez[1,2,3,4], Natalia Hermán-Sánchez[3,4,5,6], Belén Gracia-Herencia[3,4,5,6], Manuel Rodriguez-Peralvarez[1,6,7,8], Raul M Luque[1,3,4,6], Juan Luis López-Cánovas[1,2,3,4] and Manuel D. Gahete[1,2,3,4]

[1]Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Cordoba, Spain; [2]Cordoba, Spain; [3]Reina Sofia University Hospital, Cordoba, Spain; [4]CIBER Obesity and Nutrition (CIBERobn), Madrid, Spain, Cordoba, Spain; [5]Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Cordoba, Spain; [6]Department of Cell Biology, Physiology and Immunology, University of Cordoba, Cordoba, Spain; [7]Department of Hepatology and Liver Transplantation, Reina Sofia University Hospital, Cordoba, Spain; [8]CIBER Liver and Digestive Diseases (CIBERehd), Cordoba, Spain

Introduction: Nutrient availability and amino acid homeostasis are central regulators of metabolic and endocrine function in the liver. Alterations in amino acid sensing and utilization contribute to metabolic reprogramming in metabolic dysfunction–associated steatotic liver disease (MASLD), a major driver of liver-related morbidity. Increasing evidence suggests that protein synthesis and translational control link nutrient excess to cellular dysfunction. Aminoacyl-tRNA synthetases (ARSs), which connect amino acid metabolism with translation and exert additional regulatory roles, may act as key mediators of disease progression. Therefore, we aimed to characterize the expression landscape and functional relevance of ARSs during chronic liver disease progression to hepatocellular carcinoma (HCC).

Materials and Methods: We performed an extensive transcriptomic analysis encompassing 27 cytosolic and mitochondrial

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

ARSs across 16 independent *in silico* cohorts. These datasets included a wide spectrum of chronic liver disease stages and HCC. Following the identification of the most consistently dysregulated genes, mitochondrial *HARS2* and *PARS2* were selected as top candidates for functional characterization due to their robust expression patterns. For functional studies, we employed CRISPR/Cas9-mediated gene editing to generate knockout (KO) models in two distinct HCC cell lines: Hep3B and SNU-387. The functional impact of these ARSs on the malignant phenotype was rigorously assessed through a battery of assays, including cell proliferation, wound-healing migration, colony formation, and tumorsphere formation to evaluate their role in HCC.

Results: Transcriptomic analysis revealed a widespread significant dysregulation of ARSs in HCC. Mitochondrial ARSs, specifically *HARS* and *PARS2*, emerged as the most robust biomarkers, significantly discriminating between tumor and adjacent non-tumoral tissue across multiple cohorts. In the Hep3B cell line, a *HARS2*-KO was successfully generated with 95% efficiency. Functional assays demonstrated that *HARS2* depletion led to a significant reduction in cell proliferation, migratory capacity, colony-forming units, and tumorsphere volume, suggesting a protumorigenic role in HCC.

Conclusions: Our findings reveal a profound dysregulation of ARSs in the progression from chronic liver disease to HCC. Specifically, mitochondrial *HARS2* acts as a key driver of tumorigenicity, highlighting its potential as a novel therapeutic target and diagnostic biomarker within the metabolic-oncological axis.

Funding: ISCIII (PI23/00652; co-funded by the EU), MINECO (FPU20/03957), JdA (PI-0046-2024, BIO-0139), FSEEN, and CIBERobn/ehd.

Abstract citation ID: lvag096.936

EP426 - ECE_2457 - High-fat diet disrupts intestinal crypt homeostasis by modulating epithelial proliferation and immune cell dynamics in mice

Maja Antolić[1], Sanja Srakočić[2], Mirela Janjić[2], Vuk Milutinović[2], Anja Ognjenović[2], Anesa Ivić[2], Sonja Vidović Iviš[2], Hrvoje Brzica[2], Ines Glojnarić[2] and Snježana Čužić[2]
[1]*In vivo Pharmacology and Toxicology, Selvita Ltd., Zagreb, Croatia;* [2]*Selvita Ltd., Zagreb, Croatia*

Obesity and pre-diabetes are major global public health challenges, with a high-fat diet (HFD) serving as a key contributor to obesity, insulin resistance, and metabolic inflammation. HFD-induced metabolic stress can disrupt intestinal homeostasis, affecting both epithelial proliferation and immune cell composition. Mice fed a high-fat diet are commonly used to model these conditions in vivo. Among immune cells, M2-polarized macrophages are known to support epithelial regeneration and promote the resolution of intestinal inflammation. However, the effects of HFD on the interplay between intestinal epithelial proliferation and immune cell dynamics within small intestinal crypts remain incompletely understood.

In this study, 5-6-week-old C57BL/6J male mice were fed either control chow or an HFD for 20 weeks. Blood glucose and insulin levels were measured in fasted animals. Small intestine sections were analyzed using hematoxylin and eosin (H&E) staining for morphometric assessment, while immunohistochemistry (IHC) was employed to evaluate epithelial proliferation (Ki67), crypt intraepithelial T lymphocytes (CD3), and M2 macrophages (CD206) in the lamina propria surrounding mucosal crypts. Morphometric parameters included mucosal thickness, crypt depth, villus length and width. Digital image analysis was used to quantify Ki67 expression as the percentage of positive cells, the number of intraepithelial CD3-positive cells, and the CD206-positive area within the lamina propria adjacent to crypts.

HFD-fed mice exhibited significantly increased body weight, hyperinsulinemia, and hyperglycemia compared to controls. In small intestinal crypts, the percentage of Ki67-positive cells showed a decreasing trend in HFD-fed animals, whereas the number of intraepithelial CD3-positive T lymphocytes was significantly increased. In contrast, the CD206-positive area, representing M2 macrophages, was significantly reduced in the HFD group.

These findings indicate that HFD induces systemic metabolic dysfunction and disrupts small intestinal crypt homeostasis. Reduced epithelial proliferation, increased T-cell infiltration, and decreased M2 macrophage presence suggest that HFD-induced immune dysregulation may impair intestinal epithelial regeneration. The observed association between epithelial proliferation and M2 macrophages highlights the potential role of macrophage-mediated support in maintaining intestinal epithelial integrity under metabolic stress. Overall, this study demonstrates that HFD not only drives metabolic disturbances but also alters the cellular composition and regenerative capacity of small intestinal crypts, providing mechanistic insight into the gut-related consequences of obesity and pre-diabetes.

Abstract citation ID: lvag096.937

EP427 - ECE_2668 - Multifaceted beneficial effects of thiostrepton on high-fat diet-induced MASLD mice model

Tae Ho Kim[1], Sung-E Choi[2], Youngho Son[2,3], Youngha Kim[2], Suji Choi[2,3], Ja Young Jeon[2], Seung Jin Han[2], Hae Jin Kim[2], Dae Jung Kim[2], Nami Lee[2] and Kwan-Woo Lee[2]
[1]*Division of Endocrinology and Metabolism, Seoul Medical Center, Seoul, South Korea;* [2]*Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon, South Korea;* [3]*Department of Biomedical Sciences, Graduate School of Ajou University, Suwon, South Korea*

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) remains a major global health challenge, driven by a complex interplay of lipid dysregulation and mitochondrial failure. Thiostrepton (TST), while traditionally known as a thiopeptide antibiotic, has emerged as a potent modulator of inflammation and mitochondrial homeostasis. This study explores the novel therapeutic potential of TST in reversing the core pathological hallmarks of MASLD.

Methods: To simulate chronic metabolic stress, male C57BL/6J mice were challenged with a 15-week high-fat diet (HFD). Following disease establishment, TST (2.5 mg/kg) was administered intraperitoneally for 5 weeks. We performed a comprehensive evaluation integrating systemic metabolic profiling (IPGTT, IPITT), serum biochemistry (ALT, AST), and molecular/histological analysis of hepatic lipogenesis and fibrotic remodeling.

Results: TST treatment led to a profound restoration of metabolic health, significantly enhancing glucose disposal and insulin

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

sensitivity. These systemic improvements were accompanied by a sharp decline in liver injury markers. At the molecular level, TST effectively silenced the pro-steatotic program by downregulating *Srebp1c* and *Fasn*, while simultaneously inhibiting fibrogenic gene expression. Histological scoring confirmed a marked reduction in both lipid vacuoles and collagen deposition, validating the robust anti-steatotic and anti-fibrotic efficacy of TST.

Conclusions: Our study identifies Thiostrepton as a high-potential therapeutic agent that multi-targets the metabolic and structural facets of MASLD. By coordinating lipid metabolism and attenuating fibrosis, TST offers a promising multifaceted strategy for treating progressive liver disease.

Abstract citation ID: lvag096.938

EP429 - ECE_3518 - Adipose-derived stem cells and monocyte/macrophage interactions drive inflammatory responses in obesity

Davide Masi[1], Mariaignazia Curreli[1], Michele Avventaggiato[1], Serena Recalchi[1], Stefania Morrone[1], Matteo Russo[1], Mikiko Watanabe[1], Stefania Mariani[1], Daniele Gianfrilli[1], Andrea Isidori[1], Giovanni Casella[2], Elisa Petrangeli[1], Marco Tafani[1] and Carla Lubrano[1]

[1]*Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza University, Rome, Italy;* [2]*Department of Surgical Sciences, Sapienza University, Rome, Italy*

Background: Obesity-associated adipose tissue (AT) dysfunction is driven by chronic low-grade inflammation, particularly within visceral adipose tissue (VAT), where hypoxia profoundly alters stromal–immune interactions. Adipose-derived stem/stromal cells (ASCs) are key regulators of the AT microenvironment and, in obesity, may actively promote inflammatory macrophage responses.

Objective: To define how ASCs derived from subcutaneous (SAT) and visceral (VAT) fat of individuals with obesity modulate monocyte/macrophage activation and polarization under normoxic and hypoxic conditions, and to elucidate the contribution of NF-κB signaling to this crosstalk.

Methods: ASCs were isolated from paired SAT and VAT samples of patients with obesity undergoing bariatric surgery. Human THP-1 monocytes were differentiated into M0 macrophages and polarized toward M1 or M2 phenotypes, then cultured alone or co-cultured with SAT- or VAT-derived ASCs under normoxia or hypoxia (1% O_2). Macrophage proliferation, adhesion, and polarization were evaluated by cell counts, microscopy, flow cytometry (CD14, CD80, CD206), western blotting (HIF-1α, NF-κB, RAGE), and immunofluorescence. TNF-α secretion was quantified by ELISA. NF-κB involvement was assessed using the pharmacological inhibitor parthenolide.

Results: Hypoxia alone increased THP-1 proliferation and induced HIF-1α, NF-κB, and RAGE expression, enhancing inflammatory activation across macrophage phenotypes. Co-culture with ASCs markedly amplified macrophage activation, with VAT-derived ASCs exerting stronger effects than SAT-derived ASCs. VAT-ASCs significantly increased CD14, CD80, and CD206 expression in THP-1 cells and potentiated hypoxia-driven responses. Functionally, VAT-ASCs promoted elevated TNF-α secretion, particularly in M1-polarized macrophages, an effect further enhanced by hypoxia. In contrast, SAT-ASCs attenuated TNF-α release in several polarization states, even under hypoxic conditions. Hypoxia induced robust NF-κB activation and nuclear localization predominantly in M1 macrophages. Parthenolide effectively inhibited NF-κB activation, reduced inflammatory marker expression, and significantly decreased adhesion of M1 macrophages to both SAT- and VAT-derived ASCs.

Conclusions: Hypoxia and visceral ASCs synergistically drive macrophage activation and inflammatory polarization in obesity through NF-κB–dependent mechanisms. The enhanced pro-inflammatory crosstalk between VAT-ASCs and macrophages identifies a pathogenic axis contributing to adipose tissue inflammation and dysfunction, highlighting NF-κB as a potential therapeutic target in obesity-related metabolic disease.

Abstract citation ID: lvag096.939

EP430 - ECE_3900 - Early changes in circulating immune cell populations following GLP-1 receptor agonist therapy in obesity

Kleopatra Alexiadou[1], Mona Xia[1], Rajalakshmi Valaiyapathi[1], Anna Kowalka[1], Irene Guo[1], Lara Jimenez-Pacheco[1], Julia Kenkre[1], Saira Hameed[2], Chioma Izzi-Engbeaya[1], Harvinder Chahal[2], Sirazum Choudhury[2] and Tricia Tan[1]

[1]*Imperial College London, London, United Kingdom;* [2]*Imperial College Healthcare NHS Trust, London, United Kingdom*

Background: Obesity is a multisystem disease associated with numerous complications, including type 2 diabetes, cardiovascular disease and at least 13 types of cancer. Pre-clinical data and randomised controlled trials suggest that glucagon-like peptide-1 receptor agonists (GLP-1RAs) exert pleiotropic effects beyond weight reduction and glycaemic control, including cardiovascular benefits occurring prior to substantial weight loss. This observation suggests the presence of weight-independent mechanisms, which remain incompletely understood but may involve immunomodulatory effects. The aim of this study was to investigate the impact of GLP-1 receptor agonism on circulating immune cell populations. We hypothesised that GLP-1RA therapy would be associated with a shift away from a pro-inflammatory immune phenotype.

Methods: In this observational study, 19 adults with obesity initiating treatment with either semaglutide 1 mg weekly or liraglutide 3 mg daily were recruited. In addition, 12 adults with obesity commencing a low-calorie diet were recruited as a control group. Participants were assessed at baseline, 6-8 weeks and 12-16 weeks after treatment initiation. Anthropometric measurements and biochemical analyses, including fasting glucose, insulin, lipids, high-sensitivity C-reactive protein (hsCRP) and HbA1c, were performed. Peripheral blood mononuclear cells were isolated by gradient centrifugation and immunophenotyped using a comprehensive antibody panel targeting lymphoid and myeloid surface markers. Samples were analysed using a Cytek Aurora spectral flow cytometer, with downstream analysis performed using FlowJo software. We present a preliminary analysis of the GLP-1RA treatment group.

Results: Body weight decreased significantly over the study period, with a mean reduction of 4.2% (95% CI −5.3 to −3.1) at 6-8

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

weeks and 6.3% (95% CI −8.0 to −4.6) at 12-16 weeks. No significant changes were observed in fasting glucose, insulin, or hsCRP levels. Flow cytometric analysis demonstrated a significant reduction in circulating B cells and a shift in natural killer cell subsets at 6-8 weeks, characterised by an increase in $CD56^{+}CD16^{Hi}$ cells and a reduction in $CD56^{Bright}CD16^{Dim}$ cells. At 12-16 weeks, an increase in $CD3^{+}$ T cells and a reduction in neutrophils were observed.

Conclusions: GLP-1 receptor agonist therapy is associated with early dynamic changes in circulating immune cell populations, detectable within weeks of treatment initiation and preceding significant metabolic improvements. Ongoing analysis of the dietary intervention group will help determine whether these immunological changes are independent of weight loss. These immunological alterations may contribute to the pleiotropic benefits of GLP-1RAs and support their potential therapeutic applications beyond obesity and diabetes.

Abstract citation ID: lvag096.940

EP431 - ECE_2430 - Body fat (%) change thresholds predicting LDL cholesterol progression to treatment levels

Kyoung Min Kim and Su Jin Kwon
Endocrinology, Internal Medicine, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, South Korea

Background: Dyslipidemia represents a critical cardiovascular risk factor. While body composition changes influence lipid metabolism, sex-specific thresholds for body fat percentage changes that predict progression to treatment-requiring LDL levels remain undefined.

Methods: We conducted a retrospective longitudinal analysis of 30 159 adults (15 235 men, 14 924 women) who underwent repeated health screenings at Severance Hospital Health Screening Center between 2010-2023. Participants had ≥2 measurements of LDL cholesterol and body composition. Mean follow-up was 4.3 years. Multivariate logistic regression models incorporating baseline LDL-C, body fat percentage change, age, sex, and follow-up interval identified the body fat percentage change associated with ≥50% probability of reaching LDL-C ≥160 mg/dL across baseline LDL strata.

Results: Baseline characteristics showed mean age of 43.7 years, BMI 23.2 kg/m^2, and LDL-C 112.8 mg/dL. Men exhibited higher baseline LDL-C (116.8 vs 108.6 mg/dL) and triglycerides (126.9 vs 80.9 mg/dL) compared to women. Body fat percentage change correlated positively with LDL-C progression in both sexes. Critical thresholds varied markedly by baseline LDL, age, and sex. For men aged <50 years with baseline LDL 120-129 mg/dL, a 9.7% body fat increase conferred 50% risk of reaching LDL ≥160 mg/dL, decreasing to 3.2% and 0.9% for higher baseline LDL 140-149 and 150-159 mg/dL respectively. Men ≥50 years demonstrated lower thresholds: 6.7%, 3.1%, and 1.4% for respective baseline categories. Women showed distinct patterns. Those aged <50 years reached 50% risk with 13.3%, 9.2%, 5.5%, 2.5%, and 0.03% body fat increases for baseline LDL 110-119, 120-129, 130-139, 140-149, and 150-159 mg/dL respectively. Women ≥50 years required smaller increases: 10.5%, 5.0%, 2.1%, and 0.4% for baseline LDL 120-129 through 150-159 mg/dL.

Conclusions: Changes in body fat percentage are significantly associated with the risk of reaching clinically high LDL levels. Our model provides specific BF% change "cut-off" values that can be used in clinical settings to provide personalized weight management targets for preventing the progression to hyperlipidemia, particularly in patients with borderline-high baseline LDL levels.

Abstract citation ID: lvag096.941

EP432 - ECE_1355 - From fatty liver to adipokines: converging pathways linking insulin resistance to early atherosclerosis in obese children and adolescents

Ashraf Soliman, Manal Musallam, Fawziya Alyafei, Nada Alaaraj, Noor Hamed, Shayma Ahmed and Noora Alhemaidi
Pediatric Endocrinology, Hamad Medical Center, Doha, Qatar

Background: Childhood obesity is increasingly complicated by early vascular remodeling, measurable as increased carotid intima–media thickness (cIMT). Beyond excess adiposity per se, disturbances in carbohydrate metabolism and adipose derived signaling molecules appear to play a central role. Two phenotypic clusters—nonalcoholic fatty liver disease (NAFLD) and adipocytokine dysregulation—have emerged as key intermediates linking insulin resistance to subclinical atherosclerosis in pediatric obesity.

Objectives: To synthesize evidence from the past 25 years examining the associations between increased cIMT, carbohydrate metabolism abnormalities, and adipocytokines in obese children and adolescents, with particular focus on NAFLD-heavy and adipokine-heavy phenotypes.

Methods: A structured narrative synthesis was performed using validated studies summarized in Table A (NAFLD-focused) and Table B (adipokine-focused). Included evidence comprised cross-sectional studies, interventional weight-loss studies, and systematic reviews/meta-analyses published between ~2000 and 2025. NAFLD was defined by ultrasound or liver biopsy, while metabolic assessment included fasting glucose, insulin, HOMA-IR, OGTT-derived indices, and adipocytokines (eg, resistin, adiponectin subfractions, chemerin). Outcomes of interest were mean or maximal cIMT and its metabolic determinants.

Results: Across NAFLD-heavy studies, obese children with NAFLD consistently exhibited higher cIMT than obese peers without NAFLD and normal-weight controls. This association was evident even in childhood and adolescence and strengthened with greater hepatic disease severity, including biopsy-proven steatosis and steatohepatitis. NAFLD-associated increases in cIMT closely paralleled markers of insulin resistance (elevated fasting insulin, HOMA-IR) and adverse lipid profiles, supporting NAFLD as a vascular “risk amplifier” within pediatric obesity. Interventional data further demonstrated that weight loss and metabolic improvement were accompanied by reductions in cIMT, indicating partial reversibility of early vascular changes. Adipokine-heavy studies revealed that specific adipocytokines are directly and indirectly linked to cIMT. Resistin showed robust positive associations with cIMT, acting both directly and via insulin resistance and systemic inflammation (hsCRP). Alterations in adiponectin subfractions, rather than total adiponectin alone, were

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

associated with preatherosclerotic phenotypes. Chemerin levels correlated with metabolic syndrome determinants and early vascular pathology, even in obese children without overt hypertension. Collectively, these findings demonstrate that adipokine dysregulation integrates adipose inflammation with carbohydrate metabolism to drive vascular remodeling.

Conclusions: Evidence from NAFLD-heavy and adipokine-heavy pediatric studies converges on a common pathway: insulin resistance–centered metabolic dysfunction linking obesity to increased cIMT. NAFLD identifies a particularly high-risk subgroup, while adipocytokines provide mechanistic insight into early atherosclerosis. These findings support early metabolic screening, including assessment of NAFLD and adipokine-related risk, to prevent progression of cardiovascular disease in obese youth.

Abstract citation ID: lvag096.942

EP433 - ECE_1386 - Emotional and psychological dimensions of living with type 1 diabetes: a qualitative study of adolescents, parents, and healthcare providers in Nepal

Binaya Bhattarai[1,2]
[1]Endocrinology, Hams Hospital, Hams Hospital, Kathmandu, Nepal; [2]Endocrinology, HAMS Hospital, Kathmandu, Nepal

Background: Type 1 diabetes mellitus (T1DM) presents not only a chronic physical burden but also a significant psychological challenge, particularly among adolescents and young adults. Despite increasing recognition of the emotional toll of diabetes, mental health care remains inadequately integrated into routine diabetes management.

Objective: This qualitative study explores the lived psychological experiences of adolescents and young adults living with diabetes (AYALD), their parents, and healthcare professionals to identify key emotional stressors, coping mechanisms, and systemic gaps in psychosocial support.

Methods: A phenomenological design was employed using five focus group discussions (FGDs): two with AYALD, two with their parents ($n = 20$ per group), and one with healthcare professionals ($n = 15$). Discussions were audio-recorded, transcribed verbatim, and thematically analyzed using NVivo software following a six-step framework that included data familiarization, coding, theme development, and synthesis.

Results: Three major themes emerged: (1) Emotional Burden, characterized by fear, isolation, and stigma at diagnosis and during daily management; (2) Diabetes and School, highlighting inadequate institutional preparedness and experiences of stigmatization; and (3) Diabetes and Depression, revealing prevalent depressive symptoms and gaps in mental health referral and integration. Subthemes included emotional masking, parental overprotection, and the pivotal role of peer support and diabetes camps. A key finding was the disconnect between increased mental health referrals by medical professionals and low patient uptake, suggesting structural barriers within pediatric mental health care pathways.

Conclusions: Living with T1DM extends beyond metabolic regulation; it is a deeply emotional experience shaped by social, familial, and institutional factors. Effective diabetes care requires systemic reforms to integrate psychological support into routine management, strengthen peer-support networks, enhance school-level awareness, and improve interdisciplinary communication. Further research is warranted to validate emotional masking as a potential clinical indicator and to examine long-term psychosocial outcomes among youth living with diabetes.

Abstract citation ID: lvag096.943

EP434 - ECE_1489 - Hidden metabolic risk in erectile dysfunction: prevalence of undiagnosed diabetes mellitus, prediabetes, and metabolic syndrome

Emre Hepşen[1], Samet Kıpık[1], Mustafa Köse[1], Hüseyin Mert Durak[1], Neslihan Koray Fedai[2] and Sema Hepşen[2]
[1]University of Health Sciences, Ankara Etlik City Hospital, Urology, Ankara, Türkiye; [2]University of Health Sciences, Ankara Etlik City Hospital, Endocrinology and Metabolism, Ankara, Türkiye

Background: This study aimed to determine the prevalence of undiagnosed impaired glucose metabolism (IGM) and metabolic syndrome (MetS) in men presenting with erectile dysfunction (ED) and to assess whether ED severity is associated with specific IGM subgroups.

Methods: 605 consecutive men aged ≥18 years presenting with ED were evaluated for inclusion. Patients with known IGM, chronic diseases, antiandrogen use or prior testicular, pituitary, or prostate surgery were excluded. ED severity was assessed using the 5-item International Index of Erectile Function (IIEF-5). Diabetes mellitus (DM) and prediabetes were diagnosed based on the 2025 American Diabetes Association, while MetS was defined according to the revised NCEP–ATP III criteria. Clinical data, anthropometrics, and laboratory measurements were obtained.

Results: Of the 310 patients included, the mean age was 52 ± 13.3 years, the median body mass index was 27.7 kg/m^2 (19.6-42.9), and the median waist circumference was 93 cm (73-127). Hypertension was present in 84 patients (27.1%), and obesity in 49 (15.8%). Median fasting plasma glucose was 91 mg/dL (63-568), median HbA1c was 5.4% (4.2-11.7), and median 2-hour oral glucose tolerance test glucose was 192 mg/dL (124-275). MetS was identified in 94 patients (30.3%), and IGM in 82 (26.4%), including 28 newly diagnosed cases of DM (9.0%) and 54 cases of prediabetes (17.4%). Among patients with prediabetes, impaired fasting glucose (IFG) was observed in 53.7%, combined IFG and impaired glucose tolerance in 7.4%, and elevated HbA1c in 38.9%. The prevalence of IGM differed significantly across ED severity categories ($P = .042$). Testosterone were significantly lower in patients with MetS (median, 331 ng/dL; $P < .001$). The IIEF-5 score showed a moderate negative correlation with age ($r = -0.368$, $P < .001$) and weak negative correlations with HbA1c ($r = -0.192$, $P = .001$) and fasting glucose ($r = -0.180$, $P = .001$). ROC analysis showed that IIEF-5 score had a modest but statistically significant ability to discriminate IGM (AUC, 0.599; $P = .008$), with sensitivity and specificity of 0.512 and 0.639 at a cut-off of 14.5. Similarly, its discriminatory performance for MetS was limited (AUC, 0.571; $P = .047$), with sensitivity of 0.505 and specificity of 0.606.

Conclusions: Newly diagnosed IGM and MetS were detected in nearly one out of every three patients presenting with ED. These findings emphasize that patients with ED, particularly

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

those with mild or moderate symptoms, should be carefully evaluated for underlying metabolic risk, as ED may serve as an early clinical indicator of otherwise unrecognized metabolic disturbances.

Abstract citation ID: lvag096.944

EP435 - ECE_1726 - Prediabetes stage and kidney function decline in non-diabetic adults: a metabolic liver-kidney link?

Josep León Mengíbar[1,2], Rafael Simo Canonge[1], Cristina Hernandez[1], Olga Simó[1], Pedro Gil[1], Angel Michael Ortiz[1], Aaron Switzer[1] and Albert Lecube[1]
[1]Hospital Universitari Vall d'Hebrón, Barcelona, Spain; [2]Vall d'Hebron University Hospital, Barcelona, Spain

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) has been linked to chronic kidney disease (CKD), with fibrosis as the potential pathogenic factor shared by both diseases. The Fibrosis-4 (FIB-4) index is a widely used non-invasive fibrosis marker; however, its association with renal outcomes remains uncertain. We evaluated the relationship between FIB-4, estimated glomerular filtration rate (eGFR) decline and albuminuria in the ILERVAS cohort.

Methods: We included 3,940 adults aged 45-70 years from the ILERVAS study, all free of diabetes, CKD and chronic liver disease. FIB-4 was analysed categorically (<1.30 vs ≥1.30) and continuously in regression models. Renal outcomes were eGFR and albuminuria (albumin-to-creatinine ratio ≥30 mg/g) at baseline and 4 years. Multivariable linear and logistic regression models were adjusted for age, sex, hypertension, presence of prediabetes, adiposity, lipids and smoking.

Results: At baseline, 78.3% of participants were classified as low FIB-4 risk and 21.7% as indeterminate-high risk; the latter were older and had lower eGFR, whereas albuminuria prevalence was similar. At 4 years ($n = 1593$), eGFR remained lower in the indeterminate-high group, with no differences in albuminuria prevalence. In multivariable analyses, higher FIB-4 values and prediabetes independently predicted greater eGFR decline ($\beta = -1.15$ and -1.57; $P = .013$ and .023, respectively). Age, female sex, baseline eGFR and hypertension also emerged as independent predictors of eGFR decline.

Conclusions: In adults at low-to-moderate cardiovascular risk without diabetes or established liver/kidney disease, both higher FIB-4 values and prediabetes were independently associated with faster eGFR loss. FIB-4 may help to capture systemic metabolic factors related to fibrosis, suggesting its potential role in renal risk stratification.

Abstract citation ID: lvag096.945

EP436 - ECE_1798 - Irisin ameliorates low-dose endotoxemia-induced muscle atrophy via integrin αVβ5-mediated suppression of TLR4 signaling pathway

Muhammad Arif Aslam[1] and Joo Young Huh[2]
[1]Chonnam National University, Gwangju, South Korea; [2]Seoul, South Korea

Metabolic endotoxemia, defined as the chronic low-grade elevation of circulating lipopolysaccharide (LPS), is increasingly being recognized as a driver of systemic inflammation, metabolic dysfunction, and age-related muscle atrophy. However, the molecular pathways linking endotoxemia to muscle atrophy and the potential protective role of irisin, a myokine derived from fibronectin type III domain-containing protein 5 (FNDC5), remain poorly understood. This study addressed the gap between metabolic endotoxemia and muscle atrophy and investigated whether irisin could serve as a muscle-protective factor. Male C57BL/6J mice received low-dose LPS administration (300 μg/kg for 1, 3, 7, and 14 days). Muscle mass, fiber cross-sectional area, and expression of genes and proteins were analyzed. FNDC5 knockout mice were used to assess the contribution of endogenous irisin. Recombinant irisin (0.1 mg/kg/day) was administered to LPS-treated mice, with or without integrin αVβ5 blockade by cilengitide. Repeated low-dose LPS treatment induced significant muscle wasting, as reflected by reduced muscle mass, impaired physical performance, and upregulation of atrogin-1 and MuRF1. LPS activates TLR4/MD2 signaling pathway and NLRP3-mediated pyroptosis, as indicated by elevated caspase-1 and cleaved gasdermin D (GSDMD) levels while simultaneously suppressing FNDC5/irisin expression. FNDC5 deficiency further aggravated LPS-induced muscle atrophy and pyroptotic signaling. In contrast, recombinant irisin restored muscle mass and improved physical function. Mechanistically, irisin directly bound MD2, limiting TLR4/MD2 complex formation, and the muscle-protective effects of irisin were abolished by integrin αVβ5 blockade with cilengitide, confirming receptor dependence. Collectively, these findings identify the TLR4/caspase-1/GSDMD axis as a key driver of endotoxemia-induced muscle atrophy and establish irisin as a protective myokine that counters endotoxemic muscle loss through MD2 binding and integrin αVβ5 signaling, supporting its therapeutic potential for inflammation-associated muscle wasting.

Abstract citation ID: lvag096.946

EP437 - ECE_1836 - Bidirectional associations between FIB-4 severity and cardiovascular autonomic neuropathy in type 2 diabetes

Chan-Hee Jung[1], Hyun-Ju Lee[1], Yoon Young Cho[1], Bo-Yeon Kim[1], Chul-Hee Kim[1] and Ji-Oh Mok[1]
[1]Soonchunhyang University College of Medicine, Bucheon Hospital, Endocrinology and Metabolism, Diabetes Center, Internal Medicine, Bucheon-si, South Korea

Background and Aim: To our knowledge, studies examining the association between the fibrosis-4 (FIB-4) index and cardiovascular autonomic neuropathy (CAN) in patients with type 2 diabetes (T2DM) are very limited. In this study, we explored the bidirectional relationship between FIB-4 categories and the presence of CAN in T2DM, with particular interest in whether liver fibrosis indices might correspond to autonomic dysfunction.

Methods: A total of 434 T2DM patients were enrolled in this cross-sectional study. CAN was assessed using five tests according to Ewing's protocol and was defined as the presence of autonomic neuropathy points ≥2.0. FIB-4 index categories were defined using age-adjusted cut-off values. For participants <60 years, FIB-4 was categorized as low risk (<1.30), intermediate risk (1.3-2.67), and high risk (>2.67). For participants aged ≥60, FIB-4 ≤2.0 was defined as low risk, while FIB-4 >2.0 indicated elevated fibrosis risk.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: The mean age of participants was 55.9 years and 55.8% were male. The median duration of diabetes was 5 years (IQR 0-12), with 35.0% having diabetes for ≥10 years. The mean FIB-4 index was 1.28 ± 0.99, and autonomic function testing revealed a mean CAN score of 2 ± 1.3, with 61.3% meeting the criteria for CAN. Participants with CAN had significantly higher FIB-4 values compared with those without CAN (1.4 ± 1.2 vs 1.2 ± 0.7, P = .01). FIB-4 severity categories showed a trend toward higher proportions of high-risk FIB-4 in subjects with CAN than those without CAN (6.8% vs 1.8%, P = .06). The prevalence of CAN increased markedly across categories, from 40.3% in the low group to 85.7% in the high FIB-4 group (P < .001). In the bivariate correlation analyses, FIB-4 showed significant positive correlations with both parasympathetic (r = 0.164, P < .001) and sympathetic autonomic scores (r = 0.110, P < .05), and CAN total score (r = 0.168, P < .001). In multivariable logistic regression, High-risk FIB-4 severity was associated with significantly greater odds of CAN (OR 8.9, 95% CI 1.1-76.8), while CAN presence was also independently associated with High-risk FIB-4 status (OR 11.1, 95% CI 1.1-107.7).

Conclusions: FIB-4 severity and CAN presence demonstrated a bidirectional association, although estimates were modest. These findings suggest that liver fibrosis markers may reflect broader multisystem vulnerability related to autonomic dysfunction and highlight the need for larger longitudinal studies to determine clinical significance.

Abstract citation ID: lvag096.947

EP438 - ECE_1851 - Differential associations of FIB-4 index with dynapenia in younger and older patients with type 2 diabetes mellitus

Ji-Oh Mok, Chan-Hee Jung, Hyun-Ju Lee, Yoon Young Cho, Bo-Yeon Kim and Chul-Hee Kim
Soonchunhyang University College of Medicine, Bucheon Hospital, Endocrinology and Metabolism, Diabetes Center, Internal Medicine, Bucheon-si, South Korea

Background and Aim: Dynapenia is an important predictor of adverse health outcomes and may be influenced by metabolic dysfunction. The fibrosis-4 (FIB-4) index, a non-invasive marker of liver fibrosis, has been associated with systemic metabolic abnormalities; however, its relationship with dynapenia and the potential mediating role of insulin resistance remain unclear, particularly across different age groups.

Methods: We conducted a cross-sectional analysis of 582 adults with T2DM stratified by age (<60 and ≥60 years). Dynapenia was defined based on handgrip strength criteria. FIB-4 index categories were defined using age-adjusted cut-off values. For participants <60 years, FIB-4 was categorized as low risk (<1.30), intermediate risk (1.3-2.67), and high risk (>2.67). For participants aged ≥60, FIB-4 ≤2.0 was defined as low risk, while FIB-4 >2.0 indicated elevated fibrosis risk.

Results: The mean age of all participants was 5.9 years and duration of DM was 8 years. The prevalence of dynapenia was 19.1% in all subjects (11.8% in aged <60 and 28.1% in aged ≥60). When stratified by age, participants aged <60 years showed a higher prevalence of the low-risk category (71.4%), with 25.2% as intermediate risk, and 3.4% as high risk. Among participants aged ≥60 years, the proportion of low risk was lower (55.2%) while the prevalence of intermediate- and high-risk was higher (35.1% and 9.7%). FIB-4 showed significant inverse correlations with HGS and the HGS/ASMI ratio, but not with ASMI. Multivariable logistic regression analysis was performed to examine the association between FIB-4 severity and dynapenia. Among age <60 years, high FIB-4 severity was significantly associated with dynapenia (OR 13.24, 95% CI 1.7-103.6) after adjustment for covariates. After further adjustment for HOMA-IR as marker of insulin resistance attenuated the association, although effect sizes remained elevated (High risk OR 4.9). In contrast, among aged ≥60 years, the association between FIB-4 severity and dynapenia was weaker and not statistically significant.

Conclusions: Our study showed the association between FIB-4 severity and dynapenia appears to differ by age. These findings suggest that FIB-4 may serve as an early metabolic risk marker for dynapenia, particularly in younger populations. The attenuation of the association after adjustment for HOMA-IR suggests that insulin resistance may represent an important mechanistic link between liver fibrosis burden and muscle strength decline in younger adults. In contrast, the association was weaker and more heterogeneous in adults aged ≥60 years, consistent with multifactorial aging-related mechanisms.

Abstract citation ID: lvag096.948

EP439 - ECE_2035 - Association between perceived psychological stress and eating disorders in adolescent and young adults with type 1 diabetes

Ruta Navardauskaite[1,2], Vika Jaskeviciute[3], Virginija Bulikaite[1,4] and Lina Lašaitė[5]
[1]*Department of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [2]*Department of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [3]*Pediatric Department, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [4]*Department of Nursing, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [5]*Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania*

Introduction: Adolescents and young adults with type 1 diabetes mellitus (T1DM) are at an increased risk of developing eating disorders (ED) compared to their healthy peers. ED in T1DM patients ranges from 7.0% to 39.3% and is associated with poor glycemic control and impaired psychosocial well-being.

Objectives: To assess the relationship between eating disorder severity and perceived stress in adolescents and young adults with T1DM attending a specialised transition-age diabetes camp.

Methods: Levels of perceived stress and ED were assessed in 29 adolescents and young adults with T1DM (age: 17.1 ± 2.0 years; T1DM duration: 8.9 ± 4.5 years; age at diagnosis: 8.1 ± 4.1 years; HbA1c: 7.5 ± 1.4%; BMI: 23.7 ± 3.9 kg/m^2) attending the diabetes camp for transition-age patients. The Perceived Stress Scale (PSS) was used to measure stress levels (higher scores indicate greater perceived stress), and the Eating Disorder Examination Questionnaire (EDE-Q) was used to assess ED severity (higher scores indicate more severe ED symptoms).

Results: Participants were divided into two groups based on PSS scores: low perceived stress (<20, n = 14) and high perceived

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

stress (≥20, $n = 15$). Those with high perceived stress had significantly higher EDE-Q scores in restraint ($P = .004$), eating concern ($P < .001$), shape concern ($P < .001$), weight concern ($P = .002$), and global score ($P < .001$). Additionally, they reported more binge eating episodes with loss of control per month ($P = .016$). BMI was correlated with EDE-Q restraint (r = 0.377, $P = .048$), eating concern (r = 0.581, $P = .001$), global score (r = 0.447, $P = .017$), and number of compulsive exercise episodes per month (r = 0.389, $P = .041$). PSS scores were correlated with EDE-Q restraint (r = 0.470, $P = .012$), eating concern (r = 0.628, $P < .001$), shape concern (r = 0.628, $P < .001$), weight concern (r = 0.567, $P = .002$), and global score (r = 0.652, $P < .001$).

Conclusions: Adolescents and young adults with T1DM and high perceived stress exhibit higher levels of eating disorder symptoms compared to those with low perceived stress.

Abstract citation ID: lvag096.949

EP441 - ECE_2338 - The insulin-like growth factor system and the progression ofrenal complications of type 2 diabetes

Adrian Heald[1], Yasitha Illangasekera[2,3], Andreas Matheou[4], Ram Prakash Narayanan[5], Steve White[6], Hellena Habete-Asres[7], Abigail Lay[4], Liliana Shalamanova[8], William Ollier[8], Graham Hitman[9], Ritwika Mallik[9], Philip Kalra[4], Martin Whyte[10] and Martin Gibson[1]

[1]Department of Diabetes and Endocrinology, Salford Royal Hospital, Salford, United Kingdom; [2]Sheffield Hallam University, Sheffield, United Kingdom; [3]University of Peradeniya, Peradeniya, Sri Lanka; [4]University of Manchester, Manchester, United Kingdom; [5]Whiston Hospital, Prescot, Merseyside, United Kingdom; [6]University of Newcastle, Newcastle, United Kingdom; [7]Kings College Hospital, London, United Kingdom; [8]Manchester Metropolitan University, Manchester, United Kingdom; [9]Queen Mary University of London, London, United Kingdom; [10]University of Surrey, Guildford, United Kingdom

Introduction: Insulin-like growth factors (IGFs), including IGF-I and IGF-II, are members of a family of growth promoting peptides and are some of the most abundant growth factor polypeptides found in humans. The IGF family contains at least seven exclusive high-affinity IGF binding proteins (IGFBPs). In recent years, the biological role of IGFBPs within kidney disease has been increasingly recognised.

Methods: Baseline IGF/IGFBP profile was related to 2 primary outcomes: (i) change in albumin-to-creatinine ratio over time (urine ACR trend slope) and (ii) change in serum creatinine over time (creatinine trend slope) and to all-cause mortality. Trend slopes were derived for each participant using repeated measures over follow-up. IGF-I, IGF-II, IGFBP-1 and IGFBP-2 were measured by immunoassay.

Results: At baseline, 59.3% of patients were male and 40.7% were female. Mean age at baseline was 56.6 ± 9.4 years. The mean follow-up period was 17.4 ± 5.2 years. IGF-II and IGFBP-3 were found to be strongly correlated with each other (Spearman rho = 0.80), and were therefore not included simultaneously in the multivariate linear regression model to avoid co-linearity. Baseline IGF-II, IGFBP-1 and IGFBP-2 levels were both significant and independent predictors of urine ACR increase. The predictive strength of these factors remained even when adjusted for covariates. Higher IGFBP-2 was independently associated with steeper rate of ACR progression (B = 0.007, $P = .002$), while IGFBP-1 showed an inverse association (B = −0.057, $P = .009$). IGF-II also remained positively associated with ACR trend (B = 0.005, $P = .013$), whereas IGF-I showed no association. IGFBP-1 showed a significant inverse association with serum creatinine change (B = −0.038, $P = .04$). Survival analysis revealed that higher circulating IGFBP-2 levels were independently associated with higher all-cause mortality (hazard ratio [HR] per 1 standard deviation (SD) increase 1.306, 95% CI 1.151-1.483 $P = .0001$)

Conclusions: In conclusion, this longitudinal study with up to 23 years follow-up, indicated that higher IGF-II, lower IGFBP-1 and higher IGFBP-2 levels, all associated with a greater likelihood of ACR progression over time, while lower IGBFP-1 also associated with a greater change in serum creatinine over time. This was independent of standard risk factors. Higher baseline IGBFP-2 also associated with higher all cause mortality. This highlights the relevance of the IGF/IGFBP system to our understanding of renal complications in diabetes and suggests that further exploration of these associations is merited.

Abstract citation ID: lvag096.950

EP443 - ECE_3246 - Morphofunctional assessment using bioelectrical impedance vector analysis, nutritional ultrasound and handgrip strength in severe anorexia nervosa

Aida Elhadri-Egea[1], Víctor Siles-Guerrero[2], Rosa Natalia García Pérez[3] and José Manuel Romero-Márquez[4]

[1]Endocrinology and Nutrition Department, Hospital Universitario Virgen de las Nieves, Granada, Spain; [2]Endocrinology and Nutrition Department, Hospital Universitario Virgen de las Nieves, Granada, Spain; [3]Endocrinology and Nutrition Department, Hospital Universitario Virgen de las Nieves, Granada, Spain; [4]Hospital Universitario Virgen de las Nieves, Granada, Spain

Background: Monitoring physical recovery in anorexia nervosa (AN) requires functional assessment tools beyond body weight. Phase angle (PhA), nutritional ultrasound (NU) and handgrip strength provide a comprehensive and reproducible evaluation of true nutritional status.

Methods: A prospective cohort of 43 women (mean age 28.7 ± 13.5 years) admitted for severe AN to a specialized inpatient unit was evaluated. Anthropometric data, multifrequency bioelectrical impedance analysis, NU of the rectus femoris muscle and abdominal adipose tissue, and handgrip strength measured with a Jamar® dynamometer were collected. Two complementary analyses were performed: (1) stratification by PhA tertiles at admission and assessment of associations with morphofunctional parameters and length of hospital stay; (2) comparison of variables between admission and discharge.

Results: Higher PhA at admission was associated with greater body cell mass, rectus femoris muscle area and handgrip strength (all $P < .001$), as well as shorter hospital stay (41 vs 58 days; $P < .05$) and lower estimated hospital costs (€25 829 vs €36 523), calculated according to the diagnosis-related group daily cost for eating disorders. During hospitalization, significant increases were observed in body weight, fat-free mass, fat mass, handgrip strength and abdominal subcutaneous fat, while no

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

relevant changes were detected in PhA or serum protein levels.

Conclusions: The combined use of bioelectrical impedance vector analysis, nutritional ultrasound and handgrip strength enables precise monitoring of functional recovery in severe AN and helps anticipate length of stay and economic impact. Integrating these tools into clinical protocols may optimize inpatient management, support individualized decision-making and provide objective outcome measures in patients with extreme malnutrition.

Abstract citation ID: lvag096.951

EP444 - ECE_3605 - Female sexual function following glp-1 receptor agonist therapy in women with obesity: a prospective observational study

Sara Odalovic[1], Kristina Saravinovska[1,2], Dijana Jankovic[1], Antoan Stefan Sojat[1,2], Natalija Antic[1], Jana Vujnovic[1], Boban Stepanovic[1], Neda Delic[2], Ilija Gunjic[3], Mina Hagen[4], Lana Durutovic[2], Miomira Ivovic[1,2], Svetlana Vujovic[1,2] and Ljiljana Marina[1,2]

[1]Clinic of Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Belgrade, Serbia; [2]Belgrade, Serbia; [3]Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia; [4]Faculty of Media and Communications, Singidunum University, Psychology Department, Belgrade, Serbia

Introduction: Available evidence shows that women with obesity treated with glucagon-like peptide-1 receptor agonist (GLP-1 RA) exert decreased sexual function following the treatment. Moreover, compared with men, data on sexual function in women treated with GLP-1 RAs are particularly limited.

Aim: To evaluate changes in sexual function in women with obesity before and three months after initiation of GLP-1 RA therapy, and to investigate potential associations with weight loss, mental health and body image.

Methods: This prospective observational study included 25 women with obesity initiating GLP-1 RA therapy—semaglutide or liraglutide. Sexual function was assessed using the Female Sexual Function Index (FSFI). Symptoms of depression and anxiety were evaluated using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7), respectively, while body self-perception was assessed with the Body Shape Questionnaire (BSQ). All questionnaires were distributed at two time points: baseline and after 3-months of GLP-1 RA treatment initiation. Participation in clinical and psychological interventions, including weight loss-associated hospitalization and motivational interviewing with group psychological support, was assessed.

Results: 25 women completed the questionnaires, mean age 44.8 ± 6.1, mean baseline BMI 40.7 ± 8.5 kg/m^2, mean BMI after three months—34.8 ± 8 kg/m^2. 22/88% women were on liraglutide, and 3/12% on semaglutide. The mean percentage of initial BMI lost after 3 months was $11.6 \pm 6.5\%$ kg/m^2. 13/52% of women were hospitalized for weight loss, and 17/68% underwent motivational interviewing and were part of the psychological support group. Overall FSFI scores significantly increased after 3 months of GLP-1 RA treatment ($P < .001$). The type of GLP-1 RA did not affect weight loss ($P > .05$). Weight loss, type of GLP-1 RA, hospitalization, motivational interviewing with group psychological support, total GAD-7, PHQ-9 nor BSQ scores did not affect FSFI score changes ($P > .05$). Mental health indicators were overall improved after 3 months of GLP-1 RA treatment ($P < .001$). In multiple linear regression models, we found no significant predictors of weight reduction or sexual function changes.

Conclusions: Improvement of sexual function in our cohort was independent of the weight loss and was not statistically explained by clinical and psychological interventions, nor by changes in depression, anxiety or body shape perception scores. However, mental health and body shape self-perception scores were improved over the same period, which suggests an overall positive impact of the GLP-1 RA treatment. Studies with longer follow-up are needed to elucidate the long-term effects and underlying mechanisms.

Abstract citation ID: lvag096.952

EP445 - ECE_3599 - The role of endocrine disruptors and steroid hormones in gestational diabetes mellitus

Michaela Svojtková[1], Lucie Kolatorova[1], Tereza Skodova[1], Daniela Vejrazkova[1], Katerina Anderlova[2], Patrik Simjak[2], Karolina Adamcova[2], Antonin Parizek[2] and Jana Vitku[1]

[1]Department of Steroids and Proteofactors, Institute of Endocrinology, Praha 1, Czech Republic; [2]Department of Gynecology, Obstetrics and Neonatology, General University Hospital in Prague, Praha, Czech Republic

Introduction: During pregnancy, insulin resistance increases, compensated by increased insulin secretion. In predisposed pregnant women, insulin secretion is insufficient and gestational diabetes mellitus (GDM) develops. The growing use of substances that affect the endocrine system (endocrine disruptors, EDs), together with evidence of their role in the development of type 2 diabetes (DM2), has led to the hypothesis that EDs may contribute to the rising incidence of GDM.

Objectives: to describe exposure to selected EDs in women diagnosed with GDM compared to a control group and to identify changes in the steroid spectrum in relation to ED exposure and GDM.

Methods: We included 97 pregnant women from that 55 with diagnosed GDM (fetus: 30 male and 25 female) and 42 healthy controls (fetus: 15 male and 27 female). Women taking medications or having diseases affecting steroidogenesis were excluded. Maternal blood was collected two times during pregnancy, at delivery, three days and six months after delivery. Mixed fetal cord blood after delivery was collected. In all samples, steroids (nine C21 steroids, nine androgens, three estrogens and their conjugates) and EDs (bisphenols A, S, F, P, AF, AP, methylparaben, ethylparaben, propylparaben, butylparaben, benzylparaben and their conjugates) were analysed using LC MS/MS. Data were statistically analysed using the Mann–Whitney test, with fetal sex considered.

Results: No changes in ED and steroids were found in women (GDM) with a female fetus compared to controls. In women (GDM) with a male fetus, a lower level of conjugated ethylparaben and butylparaben was found compared to controls, as well as lower conjugated androstenedione, conjugated progesterone, conjugated and free 5α-dihydroprogesterone, pregnenolone, 11-deoxycortisol, 11-deoxycorticosterone and higher 11-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

ketotestosterone. Other changes were found in cord blood, where we demonstrated the occurrence of some EDs. In cord blood of girls (offspring of GDM), there were higher levels of conjugated butylparaben and lower levels of dehydroepiandrosterone and estradiol. In cord blood of boys (offspring of GDM), there were higher levels of bisphenol A and bisphenol S.

Conclusions: We demonstrated the occurrence of ED not only in pregnant women, but also in their offspring, where a higher level was found in offspring of women with GDM. We also observed alterations in steroid levels in women with GDM carrying male fetus, some of which have been described in the literature in male patients with DM2.

Acknowledgements: Supported by the project MZCR–RVO Institute of Endocrinology–EÚ 00023761.

Abstract citation ID: lvag096.953

EP447 - ECE_1385 - Associations between DXA-derived parameters of body composition and bone mass density in patients with T2DM and metabolic dysfunction-associated steatotic liver disease

Martin Kasko[1], Emil Fraenkel[1], Tomas Koky[2], Jana Figurova[1], Slavka Pacakova[2] and Ivica Lazúrová[1]

[1]Faculty of Medicine, 1st Department of Internal Medicine, Pavol Jozef Safarik University in Kosice, Kosice, Slovakia; [2]Stryn, Norway

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) appears to be associated with changes in bone mineral density (BMD) and fracture rate; however, the current data are ambiguous. The relationship between MASLD and bone metabolism remains controversial regarding the protective effect of mechanical loading vs the detrimental effects of insulin resistance and chronic inflammation. This study aimed to clarify the effects of MASLD on bone health in the setting of obesity and type 2 diabetes mellitus (T2DM) in a European population.

Methods: This cross-sectional observational study enrolled 156 patients with T2DM and MASLD (95 females, 61 males; mean age 62.85 ± 10.73 years), compared against a control cohort of 40 T2DM patients without hepatic involvement. Hepatic steatosis was rigorously quantified using vibration-controlled transient elastography (FibroScan®), with a Controlled Attenuation Parameter (CAP) threshold of >238 dB/m. BMD and detailed body composition (fat/lean mass, android/gynoid ratio) were evaluated via DXA. The biochemical profile focused on the GH/IGF-1 axis, insulin resistance (HOMA-IR), and a comprehensive panel of bone turnover markers (BTMs), including Osteocalcin, P1NP, and bCTX.

Results: Patients with MASLD exhibited significantly higher BMI (Body Mass Index), visceral adiposity, and HOMA-IR compared to controls. In the overall cohort, CAP positively correlated with total BMD ($r = 0.21$, $P = .001$). Sex-stratified analysis revealed this association was significant only in females ($r = 0.29$, $P = .004$). Conversely, in males, CAP showed a significant negative correlation with BTMs (Osteocalcin: $r = -0.35$, $P = .006$; bCTX: $r = -0.26$, $P = .04$). Multivariable ROC analysis revealed that traditional BMI-based assessments are suboptimal. The most robust diagnostic performance was achieved in females (Figure 1), where a model integrating CAP, age, and android fat % yielded an AUC of 0.746 (Sensitivity 76.4%, Specificity 71.4%). In the overall cohort, the inclusion of AGR (Android-to-Gynoid fat Ratio) (Figure 2) and ALMI (Appendicular Lean Mass Index) (Figure 3) significantly improved the identification of reduced total BMD and BMD of the hips, respectively.

Conclusions: In T2DM, the MASLD-bone relationship is sexually dimorphic: while liver steatosis correlates with higher BMD in women via android fat distribution, it impairs bone remodeling in men. Clinical screening for fracture risk in MASLD patients would benefit from evolving beyond BMI to incorporate sex-specific algorithms and DXA-derived soft tissue metrics to optimize diagnostic accuracy.

Abstract citation ID: lvag096.954

EP449 - ECE_1258 - Association between obstructive sleep apnea risk and type 2 diabetes among Emirati adults: results from the UAE Healthy Future Study

Manal Taimah[1,2]

[1]Abu Dhabi, United Arab Emirates; [2]Public Health Research Center, New York University Abu Dhabi, Abu Dhabi, United Arab Emirates

Background: Obstructive sleep apnea (OSA) is increasingly recognized as a cardiometabolic risk factor, yet its relationship with type 2 diabetes (T2DM) remains insufficiently explored in Middle Eastern populations despite high regional burdens of obesity and diabetes. Understanding this association in the United Arab Emirates (UAE), where rates of metabolic disease continue to rise, is essential for informing screening and prevention strategies.

Objective: To examine the association between OSA risk and T2DM among Emirati adults and to identify sociodemographic and anthropometric predictors of diabetes across OSA risk categories.

Methods: This cross-sectional analysis used baseline data from the UAE Healthy Future Study, collected between 2016 and 2023. A total of 4578 Emirati adults aged 18-71 years completed the STOP-BANG questionnaire and underwent standardised anthropometric measurements and blood sampling. OSA risk was categorised into low, intermediate, and high groups. T2DM was defined using American Diabetes Association diagnostic criteria, including fasting glucose, HbA1c, random glucose, and self-reported diagnosis with medication use. Logistic regression models (unadjusted and adjusted) estimated the association between OSA risk and T2DM, controlling for education, marital status, waist circumference, and smoking.

Results: Participants were young (mean age 27.5 ± 8.35 years), and 55.8% were male. High OSA risk was identified in 16.6% of the cohort, with men showing substantially higher prevalence than women. T2DM prevalence was 4.63%. In unadjusted models, intermediate (OR 2.44; 95% CI 1.78-3.35) and high OSA risk (OR 6.44; 95% CI 4.32-9.59) were strongly associated with T2DM ($P < .0001$). After adjustment, associations remained significant: intermediate OSA risk (OR 1.65; 95% CI 1.18-2.32) and high OSA risk (OR 3.44; 95% CI 2.23-5.33). Higher waist circumference, lower educational attainment, and being married or previously married were additional predictors of T2DM. Gender differences were evident, with men showing higher rates of snoring and elevated

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

neck circumference, while women reported greater daytime fatigue.

Conclusions: Among Emirati adults, higher OSA risk is independently associated with increased odds of T2DM, even after adjusting for established sociodemographic and anthropometric factors. These findings underscore the importance of incorporating OSA screening into diabetes risk assessment and suggest that targeted interventions addressing obesity and central adiposity may help mitigate dual disease burden in this high-risk population.

Note: Preferred presentation as a poster.

Abstract citation ID: lvag096.955

EP450 - ECE_2040 - Youth- and young adult–onset type 1 and type 2 diabetes: long-term complications and mortality in a Nationwide Korean Claims Cohort

Ja Young Jeon[1], Kyounghwa Ha[1], Seung Jin Han[1], Hae Jin Kim[1], Kwan-Woo Lee[1] and Dae Jung Kim[1]
[1]*Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon, South Korea*

Background: We compare long-term risks of diabetes-related complications and mortality between T1DM and T2DM diagnosed at ages 0-39 years in South Korea.

Methods: This retrospective cohort of individuals aged 0-39 years newly diagnosed with diabetes between 2003 and 2006 was constructed from nationwide claims data and followed through 2023. Idividuals were categorized into 4 groups based to diabetes types (T1DM and T2DM) and ages at diagnosis (0-19 years [youth-onset diabetes] and 20-39 years [young adult-onset diabetes]). Outcomes included acute complications, severe microvascular complications, cardiovascular complications, and all-cause mortality. Time-to-event analyses used cumulative incidence functions with competing risks and Cox proportional hazards models.

Results: A total of 72 917 participants newly diagnosed with diabetes between 2003 and 2006 were included in the study. Among youth-onset diabetes, T1DM was associated with a much higher burden of acute complications, with cumulative incidence reaching 30% at 10 years and 40% at 20 years, whereas the corresponding risk in T2DM remained below 10% even after 20 years. Severe microvascular complications rose to around 20% over 20 years in both groups, with a steeper increase in T1DM, while cardiovascular complications were rare and all-cause mortality remained relatively low and similar between T1DM and T2DM. Among young adult-onset diabetes, differences between T1DM and T2DM were even more pronounced. T1DM was associated with markedly higher cumulative incidences of acute and severe microvascular complications, approximately twofold higher risk of cardiovascular complications, and more than double the risk of all-cause mortality compared with T2DM.

Conclusions: Our findings indicate that youth- and young adult-onset T1DM remains a highly vulnerable condition despite advances in diabetes management. Given the particularly elevated risks of complications and mortality observed in young adult–onset T1DM, this subgroup needs heightened clinical attention and targeted preventive strategies.

Abstract citation ID: lvag096.956

EP453 - ECE_3084 - Two cases of immunotherapy-induced type 1 diabetes: clinical characteristics, presentation and the role of technology

Vasiliki Antonopoulou, Aggeliki Kyriakou, Dimitra Sinni, Anna Louisa Chaliasou, Sofia Georgiadi, Chrysoula Koukoula, Marinella Tzanela and Theodora Stratigou
Department of Endocrinology "D. Ikkos"- Diabetes Center- EndoERN-Evangelismos General Hospital, Athens, Greece

Background: Immune checkpoint inhibitors (ICIs), widely used in the treatment of cancer, have been associated with endocrine adverse events. Although Type 1 Diabetes Mellitus (T1DM) is a rare adverse event, its abrupt onset and rapid progression may lead to life-threatening conditions, such as diabetic ketoacidosis (DKA). Herein, we describe two cases of ICI-induced T1DM, focusing on clinical characteristics and the role of technology in diabetes management.

Case 1: A 42-year-old woman with mesothelioma, treated with chemotherapy followed by nivolumab, who was diagnosed with T1DM presenting as DKA three years ago. She reported ~10 kg weight loss and catabolic symptoms prior to diagnosis. Initial therapy included basal insulin, dapagliflozin, and dulaglutide. She experienced recurrent DKA three months later. On her first visit to our department, she was on a basal-bolus regimen plus dulaglutide. BMI was 23.4 kg/m^2 and HbA1c 8.1%, with frequent glycemic fluctuations. Islet cell autoantibodies were negative and C-peptide undetectable. Autoimmune thyroiditis was also diagnosed. Dulaglutide was stopped. The patient received basal-bolus insulin treatment, carbohydrate-counting education and continuous glucose monitoring (CGM) was initiated, improving glycemic control (TIR 59%, GMI 7.3%). Nivolumab was discontinued 10 months after diabetes mellitus (DM) onset without improvement of glycemic control. An automated insulin delivery system (AID) was later initiated, resulting in marked improvement: TIR 78%, TAR 20%, TBR: 2%, GMI 6.7%. Glycemic control remains stable nearly one year later (HbA1c:6.1%). Notably, her son was diagnosed with type1 DM with positive autoantibodies one year after her diagnosis.

Case 2: A 71-year-old man with a history of mesothelioma treated with ICIs, who presented with new-onset DM and DKA. Initial management included a basal-bolus insulin regimen. One month later, he experienced severe hypoglycemia, prompting admission for intensive diabetes education and management. Laboratory evaluation revealed negative islet autoantibodies, C-peptide 0.42ng/mL, and HbA1c 10%. During the first year, glycemic control remained suboptimal with significant glucose variability (60-220mg/dL) despite degludec (15 IU) and lispro therapy. Introduction of CGM and structured carbohydrate counting education resulted in a substantial improvement of HbA1c (7%). One and a half years later, an advanced AID was initiated, further reducing glucose fluctuations.

Discussion: Our cases indicate that early detection and intensive diabetes education are crucial for the management of ICI-induced T1DM and for minimizing acute and chronic complications. The role of technology including CGM and AID can result in optimal glycemic control and enhance safety in these patients.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.957

EP456 - ECE_2472 - Insulin autoimmune syndrome in a caucasian male: a rare cause of recurrent hypoglycemia

Kevin Veerasamy, Najmi Mohd Noor, Therese Dunleavy, Audrey Melvin and Anne Marie Hannon
University Hospital Limerick, Limerick, Ireland

Insulin autoimmune syndrome (IAS), or Hirata disease, is a rare cause of hypoglycemia mediated by insulin autoantibodies (IAA). We report a 76-year-old Caucasian male with hypertension, ischemic heart disease, and benign prostatic hyperplasia who presented with recurrent syncope and seizure-like activity over two months, necessitating his third hospital admission.

Initial workup, including CT/MRI brain, EEG, echocardiogram, and Holter monitoring, was unremarkable. During the third admission, hypoglycemia was confirmed (serum glucose 2.2 mmol/L), with markedly elevated insulin (>6945 pmol/L), C-peptide (2.48 nmol/L), and IAA titers (75%, normal <5.5%). Pancreatic imaging and endoscopic ultrasound excluded neuroendocrine tumours, and negative sulfonylurea screen confirmed IAS. The patient received intravenous hydrocortisone for two days, followed by oral prednisolone, dietary counselling for frequent low-carbohydrate meals, and continuous glucose monitoring. Rituximab was initially considered for severe, refractory hypoglycemia but was not administered due to rapid clinical and serological improvement. Follow-up revealed declining IAA titers and no further hypoglycemic episodes by five months. Historically prevalent in Japan (0.017/100 000), IAS is associated with HLA-DR4 (DRB1*0406) and triggers including sulphydryl drugs or viral infections. Rising global cases among Caucasians likely reflect increased medication use and wider IAA assay availability. IAS involves high-capacity, low-affinity IAA causing glycemic fluctuations through insulin- IAA complex dynamics. Symptoms range from mild to severe (seizures, syncope). Management is complex given an 82% spontaneous remission rate. This case highlights recognising IAS in non-Asian populations and demonstrates the efficacy of corticosteroids and dietary interventions. Recurrence is rare (<5%).

Abstract citation ID: lvag096.958

EP457 - ECE_1429 - Determinants of achieving optimal time in tight range with automated insulin delivery systems

Luís Silva Gadelho, Margarida Gonçalves, Nuno Jesus, Henrique Alexandrino, Ana Sousa, Patrícia Tavares, Gustavo Rocha and Mariana Martinho
Unidade Local de Saúde Gaia e Espinho, E.P.E., Serviço de Endocrinologia, Vila Nova de Gaia, Portugal

Background: The management of type 1 diabetes (T1D) has advanced substantially with the advent of novel technologies, such as automated insulin delivery (AID) systems, enabling more precise glycaemic control. In this context, time in tight range (TITR; glucose 70-140 mg/dL) has emerged as a clinically relevant metric, as it better reflects physiological glycaemic profiles, with commonly accepted targets above 50%. This study aimed to identify factors associated with achieving optimal TITR in adults with T1D using AID systems.

Methods: All adults with T1D followed at a tertiary centre and using AID systems for at least six months were retrospectively included. Data were collected from the visit prior to AID initiation and from the most recent follow-up visit. Patients were divided into two groups according to post-AID TITR: those achieving TITR>=50% and those with TITR<50%. Baseline and post-AID variables were compared between groups, and logistic regression analysis was performed.

Results: Fifty-six patients were included; 26 (46.4%) were female, with a median age of 27.5 years and a mean diabetes duration of 17.5 years. Most patients (85.7%) had prior experience with conventional insulin pumps (median 7 years). During follow-up, 32 (57.1%) used the t:slim X2 and 24 (42.9%) the MiniMed 780G. After AID initiation, 22 (39.3%) achieved a TITR>=50% (TITR(%), mean ± SD 57.0 ± 7.1 vs 36.6 ± 8.4; $P < .001$), without an increase in time in hypoglycaemia (TBR<70mg/dL(%), median[IQR] 1,5[1-3] vs 1[0-2]; $P = .068$; TBR<54 mg/dL(%), median[IQR] 0[0-0] vs 0[0-1]; $P = .626$). Those achieving the target were older (age, median[IQR] 33.0[26.0-41.0] vs 24.0[19.0-39.0]; $P = .027$) and had better baseline glycaemic control (TIR(%), mean ± SD 62.6 ± 16.3 vs 49.3 ± 18.0; $P = .011$). They also demonstrated higher CGM use (%, median[IQR] 97.1[95.0-99.9] vs 94.9[90.9-97.9]; $P = .011$), more time spent in automated mode (%, median[IQR] 97.5[95.0-100.0] vs 95.5[90.0-97.0]; $P = .009$), a greater number of carbohydrate entries (mean ± SD 5.5 ± 1.9 vs 3.9 ± 1.3; $P < .001$), and a lower proportion of automated boluses (%, median[IQR] 14.5[8.0-21.0] vs 22.0[15.0-34.0]; $P = .001$). Logistic regression analysis identified CGM use (OR = 1.23 [95% CI: 1.03-1.47]; $P = .0246$), number of carbohydrate entries (OR = 1.98 [95%CI: 1.25-3.15]; $P = .004$), percentage of automated boluses (OR=1.11 [95%CI: 1.03-1.19]; $P = .005$), and baseline TIR (OR=1.05 [95%CI: 1.01-1.09]; $P = .016$), TAR (OR = 1.04 [95%CI: 1.01–1.08]; $P = .024$), and HbA1c (OR=2.56 [95%CI: 1.20-5.26]; $P = .015$), as predictors of achieving the TITR target.

Conclusions: Patients with better baseline glycaemic control were more likely to achieve optimal TITR following AID initiation. Achievement of the TITR target was not associated with increased hypoglycaemia and was accompanied by higher CGM use, more frequent carbohydrate entries, and reduced reliance on automated boluses.

Abstract citation ID: lvag096.959

EP458 - ECE_2173 - Glycemic control in children and adolescents with type 1 diabetes before, during, and after attending a diabetes camp: an observational cohort study

Arshia Beigi, Shadan Ashrafi, Rui (Rachel) Huang, Huaying (Helen) Zhao, Nada Al Mahmeed and Joseph Leung
University of British Columbia, Vancouver, Canada

Background and Aims: Glycemic variability often increases during diabetes camps due to increased physical activity, social interactions, and camp-based nutrition. Careful glucose monitoring is essential to minimize fluctuations. While continuous glucose monitoring (CGM) provides valuable insight into time in range and glycemic patterns, few studies have examined these outcomes before, during, and after camp in children and adolescents with type 1 diabetes, particularly comparing those on vs not on automated insulin delivery (AID). The aim of this study was to evaluate changes in glycemic control associated with diabetes camp attendance and to assess whether these changes differed by AID.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Methods: Eighty-eight children and adolescents aged 7 to 17 years with type 1 diabetes attending the 2025 Diabetes Canada Camp Khakhamela in Vancouver, British Columbia were included in the final analysis. All participants used a CGM system and were managed with either insulin pump therapy (with or without AID) or multiple daily injections. CGM data were collected for four predefined periods: two weeks before camp, during camp, and two post-camp intervals (weeks 0-2 and weeks 2-4). Participants with less than 60% active CGM time during any interval were excluded to ensure data reliability. Demographic and treatment characteristics, including insulin delivery modality and AID use, were recorded. Paired comparisons were performed across time periods, with subgroup analyses conducted based on AID use.

Results: The mean age was 12.3 ± 2.5 years, with a mean diabetes duration of 5.8 ± 3.9 years. Of the 88 participants, 29 (33%) were boys and 59 (67%) were girls. Forty-nine (56%) used AID, including open-source (39%) and commercial systems (17%). Most participants (89%) were on insulin pump therapy. AID users consistently demonstrated a higher time in range (TIR) compared to those not using AID across all study periods. Among non-AID users, TIR increased significantly during camp compared with the pre-camp period ($P = .037$). In contrast, no significant change in TIR was observed among AID users during camp ($P = .656$).

Conclusions: Diabetes camp attendance was associated with improved glycemic control particularly among children and adolescents not using AID systems, highlighting the positive impact of structured camp environments in supporting diabetes self-management. Participants using AID maintained stable glycemic control across all periods, suggesting resilience of automated systems during periods of increased variability.

Abstract citation ID: lvag096.960

EP459 - ECE_3466 - A bioimpedance analysis of body composition and advanced glycation end-product evaluation in patients using advanced hybrid closed-loop systems, patch pumps, or multiple daily injections

Michele Baldari[1,2], Sabrina Berti[1,2], Enrico Saudelli[1,2], Simona Moscatiello[1], Sara Flamigni[1], Uberto Pagotto[1,2] and Guido Di Dalmazi[1,2]

[1]Endocrinology and Diabetes Prevention and Care Unit, IRCCS Policlinico di S. Orsola, Bologna, Italy; [2]Department of Medical and Surgical Sciences, Alma Mater Studiorum Università di Bologna, Bologna, Italy

Background and Aims: The effect of advanced hybrid closed-loop (AHCL) systems on body composition in individuals with type 1 diabetes mellitus (T1DM) remains unclear. This cross-sectional study aimed to compare body composition and, secondly, to evaluate AGEs, among patients using AHCL systems (MiniMed 780G® or t X2 Control-IQ®), multiple daily injections (MDI), or patch pumps without advanced insulin delivery algorithms.

Methods: Patients who had been using the same AHCL system for at least one year ($n = 30$) were compared with individuals using MDI ($n = 35$) or patch pumps ($n = 13$) in combination with a continuous glucose monitoring (CGM) sensor. Body composition was assessed by bioelectrical impedance analysis (BIA). Three-site skinfold thickness and handgrip strength were also measured. A sub-group of patients ($n = 39$, 21 MDI, 12 AHCL and 6 patch pump) underwent AGEs evaluation using skin autofluorescence.

Results: A total of 78 patients (mean age 39 ± 12 years) were enrolled. No significant differences were observed among the AHCL, MDI, and patch pump groups with respect to diabetes duration, sex distribution, body mass index (BMI), or waist circumference. HbA1c levels were also comparable across groups. Patch pumps users were younger ($P = .028$) than MDI users. Physical Activity did not differ among groups according to International Physical Activity Questionnaire (IPAQ). No significant differences in BIA-derived body composition parameters were detected. However, patch pump users showed a non-significant trend toward lower fat mass percentage(mean 19.7 ± 8.4% in MDI; 18.8 ± 5.8% in AHCL; 15.3 ± 5.2% in patch-pump users, $P = .086$), with corresponding trends toward higher fat free mass percentage and higher body cell mass percentage ($P = .086$). Total body water percentage was similar across groups ($P = .138$). Skinfold thickness and handgrip strength did not differ significantly among groups. Daily insulin dose per kilogram was significantly lower in MDI users compared with AHCL users (0.57 vs 0.68 U/kg; $P = .04$; 0.62 U/kg for patch-pump users). AGEs levels did not differ significantly among groups ($P = .113$). AHCL users showed glycemic control compared to MDI and patch pumps, with higher Time in Range(mean TIR 72 ± 7% vs 51 ± 18% vs 56 ± 18%, respectively), higher Time in Tight Range, lower Time Above Range and Time Below Range, lower GMI and glycemic variability.

Conclusions: Body composition assessed by BIA did not differ significantly among treatment groups. AHCL users had superior glycemic control compared with MDI and patch pumps, albeit with higher insulin requirements than MDI. AGEs levels were comparable across study groups.

Abstract citation ID: lvag096.961

EP461 - ECE_1119 - Dual-etiology diabetes associated with mitochondrial m.961T>C variant: A mother–son case

Azad Duman[1], Murat Alay[1] and Julide Ekici Duman[2]

[1]Endocrinology and Metabolism, Department of Internal Medicine, Yuzuncu Yil University, Van, Türkiye; [2]Department of Family Medicine, Van Yuzuncu Yil University, Van, Türkiye

Objective: The *m.961T>C* variant in the 12S rRNA (*MT-RNR1*) gene of mitochondrial DNA is commonly associated with sensorineural hearing loss due to aminoglycoside sensitivity. However, its association with a diabetic phenotype is extremely rare. Mitochondrial gene mutations may impair pancreatic β-cell function by disrupting energy production, oxidative stress balance, and insulin secretion. Here, we discuss the clinical significance of the *m.961T>C* variant identified in a family presenting with both autoimmune diabetes and neurosensory manifestations.

Case Report: A 19-year-old male patient was diagnosed with insulin-dependent diabetes in 2021. At diagnosis, the C-peptide level was 0.1 ng/mL, and pancreatic autoantibodies were positive. The patient had a history of bilateral sensorineural hearing loss and epilepsy since childhood. There was no known history of aminoglycoside exposure, and his body mass index was within normal limits. The patient's mother, aged 53, was diagnosed with diabetes in 2015 with HbA1c 6.5% and C-peptide 1.83 ng/mL. Oral antidiabetic therapy was initiated, followed by insulin

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

treatment in 2016, when autoantibody positivity was also detected. The mother has no hearing loss or neurological symptoms. Genetic analysis in both individuals revealed a homoplasmic *m.961T>C* variant in the mitochondrial 12S rRNA (*MT-RNR1*) gene.

Discussion: The coexistence of autoimmune diabetes, sensorineural hearing loss, and epilepsy in the son at an early age suggests a clinical expression of mitochondrial dysfunction. Although diabetes developed through an autoimmune mechanism in both individuals, the presence of neurological and auditory findings only in the son indicates that the *m.961T>C* variant may act as a phenotype-modifying factor. The mother's asymptomatic status supports the concept of variable phenotypic expression (incomplete penetrance) of this variant. As the association between this variant and diabetes has been rarely reported, this case represents a unique example of mitochondrial and autoimmune mechanisms coexisting in the same family.

Conclusions: This case highlights that the mitochondrial *m.961T>C* variant may contribute to the neurological and auditory phenotype in a family predominantly affected by autoimmune diabetes. In diabetes cases presenting with neurosensory features, incorporating mitochondrial genetic analysis alongside autoimmunity testing may strengthen diagnostic evaluation and enhance understanding of phenotypic diversity.

Keywords autoimmune diabetes, mitochondrial DNA, *m.961T>C*, epilepsy, hearing loss, phenotypic variation

Abstract citation ID: lvag096.962

EP463 - ECE_1541 - In-depth analysis of metabolic hormones and inflammatory markers following Roux-en-Y gastric bypass in humans and rodents: similarities and differences

Simon Kloock[1], Lukas Scheller[2], Julia Hasinger[1], Ilja Balonov[3,4], Max Kurlbaum[1], Martin Fassnacht[1], Ann-Cathrin Koschker[1], Florian Seyfried[5] and Ulrich Dischinger[1]
[1]Department of Internal Medicine, Division of Endocrinology and Diabetes, University of Wuerzburg, University Hospital Wuerzburg, Wuerzburg, Germany; [2]Department of Internal Medicine, Division of Haemato-Oncology, University of Wuerzburg, University Hospital Wuerzburg, Wuerzburg, Germany; [3]Department of General, Visceral and Transplantation Surgery, LMU University Hospital, Munich, Germany; [4]Comprehensive Cancer Center (CCC Munich LMU), LMU University Hospital, Munich, Germany; [5]Department of General, Visceral, Transplant, Vascular and Paediatric Surgery, University of Wuerzburg, University Hospital Wuerzburg, Wuerzburg, Germany

Background: Bariatric surgery induces alterations in metabolically active hormones that regulate energy balance. The objectives of this study were to validate a Roux-en-Y gastric bypass (RYGB) rat model by comparison with RYGB-treated humans and to examine associations between circulating amino acids and the incretin hormones GLP-1 and PYY in both species.

Methods: Fasting plasma samples were obtained from participants of the randomized controlled WAS trial (Koschker et al., Metabolism, 2023; RYGB $n = 20$, controls $n = 17$) at baseline and 12 months post-surgery, as well as from male Wistar rats with diet-induced obesity seven weeks after RYGB ($n = 12$) or sham surgery ($n = 12$). Concentrations of 18 peptide hormones and 21 amino acids were quantified using multiplex assays, ELISA, and LC–MS/MS.

Results: In humans, fasting GLP-1 and PYY3-36 levels were significantly reduced 12 months after RYGB (both $P < .001$), whereas rats showed a tendency toward increased levels. Fasting insulin concentrations declined after RYGB in both humans ($P < .001$) and rats ($P < .01$). Leptin levels were markedly decreased in humans ($P < .001$) and rats ($P < .05$). The inflammatory markers IL-6 and MCP-1 were significantly reduced in humans following RYGB ($P < .01$ and $P < .05$, respectively) but remained unchanged in rats. Notably, preoperative GLP-1 concentrations in humans correlated positively with weight loss 12 months after surgery (Pearson's $r = 0.733$; $P < .05$). In addition, leucine levels were positively associated with GLP-1 concentrations at 12 months post-RYGB in humans (Pearson's $r = 0.588$; $P < .05$), an association not observed in rats.

Conclusions: Baseline GLP-1 levels in humans are associated with postoperative weight loss after RYGB and may serve as a predictive marker. Overall, the rat RYGB model recapitulates key changes in incretin and adipokine profiles observed in humans, supporting its suitability for preclinical testing of pharmacological strategies targeting anorexigenic hormones in the treatment of severe obesity.

Abstract citation ID: lvag096.963

EP464 - ECE_2010 - Hyperphagia severity in adult patients with Bardet-Biedl Syndrome—a mixed-methods cross-sectional study in the United Kingdom

Jean Mossman[1], Sarah Flack[2], Elise Gamertsfelder[3], Nicolas Touchot[4], Eric Low[3] and Phil L. Beales[5]
[1]Department of Health Policy, Medical Technology Research Group, London School of Economics, London, United Kingdom; [2]Great Ormond Street Hospital for Children, London, United Kingdom; [3]Eric Low Consulting Ltd, East Lothian, United Kingdom; [4]Rhythm Pharmaceuticals, Inc, Boston, United States; [5]Genetics and Genomic Medicine Research and Teaching Department, UCL GOS Institute of Child Health, London, United Kingdom

Background: Bardet-Biedl Syndrome (BBS) is a rare genetic disease frequently associated with hyperphagia, an insatiable feeling of hunger, persistent food-seeking behaviours and abnormal food intake. This can have behavioural, emotional, social and health consequences, and may lead to early-onset obesity. Quantifying the severity of hyperphagia in adult patients with BBS remains challenging due to the limited availability of assessment tools.

Objective: To assess the level of severity of hyperphagia in adult patients with BBS and obesity living in the UK using an exploratory mixed-method approach.

Methods: This sub-analysis of a non-interventional, cross-sectional study included 39 adult patients with BBS and obesity. Patients were excluded if they were currently prescribed or had previously taken setmelanotide or if they had a BMI <30 kg/m^2. Patients were 41% male, 56% were aged 18-34 years and 82% were of white ethnicity. Patients had a mean (SD) age at diagnosis of BBS of 8.7 (8.1) years. Patients completed a 14-item hyperphagia questionnaire combining multiple-choice and open-ended questions; a subset ($n = 13$) participated in follow-up semi-structured interviews. Interview transcripts were systematically coded by a qualitative researcher and jointly reviewed with a BBS clinical expert to assign severity ratings. Interviews were designed to contextualise and overcome known limitations of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

self-reporting in this population, including the disability paradox, stigma, and cognitive difficulties.

Results: Based on the interviews, 69% (9/13) of patients were classified as having severe hyperphagia, 31% (4/13) as moderate, and none as mild. Questionnaire data classified 8% of patients as having severe hyperphagia, 51% as moderate, and 41% as mild. Notably, 92% (12/13) of patients were assigned a higher severity level via interviews than by questionnaire responses, while only 1 patient had the same severity classification across both methods.

Conclusions: This study reveals a high prevalence of severe hyperphagia in adult patients with BBS and obesity, and suggest substantial underreporting with self-reported questionnaires. The findings highlight the limitations of questionnaire-based assessments in estimating hyperphagia severity and support the incorporation of expert-led interviews as a more accurate mixed-method approach to better capture the true burden of hyperphagia in adult patients with BBS.

Abstract citation ID: lvag096.964

EP465 - ECE_2085 - Cognitive training as an adjunct to intensive health behaviour and lifestyle treatment in childhood obesity: sleep and neurobehavioural outcomes

Deny Menghini, Gabriele Scozia, Valentina Russo, Nicoletta Gianni, Elena Madonna, Maria Rea, Francesco D'aniello, Stefano Cianfarani, Danilo Fintini and Melania Manco
Ospedale Pediatrico Bambino Gesù, Roma, Italy

Background: Paediatric overweight and obesity are frequently accompanied by sleep disruption, sedentary behaviours, and emotional-behavioural difficulties, factors that can undermine adherence to lifestyle change. Growing evidence also links excess weight with weaknesses in executive and memory functions that are central to self-regulation, suggesting that cognitive training may represent a useful adjunct to Intensive Health Behaviour and Lifestyle Treatment (IHBLT). Objective: To test whether adding computerized cognitive training (CT) to an 8-week multidisciplinary Intensive Health Behaviour and Lifestyle Treatment (IHBLT) improves sleep and neurobehavioural outcomes beyond IHBLT alone.

Methods: Eighty-four children aged 6-11 years with overweight/obesity (mean age 8.97 ± 1.70; 49 females) were assessed at baseline (T0) and post-intervention (T1). Families received caregiver-inclusive dietary and physical-activity education and an individualized Mediterranean-style diet. Using age- and gender-stratified block randomisation, participants were assigned to IHBLT (online physical-activity training twice weekly; $n = 19$) or CT+IHBLT (IHBLT plus adaptive Cogmed training, 3×25 minutes/week; $n = 24$). A parallel education-only cohort (Educational group; $n = 41$) participated when training was not feasible. Outcomes included sleep (Sleep Disturbance Scale for Children), quality of life (PedsQL), emotional-behavioural symptoms (CBCL), social functioning (ABAS-II; SRS), and neuropsychological measures of learning, attention, and working memory.

Results: Sleep disturbance improved overall, with a significant Time×Group interaction driven by larger reductions in CT+IHBLT ($F(2,81) = 4.83$, $P < .010$). Quality of life increased and CBCL symptoms decreased over time without differential group effects. CT+IHBLT showed greater gains in verbal immediate learning ($F(2,82) = 3.16$, $P = .047$) and visuospatial short-term memory (Corsi forward: $F(2,82) = 8.51$, $P < .001$); both training arms improved visuospatial working memory (Corsi backward: $F(2,82) = 4.62$, $P = .012$) relative to education only.

Conclusions: A brief, largely remote, family-centred IHBLT improved psychosocial outcomes in paediatric overweight and obesity, while adding CT yielded incremental benefits for sleep and selected memory domains relevant to self-regulation.

Abstract citation ID: lvag096.965

EP466 - ECE_3529 - Physical Activity analysis in Patients with Diabetes in Lithuania

Deimante Paskeviciene[1], Rasa Verkauskiene[1], Lina Radzeviciene[1] and Diana Simoniene[2]
[1]*Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [2]*Department of Endocrinology, Hospital of Lithuanian University of Health Science Kauno Klinikos, Kaunas, Lithuania*

Background: Physical activity (PA) is widely recommended to improve glycemic control in diabetes, whereas prolonged sedentary behavior is linked to adverse cardiometabolic risk. Regular daily activity is critical to healthy aging and reducing risk for falls, maintaining function, and reducing premature morbidity. Multiple national guidelines recommend a multimodal exercise as the single most beneficial intervention to improve health in older adults. Regular PA enhances β-cell function, insulin sensitivity, and vascular function, which leads to better diabetes and health management as well as disease risk reduction. This study aimed to analyze physical activity and sitting time assessed by the IPAQ short questionnaire (IPAQ-SF) and their associations with key demographic and clinical factors in adults with diabetes.

Methods: In this cross-sectional study of 137 adults with diabetes (type 1, $n = 69$, type 2, $n = 68$), physical activity was assessed using the IPAQ-SF, with total MET-min/week calculated according to standard scoring rules. Participants were classified into low (<600 MET-min/week), moderate (600-3000 MET-min/week), or high (>3000 MET-min/week.) PA level. Sitting time was grouped as <6 or ≥6 hours/day. PA and sitting metrics were compared across sex, BMI group, diabetes type, education level, HbA1c, complications status, and age. Data on patients' clinical characteristics were collected from medical records.

Results: The median diabetes duration was 15 years, age—55 years. 57.7% of participants were women. By IPAQ classification, 10.9% of participants had low, 45.3% moderate, and 43.8% high PA level. A progressive decrease in BMI with increase in PA level was found ($P < .05$). In subgroup analyses, PA category did not differ significantly by sex ($P = .70$), diabetes type ($P = .13$), HbA1c level ($P = .98$), complication status ($P = .67$), or age group ($P = .71$). However, significant differences were apparent when analyzing social status: patients with higher education were more often in the moderate/high PA groups compared to patients with lower education ($P < .05$). 54.7% of participants reported sitting time <6h/day. Median sitting time was 300 (180-360) min/day with no differences by any subgroup.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: In this cohort of people with diabetes, most patients achieved at least moderate IPAQ-defined activity levels. PA level varied significantly only by education level and BMI. Higher-educated individuals are more likely to engage in moderate or high levels of PA. Nearly half of patients reported prolonged sitting time. These findings highlight the need to promote greater PA and reduce sedentary behavior in diabetes care, especially targeting individuals with lower education.

Funding: EEA Financial Mechanism 2014-2021 "The Baltic Research Programme"EEA-RESEARCH-60.

Abstract citation ID: lvag096.966

EP467 - ECE_3687 - Mesenteric adipose tissue in Crohn's disease increases angiogenesis and fibrosis

Fernando Gutiérrrez-Martínez[1], Carlos Lopez-Gomez[1], Imane Kentaoui-Bousellam[1], Marina Herraiz-Vilela[1], Guillermo Alcain Martinez[1], Raquel Camargo Camero[1], Juan Victor Martos Vandussen[1], Alejandra Fernandez Castañer[1], Francisco Rodríguez González[1], Laura Camacho Martel[1], Cristina Rodríguez Díaz[1] and Eduardo García-Fuentes[1,2]

[1]Instituto de Investigación Biomédica de Málaga (IBIMA)-Plataforma Bionand, UGC Aparato Digestivo, Hospital Universitario Virgen de la Victoria, Malaga, Spain; [2]Malaga, Spain

Background: The presence of "creeping fat" (CrF), a specific type of mesenteric adipose tissue (MAT) that infiltrates and envelops inflamed intestinal segments, is one of the key factors underlying the Crohn's disease (CD) pathogenesis. It is associated with small intestinal transmural fibrosis and stricture formation. MAT is also an endocrine organ that appears to be a significant risk factor for the severity of intestinal fibrostenosis. It secretes a considerable number of adipokines (secretome), which appear to exert an influence on the pathogenesis of CD.

Aim: To conduct a study with the objective of examine the impact of this MAT secretome on the angiogenic and fibrosis processes.

Material and Methods: Twelve patients with CD undergoing ileocecal resection were included. The hypertrophic MAT adjacent to stenotic ileum (CD-CrF) and from the resection margin (ileal segments from non-affected area (CD-NA)) were obtained. MAT from non-CD subjects (control group (Control-MAT)) were obtained from 10 patients who underwent laparoscopic cholecystectomy. The MAT was immediately placed in DMEM and cultured for 24 hours at 37°C. This MAT-conditioned media (MAT secretome) was collected and frozen at −80°C. After, we analyzed the effect of the MAT secretome on fibrosis in intestinal myofibroblasts by the wound healing and cell proliferation assays. The effect on angiogenesis was analized in HUVECs cells by the endothelial cell cord and cell proliferation assays.

Results: Treatment with CD-NA substantially increased the wound healing ($P < .05$) and the proliferation of myofibroblasts ($P < .05$). Meanwhile, CD-CrF secretome increased the wound healing ($P < .05$) and the proliferation of myofibroblast, althought not significantly. But the analysis of soluble collagen into the culture medium showed a significant decrease after the incubation of miofibroblasts with CD-NA and CD-CrF ($P < .05$, respectively). Treatment with CD-NA and CD-CrF secretomes substantially increased the endothelial cell tube formation ($P < .05$). However, only CD-CrF secretome increased HUVECs proliferation ($P < .05$).

Conclusions: The present study highlights the association between MAT and the pathogenesis of CD. The MAT secretome from CrF may exhibit greater angiogenic and profibrotic effects than the MAT from a non-affected area, and particularly than MAT from control subjects.

Acknowledgements: CIBER de Enfermedades Hepáticas y Digestivas is an ISCIII project.

Funding: This study has been funded by the proyect PID2021-127764OB-I00 from the Agencia Estatal de Investigación del Ministerio de Ciencia, Innovación y Universidades, and co-funded by European Union.

Abstract citation ID: lvag096.967

EP468 - ECE_2754 - Molecular mechanisms of liver injury induced by selective progesterone receptor modulator ulipristal acetate

Aleksandra Lupinska[1], Donata Ponikwicka-Tyszko[2,3], Oana Lupu[1,3], Weronika Lebiedzinska[1], Ewelina Palak[1], Gabriela Milewska[1], Kamila Pulawska[3], Anatol Panasiuk[4,5], Mariusz Koda[6], Robert Milewski[7], Mateusz Maclejczyk[8], Magdalena Niemira[2], Karolina Chwialkowska[2,9], Chen-Che Huang[10], Ilpo Huhtaniemi[3,11], Slawomir Wolczynski[1] and Nafis Rahman[1,3]

[1]Department of Reproduction and Gynecological Endocrinology, Medical University of Bialystok, Bialystok, Poland; [2]Clinical Research Centre, Medical University of Bialystok, Bialystok, Poland; [3]Institute of Biomedicine, Integrative Physiology and Pharmacology, University of Turku, Turku, Finland; [4]Bialystok, Poland; [5]Department of Clinical Medicine, Medical University of Bialystok, Bialystok, Poland; [6]Department of General Patomorphology, Medical University of Bialystok, Bialystok, Poland; [7]Department of Statistics and Medical Informatics, Medical University of Bialystok, Bialystok, Poland; [8]Department of Hygiene, Epidemiology and Ergonomics, Medical University of Bialystok, Bialystok, Poland; [9]Centre for Bioinformatics and Data Analysis, Medical University of Bialystok, Bialystok, Poland; [10]Department of Anatomy, Physiology and Pharmacology, Auburn University College of Veterinary Medicine, Auburn, United States; [11]Department of Digestion, Metabolism and Reproduction, Imperial College London, London, United Kingdom

Drug-induced liver injury (DILI) is a major in clinical and drug development challenge due to its unpredictable nature. While most of the research focus on direct hepatotoxicity, the role of the endocrine signaling in DILI susceptibility remains largely underexplored. As the liver is a central metabolic and endocrine organ, understanding how steroid receptor modulators interact with hepatic metabolism is critical for elucidating individual susceptibility to liver injury. Taken the advantage of using the selective progesterone receptor modulator (SPRM) ulipristal acetate (UA), a clinically effective drug for uterine leiomyomas (ULs) that carries a hepatotoxicity risk, hereby, we investigated the molecular mechanisms underlying steroid-related DILI.

We employed a patient-derived xenograft (PDX) mouse model, where human ULs transplanted into NOD.CB17-Prkdc^{scid} mice,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

uterine leiomyomas were treated with UA to assess DILI. Hepatic effects were evaluated through histopathology, serum biochemistry, and transcriptomic profiling. Complementary *in vitro* cytotoxicity assays were performed in HepaRG cells with UA alone or in combination with steroid hormones.

In the PDX model, UA treatment induced a spectrum of liver injury (mild, 2.5%; moderate, 5%; to severe 5%) of animals, characterized by necrosis, cholestasis, and systemic inflammation. Transcriptomic analysis revealed dysregulation of xenobiotic metabolism, impaired bile acid homeostasis, and activation of stress- and injury-associated pathways. Namely, *Pgrmc1* expression remained unchanged, whereas *Tgfβ-1*, *Tgfβ-3*, *TgfβR2*, and *Eng* were upregulated, accompanied by upregulated *Smad1* and downregulated *Smad2*, *Smad3*, and *Smad8* expression. Notably, we observed zonal enhancement of progesterone receptor membrane component 1 (PGRMC1) protein localization in injured livers and a dysregulated hepatic TGF-β/Smad signaling axis. *In vitro*, UA's cytotoxicity in HepaRG cells was potentiated by co-treatment with estradiol and progesterone in a time- and dose-dependent manner.

Our results suggest that UA-associated liver injury DILI was mediated, in part, by PGRMC1, acting as a zonal integrator of steroid signaling and cellular stress. These findings provide a novel mechanistic framework for SPRM-induced DILI mechanisms, highlighting endocrine context as a critical determinant of individual susceptibility and informing the development of safer therapeutics.

Abstract citation ID: lvag096.968

EP469 - ECE_1901 - Acute and long-term impact of tight vs liberal blood glucose control in corticosteroid-treated critically ill patients

Eline Vanderwegen[1], Ilse Vanhorebeek[1], Fabian Güiza[2], Dominique D. Benoit[3], Eric Hoste[3], Alexander Wilmer[4], Björn Stessel[5], Jasperina Dubois[5], Greet Van den Berghe[6] and Jan Gunst[2]

[1]Laboratory of Intensive Care Medicine, KU Leuven, Leuven, Belgium; [2]Clinical Division and Laboratory of Intensive Care Medicine, KU Leuven, Leuven, Belgium; [3]Department of Intensive Care Medicine, Ghent University Hospital, Ghent, Belgium; [4]Medical Intensive Care Unit, KU Leuven, Leuven, Belgium; [5]Department of Anesthesiology and Intensive Care Medicine, Jessa Hospital, Hasselt, Belgium; [6]Leuven, Belgium

Introduction: Iatrogenic severe hyperglycemia by early parenteral nutrition (PN) was shown harmful in critical illness. We hypothesized that corticosteroids in ICU are another iatrogenic cause of severe hyperglycemia, increasing vulnerability for its acute and long-term harmful effects.

Methods: The hypothesis was tested in a secondary analysis of the multicenter TGC-Fast trial, in which patients not receiving early PN were randomized to tight (TGC) or liberal (LGC) glucose control.[1] We assessed whether baseline corticosteroids, defined as systemic corticosteroids initiated on ICU d-1 or 2, statistically interacted with randomization for impact on acute and 2-year outcomes via multivariable regression. The effect of TGC vs LGC was reported for patients with and without baseline corticosteroids, unadjusted and adjusted for baseline risk factors. $P < .05$ and interaction-$P < .1$ were considered significant.

Results: Of 9230 randomized patients, 2293 (24.8%) received baseline corticosteroids. Patients with baseline corticosteroids had higher blood glucose concentrations and insulin needs than patients without corticosteroids. There was significant interaction between baseline corticosteroids and randomization to TGC vs LGC on occurrence of in-ICU delirium, reduced from 33.1% to 27.5% in the first week ($P = .005$) with TGC for patients on corticosteroids only. At 2-year follow-up, significant interaction was present for mortality and mental health outcomes. For patients on corticosteroids only, TGC reduced 2-year mortality from 32.8% to 28.7% ($P = .03$), improved SF-36 mental component scores from 44.5 ± 12.8 to 46.0 ± 12.8 ($P = .02$), and improved subscores for vitality ($P = .03$) and mental health ($P = .03$). Similar results were obtained after adjustment for baseline risk factors.

Conclusions: Corticosteroids in ICU increased the severity of hyperglycemia and TGC in corticosteroid-treated patients reduced in-ICU delirium and improved long-term survival and mental health outcomes.

Reference

1. Gunst JD, Søgaard OS. Host receptor targeting to treat Covid-19. *NEJM Evid*. 2023;2(11):EVIDe2300222. https://doi.org/10.1056/EVIDe2300222

Abstract citation ID: lvag096.969

EP470 - ECE_2727 - Secretome and exosomes from conditioned medium of human adipose-derived mesenchymal stem cells (hAMSCs) acutely treated with dexamethasone (Dex) reduce atrophic signals in C2C12 myocytes

Nunzia Magnacca[1], Mariarosaria Negri[2], Feliciana Amatrudo[2], Francesco Cecere[3], Maria Anna Marciano[4], Bruno Hay Mele[5], Cristina De Angelis[1], Chiara Simeoli[1], Erminio M. Crescenzo[1], Raffaella Crescenzo[4], Annamaria Colao[1,6], Rosario Pivonello[1,6] and Claudia Pivonello[7]

[1]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione—Università Federico II di Napoli, Naples, Italy; [2]Dipartimento di Psicologia e Scienze della Salute, Università Telematica Pegaso, Naples, Italy; [3]UOS Laboratori di Ricerca e Biobanca, UOC Ricerca Clinica e Traslazionale, AORN Santobono-Pausilipon, Naples, Italy; [4]Department of Biology, Federico II University, Naples, Italy; [5]Department for the Promotion of Human Science and Quality of Life, San Raffaele Open University, Rome, Italy; [6]UNESCO Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy; [7]Dipartimento di Sanità Pubblica, Università degli Studi di Napoli Federico II, Naples, Italy

While chronic glucocorticoids (GC) exposure is associated with skeletal muscle (SM) atrophy and increased adiposity, the effects of acute GC treatment on the adipose-muscle axis remain poorly understood. The current study investigated whether acute Dex exposure (48h) modulates the secretome and the profile of miRNAs cargo in released exosomes of hAMSCs with a consequent impact on SM homeostasis.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Following acute Dex exposure, hAMSCs, differentiated into white adipocytes, exhibited a significant reduction in lipid droplet accumulation (−15.64%, $P < .0001$) quantified by Oil-Red-O staining, indicating suppression of lipogenesis. Cell miRNAs analysis, evaluated by miRNAs arrays, revealed an interesting upregulation of miR-103a-3p ($P = .008$), miR-130b-3p ($P = .04$), and miR-204-5p ($P = .01$), consistent with bioinformatic predictions linking these miRNAs to SM homeostatic pathways. miRNAs expression levels were also evaluated by RT-qPCR in exosomes released by Dex-treated (Exo Dex) and not-treated (Exo) hAMSCs. Accordingly, miR-103a-3p ($P = .03$), miR-130b-3p ($P = .04$) and miR-204-5p ($P = .04$) were upregulated in Exo Dex hAMSCs. hAMSCs secretome, evaluated by proteome profiler human adipokine array, showed decreased levels of several adipokines (Angiopoietin-1 ($P = .0003$), Angiopoietin-2 ($P = .004$), Cathepsin D ($P = .02$), Cathepsin L ($P = .002$), CRP ($P = .01$), IGFBP-3 ($P = .0005$), IGFBP-6 ($P = .007$), MIF ($P = .01$)), with a consequent shift toward a muscle-supportive environment.

To evaluate the functional impact of these changes on SM, C2C12 myotubes were exposed to conditioned medium (CM) or Exo Dex. Both exposure conditions ameliorated SM catabolic signalling, by reducing the protein levels of Atrogin-1 (CM: -11.1%, $P = .04$; CM+Dex: −17.3%, $P = .04$; Exo Dex: −33.9%, $P = .03$ vs control) and MuRF1 (CM: −36.25%, $P = .02$; CM+Dex: −28.5%, $P = .02$; Exo: −16.4%, $P = .0006$; Exo Dex: −44.16%, $P = .0006$ vs control; Exo vs Exo Dex: −27.7%, $P = .014$), evaluated by western blot. To directly assess the contribution of exosomal identified miRNAs to these findings, C2C12 cells were transfected with mimics or inhibitors. Consistently, immunofluorescence revealed that mimics transfection reduced Atrogin-1 (miR-204-5p $P < .0001$) and MuRF1 (miR-103a-3p $P = .009$, miR-130b-3p $P = .003$ and miR-204-5p $P = .05$) protein expression as observed with Exo Dex, while inhibitors transfection reversed it, confirming the impactful contribution of these exosomal miRNAs in modulating muscle catabolism.

Overall, the results of the study reveal that acute Dex treatment elicits adipose tissue responses distinct from those induced by the well-known chronic GC exposure. This in vitro study highlights a previously unrecognised mechanism by which the acute Dex exposure generates an exosomal miRNAs cargo release by differentiated hAMSCs that mitigates SM catabolic pathways, emphasising the functional importance of the adipose-muscle crosstalk in modulating SM homeostasis in conditions of acute GC treatment.

Abstract citation ID: lvag096.970

EP473 - ECE_1731 - Diabetic retinopathy after liver transplantation: impact of diabetes type

Keren Kaminer[1], Mor Atlas[2], Gloria Tsvetov[1], Amit Akirov[1] and Talia Diker Cohen[1]
[1]*Rabin Medical Center, Petah Tikva, Israel;* [2]*Ono Academic College, Kiryat Ono, Israel*

Objectiveראש הטופס: Diabetic retinopathy (DR) is a microvascular complication of diabetes mellitus (DM). Among liver transplant recipients, DM may be present prior to transplantation or may develop post-transplant. Despite the well-recognized burden of diabetes in this population, data on the incidence, progression, and management of diabetic retinopathy after liver transplantation remain limited.

Design: A retrospective study of patients who underwent liver transplantation between 1996 and 2020 and were followed for at least one year post-transplantation in a tertiary referral center. All patients had no evidence of retinopathy at baseline.

Methods: Patients with less than one year of follow-up and/or without an ophthalmologic examination were excluded. Participants were classified into two groups according to diabetes type—type 2 diabetes mellitus (DM2) or new-onset diabetes after transplantation (NODAT)—and were assessed for diabetic retinopathy at baseline and at 1, 3, 5, 10, 15, 20, and 25 years following transplantation.

Results: Eighty-eight patients were included (mean age 53 ± 11 years; 33% female). Pre-transplant diabetes mellitus was present in 50% of patients, while the remaining 50% developed NODAT. Diabetic retinopathy developed in 13.6% of the cohort (n = 12). Patients who developed retinopathy had a higher prevalence of neuropathy (30% vs 6.8%, $P = .06$) and hypertension (50% vs 19.1%, $P = .08$) at baseline, as well as higher baseline HbA1c levels (8.6 ± 2.5 vs 7.0 ± 2.3, $P = .09$). Patients with DM2 exhibited more than a sixfold increased risk of developing diabetic retinopathy during follow up compared with those with NODAT (HR = 6.527; 95% CI: 1.62-26.27; $P = .008$). Notably, retinopathy in patients with NODAT occurred only 15 years post-transplantation. The incidence rate of developing retinopathy was 1600 per 100 000 person-years. When stratified by diabetes type, patients with NODAT had a markedly lower incidence rate (628 per 100 000 person-years) compared with those with pre-transplant diabetes (3296 per 100 000 person-years).

Conclusions: In liver transplant recipients, the risk of developing diabetic retinopathy among patients with NODAT is low, with retinopathy occurring only after prolonged follow-up, beyond 15 years post-transplantation.

Abstract citation ID: lvag096.971

EP474 - ECE_3126 - Diabetic striatopathy- a clinical conundrum

Huma Razzaqe and Julia Ioana
Diabetes and Endocrinology, Our Lady of Lourdes, Drogheda, Ireland

Diabetic Striatopathy, also known as Non-ketotic hyperglycaemic hemichorea-hemiballismus is an uncommon complication of hyperglycaemia with an estimated prevalence of 1 in 100 000 individuals which can occur in patients with long-standing, poorly controlled diabetes or may present as an initial manifestation of diabetes. Patients usually present with unilateral ballismus or choreiform movements. Biochemical findings show significant hyperglycaemia following altered signal intensities in the basal ganglia on brain imaging.

The case report describes this rare presentation of hyperglycaemia in a non-compliant diabetic patient. A 53 years old woman with a one year history of poorly controlled type 2 diabetes mellitus and hypertension presented with 2 weeks history of ataxic gait and involuntary right sided jerky movements. Biochemical investigations revealed near HHS(Hyperosmolar Hyperglycaemic State) levels of serum glucose (32 mmol/l) and osmolality (295 mOsm/kg) followed by HBa1c of 173 mmol/mol.

Brain imaging included CT showed hyper dense changes in left striatum, mimicking left striatal infarction; however later T1-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

weighted MRI brain showed hyper intensity in the basal ganglia contralateral to the choreiform movements. This finding together with the clinical picture pointed towards the diagnosis of hyperglycaemic chorea.

Patient was started on an aggressive fluid and electrolyte replacement therapy along with basal and short-acting insulin. Neurology input was sought, and tetrabenazine was commenced.

The patient's symptoms began to improve as blood glucose levels decreased to 12-14 mmol/l and completely resolved once euglycaemia was achieved. Her gait returned to normal following stabilization of blood glucose levels to 8-10 mmol/L.

This case highlights the importance of recognising hyperglycaemia as a cause of acute hyperkinetic movement disorder. Prompt recognition and stringent glycaemic control, play a crucial role in symptom reversal.

Abstract citation ID: lvag096.972

EP476 - ECE_1100 - Adalimumab-associated hypertriglyceridemia in clinical practice

JeeHee Yoon[1,2], Hee Kyung Kim[1], Jungmin Kim[3], Heung Yong Jin[4] and Ho-Cheol Kang[1]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Chonnam National University Medical School, Chonnam University Hwasun Hospital, Hawsun, South Korea; [2]Chonnam National University Medical School, Hawsun, South Korea; [3]Division of Endocrinology and Metabolism, Department of Internal Medicine, St. Carollo Hospital, Suncheon, South Korea; [4]Division of Endocrinology and Metabolism, Department of Internal Medicine, Jeonbuk National University Medical School, Jeonju, South Korea

Background: Adalimumab, a tumor necrosis factor-alpha (TNF-α) inhibitor monoclonal antibody, is widely used to reduce systemic inflammation in chronic inflammatory diseases. Unlike other biologics, it has not been linked to significant increases in LDL cholesterol. However, data on adalimumab-associated triglyceride changes are limited. This study investigated real-world lipid profile patterns, focusing on triglyceride dynamics during adalimumab therapy.

Method: We retrospectively analyzed patients with ankylosing spondylitis or rheumatoid arthritis who had been treated with adalimumab at Bitgoeul Chonnam National University Hospital between 2007 and 2023. Changes in lipid parameters before and during adalimumab treatment, as well as the use of lipid-lowering therapy, were analyzed.

Results: After excluding patients with incomplete data, no follow-up lipid profiles, or early discontinuation of adalimumab (eg, pregnancy), 581 patients were included in the final analysis. The mean duration of lorlatinib treatment was 144.3 months. Among 341 patients with baseline lipid profiles available prior to adalimumab initiation, total cholesterol (36.4 ± 2.0 vs 196.4 ± 43.8, $P < .001$) and triglyceride (108.6 ± 70.9 vs 249.5 ± 262.3, $P < .001$) levels increased after treatment, whereas HDL (48.5 ± 12.4 vs 49.3 ± 12.2, $P = .398$) and LDL cholesterol(101.7 ± 30.4 vs 106.6 ± 32.6, $P = .112$) levels showed no significant changes. Hypertriglyceridemia (triglycerides >200 mg/dL) was observed in 41.4% of patients, and severe hypertriglyceridemia (>500 mg/dL) occurred in 37 patients (6.3%). In 113 patients who underwent lipid testing after discontinuing adalimumab, total cholesterol (190.0 ± 33.7 vs 183.0 ± 33.5, $P < .001$) and triglyceride (198.9 ± 164.9 vs 116.7 ± 68.3, $P < .001$) levels showed a significant decline compared with levels during treatment.

Conclusions: Although the lipid alterations observed during adalimumab therapy were generally mild and reversible, severe hypertriglyceridemia may develop in certain cases. Therefore, careful monitoring and timely management are essential to mitigate the potential risk of pancreatitis.

Keywords adalimumab, lipid, triglyceride, reversible

Abstract citation ID: lvag096.973

EP477 - ECE_1350 - The impact of hyperinsulinemia on short-term prognosis in patients with hypertriglyceridemia induced acute pancreatitis: A Single-Center Retrospective Analysis

tianke Li

Chongqing, China

Purpose: The short-term prognosis of hyperinsulinemia in patients with hyperlipidemia resulting in acute pancreatitis remains uncertain, so this research explores the correlation between them.

Material and Methods: This study retrospectively analyzed patients treated for hypertriglyceridemic acute pancreatitis at XX Hospital between January 2020 and April 2023. Patients were divided into two groups based on laboratory diagnosis: the hyperinsulinemia group(HINS) and the non-hyperinsulinemia group (NHINS). The study aims to evaluate the short-term effects of hyperinsulinemia on acute pancreatitis.

Results: A total of 92 patients with hypertriglyceridemic pancreatitis were included in the study before receiving lipid-lowering therapy, with 44 in the HINS group and 48 in the NHINS group. Significant differences were observed between the two groups in terms of white blood cell count (WBC), hypersensitive C-reactive protein (CRP) levels, and fasting blood glucose at 2, 3-4, and 5-7 days after initiation of lipid-lowering intervention ($P < .05$). Following admission, patients received symptomatic interventions. However, there was a significant difference in the rate of decrease compared to the baseline between the fifth and seventh days ($P < .05$). Additionally, the groups showed significant differences in the readmission rates for recurrent pancreatitis within 30 days post-ICU transfer and discharge ($P < .05$). No statistically significant distinctions were noted in the length of hospital stay or quality of life scores fifteen days post-discharge.

Conclusions: Hyperinsulinemia adversely affects the recovery process of patients with Hypertriglyceridemia-induced acute pancreatitis.

Keywords acute pancreatitis, hypertriglyceridemia, hyperinsulinemia, short-term prognosis, endocrine

Abstract citation ID: lvag096.974

EP478 - ECE_2212 - Enhanced ER–Mitochondria Contacts as Early Drivers of Hepatic Steatosis under Protein Undernutrition

Thiago Araujo[1,2,3,4], Mariana Muniz[1], Joel Junior[1], Lohanna Barreto[1] and Everardo Carneiro[1]

[1]Universidade Estadual de Campinas, Campinas, Brazil; [2]Instituto de Biologia, Campinas, Brazil; [3]Instituto de Biologia, Campinas, Brazil; [4]IB, Campinas, Brazil

Undernutrition remains a persistent nutritional challenge in low-income countries. Metabolic adaptive responses to protein

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

undernutrition are well-established contributors to the development of metabolic dysfunction–associated fatty liver disease (MAFLD). However, the molecular mechanisms underlying MAFLD onset in this context remain incompletely understood. This study aimed to investigate the role of endoplasmic reticulum (ER)–mitochondria contacts in the initiation and progression of MAFLD during protein undernutrition. To address this objective, the human hepatoma cell line HepG2 was cultured under control (C; 100% amino acids) or amino acid restriction (AaR; 10% amino acids) conditions for up to 48 hours. Additionally, thirty-day-old male C57BL/6J mice were fed for 30, 60, or 90 days with diets containing either 14% protein (control, C) or 6% protein (protein-restricted, R). Statistical analyses were performed using Student's *t*-test or the Mann–Whitney test, with significance set at $P < .05$. It was demonstrated that HepG2 cells subjected to AaR exhibited increased lipid accumulation (87%) relative to C cells. This was accompanied by a marked increase in ER–mitochondria contacts, with a 400% increase detected by proximity ligation assay and a 250% increase measured by Mitotracker/PDI colocalization. In AaR cells, the enhanced ER–mitochondria coupling was accompanied by a 200% increase in intramitochondrial calcium influx and an 89% rise in reactive oxygen species (ROS) production. Moreover, AaR cells displayed significantly reduced basal oxygen consumption (−38%), ATP-linked respiration (−42%), and maximal respiratory capacity (−59%) relative to C cells. Notably, increased ER–mitochondria contact (550%) was detected early, after 24 hours of AaR exposure, whereas elevated ROS production, impaired mitochondrial respiration, and increased lipid accumulation were observed only after 48 hours. Confirmatory analyses revealed that livers from R mice exhibited increased ER–mitochondria contact as early as 30 days of low-protein diet intake (39%), whereas a significant increase in hepatic triglyceride content (51%) was observed only after 90 days of dietary intervention. Collectively, these findings demonstrate that alterations in ER–mitochondria contacts precede the cellular disturbances induced by AaR. Therefore, enhanced ER–mitochondria coupling promotes oxidative stress, impairs mitochondrial function, and reduces fatty acid oxidation in hepatocytes under protein undernutrition. Elucidating these early molecular events may facilitate the development of targeted therapeutic strategies to prevent or attenuate MAFLD in undernourished populations.

Abstract citation ID: lvag096.975

EP479 - ECE_2608 - FIB-4 levels are associated with presentation of chronic kidney disease in patients with type 2 diabetes mellitus

Dimitrios S. Karagiannakis[1], Katerina Stefanaki[2], Maria Manolakopoulou[3], Stefania Magkou[4], Paraskevi Kazakou[2], Panagiota Zacharaki[2], Melpomeni Peppa[5], Evanthia Kassi[6], Theodora Psaltopoulou[2] and Stavroula A. Paschou[2]

[1]4th Department of Internal Medicine, Academic Hospital "Attiko", Medical School, National and Kapodistrian Univesity of Athens, Athens, Greece; [2]Endocrine Unit and Diabetes Center, Department of Clinical Therapeutics, Alexandra Hospital, Medical School, National and Kapodistrian Univesity of Athens, Athens, Greece; [3]Department of Clinical Therapeutics, Alexandra Hospital, Medical School, National and Kapodistrian Univesity of Athens, Athens, Greece; [4]Medical School, National and Kapodistrian Univesity of Athens, Athens, Greece; [5]Endocrine Unit, 2nd Dept of Internal Medicine-Propaedeutic, Research Institute and Diabetes Center, Medical School, National and Kapodistrian Univesity of Athens, Athens, Greece; [6]1st Department of Propaedeutic Internal Medicine, Medical School, National and Kapodistrian Univesity of Athens, Athens, Greece

Background/Aim: Metabolic dysfunction-associated steatotic liver disease (MASLD) is highly prevalent among patients with type 2 diabetes mellitus (T2DM) and is increasingly acknowledged as a multisystem disorder with significant extrahepatic implications, including chronic kidney disease (CKD). Increased Fibrosis-4 (FIB-4), a marker used to evaluate liver fibrosis, has been associated with a higher risk of CKD in patients with MASLD. However, its role in broader patient populations with T2DM remains less clearly defined. We aimed to investigate the association between FIB-4 and CKD in patients with T2DM.

Methods: We retrospectively analyzed data from consecutive patients aged ≥18 years with a history of T2DM admitted to our diabetes center. Epidemiological and somatometric characteristics, as well as baseline blood tests, were recorded. A diagnosis of CKD was established with a CKD-EPI score of ≤60 ml/min/1.73 m^2. We also evaluated the Hellenic score II, the FIB-4 index, and the Aspartate Aminotransferase (AST)-to-Platelet Ratio Index (APRI) score at enrollment.

Results: Two hundred fourteen consecutive patients were enrolled—158 (73.8%) males and 56 (26.2%) females. The mean age was 67.6 ± 10.3 years. The mean duration of T2DM before recruitment was 10 ± 8.1 years. Nighty six (44.8%) patients had normal kidney function, and 54 (25.2%) had CKD at enrollment. For the remaining 64/29.9% patients, the GFR could not be calculated due to missing data. Patients with CKD were significantly older ($P < .001$), had a higher Hellenic score II ($P = .007$), higher AST levels ($P = .011$), lower platelet counts ($P = .007$), higher APRI ($P = .006$), and higher FIB-4 ($P < .001$). Additionally, they had a FIB-4≥1.3, a history of hypertension, and a history of cardiovascular disease more frequently than the non-CKD group ($\chi^2 = 18.8$, $P < .001$; $\chi^2 = 13.5$, $P < .001$; $\chi^2 = 14.2$, $P < .001$, respectively). In the multivariate analysis, sex (male: OR: 0.14, 95%CI: 0.03-0.7, $P = .022$), hypertension (OR: 4.6, 95%CI: 1.06-19.7, $P = .042$), and FIB-4 (≥1.3 vs <1.3: OR: 8.4, 95%CI: 1.9-36.2, $P = .004$) were independently associated with the presence of CKD. The area under the receiver operating characteristic (AUROC) curve for FIB-4 in identifying the presence of CKD was 0.769 (95% CI: 0.668-0.869).

Conclusions: Elevated FIB-4 is associated with a higher prevalence of CKD in patients with T2DM.

Abstract citation ID: lvag096.976

EP480 - ECE_2629 - Can glucagon-like peptide (GLP)-1 agonists and dual glucose-dependent insulinotropic polypeptides (GIP/GLP-1) agonists assist in managing hyperphagia and obesity in Prader-Willi syndrome?

Magdalena Goralska[1,2,3], Urszula Ambroziak[1], Beata Rak-Makowska[4], Jerzy Malek[1] and Agnieszka Stańczyk[1]

[1]Endocrinology and Internal Medicine Department, Warsaw Medical University, Warsaw, Poland; [2]Endocrinology and Internal Medicine, Warsaw Medical University, Warsaw, Poland; [3]Endocrinology,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Medical University of Warsaw, Warszawa, Poland; [4]Centrum Medyczne Kształcenia Podyplomowego, Warszawa, Poland

Introduction: Prader-Willi syndrome (PWS) is a complex genetic disorder characterized by a constellation of phenotypic features and hypothalamic dysfunction, including multiple endocrine abnormalities, short stature, and severe hyperphagia associated with satiety center dysfunction that leads to morbid obesity. Hormone deficiencies diagnosed and managed in childhood necessitate lifelong continuation and monitoring into adulthood.

Material and Methods: This retrospective observational study included 14 young adult patients with Prader-Willi syndrome (aged 18-30 years) who received GLP-1 receptor agonist therapy (semaglutide; $n = 10$) or dual GLP-1/GIP receptor agonist therapy (tirzepatide; $n = 4$) over 12 months. Semaglutide treatment was initiated at a dose of 0.25 mg once weekly and gradually escalated every 4 weeks up to a maximum dose of 1.7 mg/week, whereas tirzepatide treatment was started at 2.5 mg/week and maintained at 5 mg/week (without dose escalation due to economic constraints). None had type 2 diabetes mellitus. Body weight, BMI, and body fat percentage were evaluated in all patients, while fasting glucose, insulin, lipid profile, glycated hemoglobin, and hormone levels were measured and statistically analyzed with between-group comparisons.

Results: The mean age in the tirzepatide-treated group was 21.25 years (±SD 4.7; range 18-28 years), whereas in the semaglutide-treated group it was 23.9 years (±SD 3.03; range 20-30 years). Mean baseline BMI in the tirzepatide group was 40.68 kg/m^2 (±SD 0.98; range 39.47-41.86) compared to 42.3 kg/m^2 (±SD 9.49; range 27.2-54.68) in the semaglutide group. After 12 months of treatment, no significant between-group differences were observed in ΔBMI ($P = .945$; mean ΔBMI −2.59 in the tirzepatide group vs −2.66 in the semaglutide group), potentially attributable to the small sample size in the tirzepatide cohort and the low doses administered (due to economic constraints). Both treatment groups demonstrated improvements in metabolic control, including reductions in HbA1c, fasting glucose, and lipid profile parameters. Caregivers reported better appetite regulation, with decreased active food-seeking behavior—particularly at night. No serious adverse effects were reported.

Conclusions: The main aim of PWS clinical management in adulthood is prevention of obesity and its comorbidities, treatment of hormonal disorders and mental health stabilization. GLP1 receptor agonist (semaglutide) and dual GLP-1/GIP receptor agonist (tirzepatide) therapy appears safe in PWS patients and may have potential benefits for weight, metabolic and appetite control. Further research and long-term clinical studies are essential to confirm these benefits and refine therapeutic strategies.

Abstract citation ID: lvag096.977

EP483 - ECE_3415 - From early-onset diabetes to a progeroid syndrome: a case of werner syndrome

Filipa Barros Alves[1], Marta Castro Tomé[1], Tânia Fernandes[1], Rosa Maria Príncipe[1,2], Ana Rita Soares[3], Isabel Serra Nunes[3] and Francisco Simões de Carvalho[1,2]

[1]Local Health Unit of Matosinhos, Matosinhos, Portugal; [2]Faculty of Medicine, University of Porto, Porto, Portugal; [3]Local Health Unit of Santo António, Porto, Portugal

Introduction: Werner syndrome (WS) is a rare autosomal recessive progeroid disorder caused by biallelic pathogenic variants in the *WRN* gene, which encodes a helicase involved in DNA repair and genomic stability. WS is characterized by premature aging and a high prevalence of metabolic and endocrine abnormalities. Diabetes mellitus (DM), hypogonadism, thyroid dysfunction and osteoporosis are among the most frequently reported endocrinopathies.

Case Presentation: We report a 37-year-old man with diabetes mellitus diagnosed at 18 years of age during routine laboratory testing. He had a normal BMI (21 kg/m^2) and no family history of diabetes. Autoimmune markers were negative and C-peptide levels were preserved. At 24 years of age, he was diagnosed with primary hypothyroidism of unknown etiology, adequately controlled with levothyroxine. At 33 years, he developed Achilles tendinopathy and underwent surgical osteosynthesis for a calcaneal fracture, which was complicated by chronic ulceration and secondary infection, requiring repeated surgical debridement, prolonged antibiotic therapy and adjunctive hyperbaric oxygen therapy, with complete healing achieved only after 20 months. During follow-up, additional endocrine abnormalities were identified, including hypogonadotropic hypogonadism, with low total testosterone levels (108 ng/dL) and inappropriately normal gonadotropins (LH 0.56 mIU/mL; FSH 2.59 mIU/mL). Physical examination revealed short stature, premature graying, alopecia, skin atrophy with sclerodermiform changes and normal-to-low body weight, raising suspicion of a progeroid syndrome. He denied a history of ocular abnormalities or malignancy. Whole-exome sequencing identified compound heterozygosity in the WRN gene (c.1105C>T and c.3879dup), confirming the diagnosis of Werner syndrome. Metabolic evaluation revealed marked insulin resistance and severe hypertriglyceridemia, consistent with the lipodystrophy-like phenotype described in WS. Bone mineral density was within the normal range. Pituitary MRI showed a 5mm microadenoma. Therapeutic management was adapted to the pathophysiology of the disease, prioritizing insulin sensitivity with metformin and pioglitazone, resulting in sustained improvement in glycemic control. Levothyroxine replacement and testosterone therapy were initiated according to endocrine deficits, and cardiovascular surveillance was implemented.

Conclusions: This case highlights Werner syndrome as a multisystemic endocrine disorder in which diabetes, thyroid dysfunction, hypogonadism and impaired tissue repair may serve as early clinical clues. Early recognition enables a pathophysiology-based therapeutic approach and allows timely cardiac and cancer surveillance in young patients with atypical endocrine presentations.

Abstract citation ID: lvag096.978

EP484 - ECE_1094 - Physical activity and liver fibrosis: a stratified analysis by obesity and diabetes status

Sunghwan Suh[1], Jung-Hwan Cho[1], Ji Min Han[1] and Ji Cheol Bae[1]

[1]Division of Endocrinology and Metabolism, Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Changwon, South Korea

Background: Metabolic dysfunction–associated steatotic liver disease (MASLD) represents a hepatic manifestation of metabolic syndrome. We investigated the association between leisure-time

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

physical activity (LTPA) and liver fibrosis, and whether this relationship differs by obesity and diabetes status.

Methods: We conducted a cross-sectional analysis using data from the National Health and Nutrition Examination Survey (NHANES) 2017-March 2020 cycle. LTPA was assessed using the Global Physical Activity Questionnaire (GPAQ) and classified as physically active if engaging in ≥600 metabolic equivalent (MET)-minutes per week of moderate-to-vigorous activity, or inactive. Clinically significant liver fibrosis was defined as liver stiffness measurement (LSM) ≥ 8.0 kPa on transient elastography. Multivariable logistic and linear regression models estimated adjusted odds ratios (ORs) for significant liver fibrosis, with additional subgroup analyses according to obesity and diabetes status.

Results: In 7,662 U.S. adults, physically active participants ($n = 2721$) had a lower prevalence of significant fibrosis than inactive individuals (5.4% vs 11.4%, $P < .001$). In multivariable analysis, Participants who were physically active were associated with 42% lower odds of having fibrosis (OR 0.58, 95% confidence interval [CI] 0.41-0.82; $P = .004$). This association remained consistent in subgroup analyses stratified by obesity and diabetes status, even in the non-obese subgroup with body mass index (BMI) <30 kg/m^2 (OR 0.54, 95% CI 0.32-0.91; $P = .022$) and the non-diabetic subgroup (OR 0.59, 95% CI 0.39-0.90; $P = .016$).

Conclusions: Regular moderate-to-vigorous LTPA was independently associated with lower likelihood of clinically significant liver fibrosis. This beneficial association was significant regardless of obesity or diabetes status, suggesting that LTPA may play a clinically meaningful role in populations at high risk for progressive liver disease.

Abstract citation ID: lvag096.979

EP486 - ECE_1707 - Body mass index and discharge destination after major elective orthopedic surgery: a retrospective cohort study

Dana Kagansky[1,2], Ofir Vinograd[1], Hitam Hagog Natour[3], Michal Bitan[4] and Orna Tal[1]

[1]Shamir Medical Center (Assaf Harofeh), Endocrine Institute, Affiliated to the Gray Faculty of Medical & Health Sciences, Tel Aviv University, Beer Yaakov, Israel; [2]Shamir medical Center, Endocrine Institute, Affiliated to the Gray Faculty of Medical & Health Sciences, Tel Aviv University, Beer Yaakov, Israel; [3]Meir Medical Center, Institute of Endocrinology, Diabetes and Metabolism, Kfar Saba, Israel; [4]The College of Management Academic Studies, School of Computer Science, Rishon LeZion, Israel

Background: Discharge destination after elective major orthopedic surgery influences health system capacity, costs, and post-acute care utilization. Although body mass index (BMI) is routinely documented in preoperative risk assessment, it is not a formal criterion for discharge planning, and evidence regarding its independent association with discharge destination remains limited. This study examined the association between BMI and discharge destination following major orthopedic surgery.

Methods: We conducted a retrospective cohort study of adult patients undergoing major elective orthopedic surgery at a tertiary medical center between 2015 and 2025. Eligible procedures included spine surgery, total knee replacement, and total hip replacement. BMI was calculated at admission and analyzed both categorically and continuously. The primary outcome was discharge destination, classified as home or institutional rehabilitation. Multivariable logistic regression was used to evaluate the association between BMI and discharge to institutional rehabilitation, adjusting for age, sex, type of surgical procedure, and length of hospital stay.

Results: The final cohort included 3617 patients (mean age 65 years; 55% female), of whom 22% were discharged to institutional rehabilitation. Discharge to rehabilitation increased across BMI categories, from 20% among patients with BMI <25 kg/m^2 to 25% among patients with BMI >30 kg/m^2 ($P <$ .001). In multivariable analysis, higher BMI was independently associated with discharge to rehabilitation (OR 1.03 per kg/m^2; 95% CI 1.01-1.04), after adjustment for age, sex, surgical procedure, and length of hospital stay.

Conclusions: Higher BMI was independently associated with discharge to institutional rehabilitation following major elective orthopedic surgery, beyond differences explained by hospitalization duration and procedural factors. These findings suggest that discharge destination represents a consequential and potentially system-influenced outcome, highlighting the need for more standardized, function-based discharge criteria.

Abstract citation ID: lvag096.980

EP487 - ECE_2748 - Preoperative GLP-1 receptor agonist therapy and body composition outcomes in bariatric surgery: a real-world study

Sonsoles Gutierrez-Medina[1], Isabel Higuera[1], Gloria Velasco[2], Isabel Yagüe[1], Elena Sánchez[1], Belén García Izquierdo[1], Marta Mediero Benítez[1], Fernando Lapuente[2], José María Lopesino2, Sonsoles Guadalix[1], Javier Escalada[3] and Magdalena De la Higuera[1]

[1]Endocrinology and Nutrition, Clínica Universidad De Navarra, Universidad de Navarra, Madrid, Spain; [2]Surgery, Clinica Universidad de Navarra, Madrid, Spain; [3]Endocrinology and Nutrition, Clinica Universidad de Navarra, Pamplona, Spain

Background: Glucagon-like peptide-1 receptor agonists (GLP-1 RA) are increasingly used in obesity management and are often combined with bariatric surgery (BS). While their role as adjuvant therapy after surgery is well established, evidence regarding their preoperative use and its impact on body composition remains limited, particularly in clinical practice.

Aims: To evaluate the effects of preoperative GLP-1 RA therapy on weight loss and body composition in patients undergoing BS, compared with patients managed without pharmacological treatment before surgery.

Methods: We conducted a retrospective observational study including adults undergoing BS at Clínica Universidad de Navarra between 2017 and 2023. Patients were classified according to exposure to GLP-1 RA therapy before surgery. Anthropometric parameters and body composition, assessed by bioelectrical impedance analysis, were evaluated at baseline, pre-surgery, and at 1 and 6 months post-surgery. Multivariable analyses were performed adjusting for baseline body mass index, age, and type of surgery.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: A total of 86 patients were included (mean age 46.6 ± 12 years; 66% women); 80.2% underwent sleeve gastrectomy and 19.8% gastric bypass. Preoperative GLP-1 RA therapy was prescribed in 34.8% of patients (63.4% liraglutide, 36.6% semaglutide) for a mean duration of 21.7 ± 15.9 weeks. Due to drug availability during the study period, semaglutide dosing reached a maximum of 1 mg weekly. Patients receiving GLP-1 RA achieved significantly greater pre-surgical weight loss compared with controls (5.1 ± 4.9% vs 2.4 ± 3.7%; $P = .005$). This difference persisted at 1 month post-surgery (15.4 ± 5.2% vs 13.0 ± 3.8%; $P = .03$), but was no longer significant at 6 months. At the time of surgery, fat mass was significantly lower in the GLP-1 RA group [53.3 kg (95% CI 50.7-56.0) vs 58.6 kg (95% CI 56.6-60.5); $P = .01$]. No significant differences in lean mass were observed, and no between-group differences in body composition parameters were detected at 6 months post-surgery. Adverse events were mild and mainly gastrointestinal (nausea 6.9%, dyspepsia 2.3%, constipation 1.1%).

Conclusions: In this real-world study, preoperative GLP-1 RA therapy was associated with greater pre-surgical weight loss and reduced fat mass at surgery, without additional lean mass loss. Although the early weight loss benefit was not sustained at 6 months, the favorable body composition profile supports a potential role for GLP-1 RA as a neoadjuvant strategy. Prospective studies with optimized dosing regimens and longer follow-up are needed to define the long-term clinical value of this approach.

Abstract citation ID: lvag096.981

EP488 - ECE_2506 - Renal function in patients with type 2 diabetes mellitus and ischemic heart disease with and without obstructive coronary atherosclerosis

Yanina Rebrova[1,2,3], Yanina Saienko[1] and Borys Mankovsky[1]
[1]*D. F. Chebotarev Institute of Gerontology of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine;* [2]*The Scientific and Practical Medical Center of Pediatric Cardiology and Cardiac Surgery of the Ministry of Health of Ukraine, Government Institution, Kyiv, Ukraine;* [3]*Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine*

Background: Type 2 diabetes mellitus (T2DM) is associated with a high risk of both ischemic heart disease and chronic kidney disease (CKD). In addition to obstructive coronary artery disease (CAD), increasing attention has been paid to ischemia with non-obstructive coronary arteries (INOCA), particularly microvascular angina, which is considered a manifestation of systemic microvascular dysfunction. However, data on renal function according to different forms of ischemic heart disease in patients with T2DM remain limited.

Aim: To compare renal function and markers of chronic kidney disease in patients with T2DM with INOCA and obstructive CAD.

Methods: The study population consisted of 80 patients with type 2 diabetes mellitus, who were categorized into INOCA ($n = 30$) and obstructive coronary artery disease ($n = 50$) groups. Age, duration of T2DM, fasting glucose, glycated hemoglobin (HbA1c), plasma creatinine, estimated glomerular filtration rate (eGFR, CKD-EPI), urine albumin-to-creatinine ratio (ACR), and plasma potassium levels were assessed. Data are presented as mean ± standard deviation. Between-group comparisons were performed using Student's t-test, and correlations were analyzed using Pearson's method.

Results: Patients with obstructive CAD were older than those with INOCA (66.8 ± 8.3 vs 58.9 ± 11.3 years). Glycemic control parameters did not differ significantly between groups (HbA1c: 6.9 ± 1.4% vs 6.7 ± 1.7%). Renal impairment was more pronounced in the obstructive CAD group, with significantly lower eGFR (51.2 ± 15.8 vs 74.3 ± 16.8 ml/min/1.73 m^2; $\mathbf{P < .001}$) and higher ACR (82.3 ± 115.8 vs 32.7 ± 34.3 mg/g; $\mathbf{P = .028}$) compared with the INOCA group. An inverse association between eGFR and ACR was observed in both INOCA and obstructive CAD groups, with a stronger correlation in patients with obstructive disease, indicating a consistent link between renal dysfunction and albuminuria across subgroups.

Conclusions: In patients with type 2 diabetes mellitus, obstructive coronary artery disease is associated with more severe renal dysfunction compared with INOCA, despite similar glycemic control. The inverse relationship between eGFR and albuminuria highlights shared cardiorenal mechanisms underlying target organ damage in T2DM

Abstract citation ID: lvag096.982

EP490 - ECE_1508 - Real-world comparison of the effects of loxenatide with other GLP-1RAs on renal outcomes in patients with type 2 diabetes: a subgroup analysis of the fighting-1 cohort study (fighting-3)

Hong Wu[1], Lianyong Liu[1], Yale Duan[2], Shaowei Duan[3], Zhizhen Hu[3] and Dajin Zou[1]
[1]*Punan Hospital, Shanghai, China;* [2]*Department of Medical Affairs, Jiangsu Hansoh Pharmaceutical Group Co., Ltd., Shanghai, China;* [3]*Jiangsu Hansoh Pharmaceutical Group Co., Ltd., Shanghai, China*

Background: Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have demonstrated renoprotective effects in clinical trials. However, real-world evidence comparing the renal outcomes of different GLP-1RAs remains limited. FIGHTING-3 is a subgroup analysis of the FIGHTING-1 cohort study. FIGHTING-3 aimed to evaluate the real-world effectiveness of loxenatide vs other GLP-1RAs on renal outcomes in patients with type 2 diabetes (T2D).

Methodology: This multicentric retrospective, real-world study, was conducted using data from the Tianjin Health Care Data Platform, which includes records from 82 hospitals in China. Adults with T2D who started and continued treatment with different GLP-1RAs for at least 12 months were included. Propensity score matching (caliper = 0.1) was used to balance 10 baseline covariates, including age, sex, diabetes duration, history of cardiovascular disease, dyslipidemia, hypertension, renal disease, use of sodium-glucose co-transporter-2 inhibitors, and antihypertensive and lipid-lowering therapies. The composite renal outcome defined as a 50% sustained decline in estimated glomerular filtration rate (eGFR), onset of renal failure, or all-cause mortality. The cox proportional hazards regression model was applied to estimate hazard ratio (HR) along with their 95% confidence intervals (CIs).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: In the cohorts, the median follow-up duration was 29.5 months for patients receiving loxenatide, 22.9 months for semaglutide, 27.2 months for liraglutide, and 27.8 months for dulaglutide. The proportion of days covered (PDC) was 69.5%, 47.7%, 46.7%, and 51.6%, respectively. The proportion of patients receiving high-dose treatment was 100.0% (loxenatide 0.2 mg), 52.3% (semaglutide 1.0 mg), 32.1% (liraglutide 1.8 mg), and 3.8% (dulaglutide 1.5 mg). Loxenatide was matched 1:1 with semaglutide ($N = 974$), liraglutide ($N = 798$), and dulaglutide ($N = 501$). Loxenatide was associated with a reduction of composite renal endpoint vs semaglutide (HR: 0.69, 95% CI: 0.07-7.29), liraglutide [HR: 0.15, 95% CI: 0.02-1.34], and dulaglutide (HR: 0.53, 95% CI: 0.05-5.99). However, these differences were not statistically significant (all $P > .05$).

Conclusions: Loxenatide exhibits comparable renal protection to other GLP-1RAs in T2D, aligning with the class's established benefits. However, low event rates highlight the need for larger trials to validate these findings.

Keywords type 2 diabetes, loxenatide, renal outcome

Abstract citation ID: lvag096.983

EP491 - ECE_2116 - Prevalence of additional autoimmune diseases in adults with Type 1 diabetes and thyroid and/or celiac disease: a real-world cross-sectional study

Valerio Velardi, Lidiana Sanson, Barbara Toffoli, Federico Favaro, Fabio Fischetti, Bruno Fabris and Stella Bernardi
University of Trieste, Trieste, Italy

Aims: Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease that is often associated with other autoimmune conditions, mostly autoimmune thyroid disease (AITD) and celiac disease. Guidelines recommend screening subjects with T1DM for thyroid and celiac disease. Nevertheless, in case of their positivity, indicating the presence of an autoimmune polyendocrine syndrome, there is a lack of guidance on how to proceed. In other words, should we screen these patients for other autoimmune diseases? The aim of our study was to evaluate the number of additional autoimmune conditions in a cohort of T1DM patients with AITD and/or celiac disease.

Methods: This is a real-world cross-sectional study. Adult patients with T1DM followed in the ASUGI Diabetes Center (Trieste, Italy) were identified with the use of electronic medical records. Among them, we selected those who had a diagnosis of AITD or celiac disease and prescribed further exams to exclude other autoimmune conditions.

Results: 639 T1DM patients were identified and 198 of them had AITD or celiac disease. A total of 139/198 (70%) agreed on performing further analyses. In the end, 65/139 (47%) patients presented a previously unknown autoantibody positivity, which led us to diagnose 16 new pathological conditions in 15/139 patients (11%). Taking into account the newly diagnosed autoimmune conditions, as well as those that were already known, 43/139 (31%) patients had at least 3 autoimmune diseases.

Conclusions: Our data show that 31% of patients with T1DM and AITD or celiac disease have at least another (ie, a third) autoimmune disease. These data shed light on the fact that once thyroid and celiac disease screening are positive in patients with T1DM, patients should receive the diagnosis of APS, which should prompt for a broader evaluation of additional autoimmune diseases and raise medical awareness during patient follow-up.

Abstract citation ID: lvag096.984

EP492 - ECE_3018 - Impact of the Dexcom G7-Tandem t:slim X2 with Control-IQ system on glycemic control in patients with type 1 diabetes: a retrospective real-world study

Javier Panizo Fra[1], Selena Rodriguez Fernandez[2], Kevin David Díaz Gorrín[1], Paula Pérez[1], MacArena Sánchez-Gallego Alonso[1], Óliver Quintero Rodríguez[1], Ana Paola Leon Ocando[1], Orvelindo Rodríguez Hernández[1], Elena Rodríguez Sosa[1], Laura Mesa Suárez[1] and Juan Ignacio Márquez De La Rosa[1]
[1]San Cristóbal de La Laguna, Spain; [2]Endocrinology and Nutrition, Hospital Universitario de Canarias, San Cristóbal de La Laguna, Spain

Introduction: Optimal glycaemic control is essential to reduce complications in type 1 diabetes mellitus (T1DM). Hybrid closed-loop systems allow automatic insulin adjustment to optimise glycaemic control. The Dexcom G7–Tandem t:slim X2 with Control-IQ system integrates an insulin pump, a continuous glucose monitoring (CGM) sensor, and an automated control algorithm.

Objective: To retrospectively evaluate the effect of using the Dexcom G7–Tandem t:slim X2 with Control-IQ system on glycaemic control parameters (HbA1c and CGM metrics) in 15 patients with T1DM during the first 6 months of use, followed in the outpatient Endocrinology and Nutrition clinics at the Hospital Universitario de Canarias.

Materials and Methods: The variables analysed included age, sex, duration of diabetes, HbA1c, total daily insulin dose, time in range (TIR), time in hypoglycaemia, time in hyperglycaemia, coefficient of variation (CV), and percentage of time with Control-IQ activated. Data were collected for the month prior to system initiation (Dexcom Clarity) and at 6 months after starting system use (Glooko).

Statistical Analysis: Paired Student's *t*-test was used for variables with normal distribution (TIR, CV, hypoglycaemia), while the Wilcoxon signed-rank test was applied for HbA1c comparisons due to non-normal distribution.

Results: HbA1c: A significant reduction of 0.6 percentage points was observed (7.32% at baseline vs 6.63% at 6 months, $P = .010$). TIR (70-180 mg/dL): Mean increase of 11% (54.07% ± 20.67% at baseline vs 65.13% ± 7.11% at 6 months, $P = .0295$). Hypoglycaemia (<70 mg/dL): Slight reduction (2.07% ± 1.22% at baseline vs 1.47% ± 1.36% at 6 months, $P = .228$). CV (%): Mild, non-significant reduction (36.65% ± 6.03% at baseline vs 35.49% ± 5.29% at 6 months, $P = .509$).

Conclusions: This study demonstrates a significant improvement in TIR and HbA1c without an increase in hypoglycaemia. These findings support the effectiveness of hybrid closed-loop systems in real-world clinical practice, improving glycaemic control in patients with T1DM.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.985

EP493 - ECE_3056 - Management of corticosteroid-induced hyperglycemia in hospitalized patients with Type 2 diabetes mellitus treated by the Endocrinology Department

Javier Panizo Fra, Selena Rodriguez Fernandez, Kevin David Díaz Gorrín, Paula Pérez MacHín, MacArena Sánchez-Gallego Alonso, Óliver Quintero Rodríguez, Ana Paola Leon Ocando, Laura Mesa Suárez, Elena Rodríguez Sosa, Patricia León González and Juan Ignacio Márquez De La Rosa
San Cristóbal de La Laguna, Spain

Introduction: The use of glucocorticoids in hospitalised patients with type 2 diabetes mellitus (T2DM) frequently triggers severe glycaemic decompensation, complicating clinical course and patient management. These patients often require basal–bolus insulin therapy to achieve optimal glycaemic control.

Objective: To evaluate glycaemic control and therapeutic strategies used in hospitalised patients with T2DM treated with systemic corticosteroids who were assessed by the Endocrinology service.

Materials and Methods: A prospective, observational study was conducted. Twenty-six patients with T2DM receiving corticosteroid therapy and admitted to different departments of the Hospital Universitario de Canarias (HUC) were included. All patients were assessed and followed through endocrinology consultation over a 6-month period. Glycaemic values before and after intervention, corticosteroid dose (prednisone equivalent), and the need for insulin therapy according to prior diabetes treatment were analysed.

Results: Of the 26 patients included, 57.7% were male and 42.3% female, with a mean age of 70.1 years. Mean glycated haemoglobin (HbA1c) was 7.52%. The mean daily corticosteroid dose (prednisone equivalent) was 34.8 mg. A statistically significant reduction in mean capillary blood glucose was observed, from 289.2 ± 62.1 mg/dL at the start of the intervention to 156.4 ± 29.8 mg/dL at discharge ($P < .001$). When stratified by prior treatment, patients previously treated with insulin had higher HbA1c levels (7.95% vs 6.9%, $P = .028$) and a greater number of severe hyperglycaemic episodes (>250 mg/dL) during hospitalisation (5.4 vs 2.3 episodes, $P = .005$) compared with those treated with oral antidiabetic drugs (OADs). No statistically significant differences in final glycaemic control were observed between patients treated with prednisone or dexamethasone. The incidence of hypoglycaemia was negligible. A statistically significant positive correlation was found between corticosteroid dose and insulin requirements at discharge ($r = 0.62$; $P < .005$). After stratification by prior treatment, insulin-treated patients exhibited greater glycaemic variability (mean of 5.4 episodes >250 mg/dL) compared with those treated with OADs (2.3 episodes; $P = .005$). No cases of severe hypoglycaemia were observed, with a mean of 0.4 events per patient.

Conclusions: Endocrinology follow-up of hospitalised patients with T2DM receiving corticosteroid therapy resulted in significant improvement in glycaemic profile. A direct and significant relationship exists between glucocorticoid dose and insulin requirements. Patients with previously insulin-treated T2DM show poorer glycaemic control and a higher number of hyperglycaemic episodes, representing the subgroup that benefits most from endocrinological intervention.

Principio del formulario
Final del formulario

Abstract citation ID: lvag096.986

EP494 - ECE_3857 - Preliminary six-month prospective analysis of glycemic control and lipid profile changes following automated insulin delivery initiation in adults with type 1 diabetes

Mafalda Canudas Costa, Helena Urbano Ferreira, Ines Pereira, João Menino, Ana Rita Leite, Patricia Ferreira, Ana Luísa Barbosa, Anabela Costa, Carmo Redondo, Sílvia Monteiro, Sandra Belo, João Neves, Celestino Neves, Joana Queirós and Juliana Gonçalves
Department of Endocrinology, Diabetes and Metabolism, São João Local Health Unit, Oporto, Portugal

Background: Automated insulin delivery (AID) systems improve glycemic control in adults with type 1 diabetes (T1D), but their impact on lipid metabolism remains unclear.

Methods: Baseline, 3-, and 6-month data were analyzed from a prospective cohort of adults with T1D followed at a tertiary center who initiated either Tandem t:slim X2™ Control-IQ (CIQ) or MiniMed™780G (MM780G) since July 2023. Participants without baseline and at least one follow-up measurement of lipid profile or glycemic control were excluded. Associations between glycemic metrics and lipid parameters were evaluated using linear regression models—cross-sectional at baseline and longitudinal for within-person changes—and a linear mixed-effects model including repeated measures at 0, 3, and 6 months. Analyses were unadjusted and adjusted for age, sex, BMI, and statin therapy. Continuous variables were summarized as mean ± SD or median (IQR) according to distribution.

Results: Seventy-three adults were included (37.30 ± 11.80y; 34.30% male), 38.40% under statin therapy, 49.00% using MM780G. Baseline HbA1c was 7.60 ± 1.00%, TIR 55.13 ± 14.23%, LDL-C 86.00 (63.50-104.00) mg/dL, BMI 24.60 (22.51-27.41) kg/m^2. Higher TIR correlated with lower ApoB at baseline ($\beta = -.39$, 95%CI−0.77;−0.01, $P = .048$), not sustained after adjustment. Cross-sectionally, higher TIR associated with lower triglycerides ($\beta = -.01$, 95%CI–0.02; 0.00, $P = .049$); higher TAR showed no baseline association but was positively associated with triglycerides longitudinally ($\beta = .01$, 95%CI 0.00; 0.02, $P = .040$). BMI independently predicted higher triglycerides ($\beta = .05$, 95%CI 0.02; 0.08, $P = .001$) and LDL-C ($\beta = 1.18$, 95%CI 0.07; 2.29, $P = .040$), while statin use correlated with lower LDL-C ($\beta = -14.50$, 95%CI−23.30; −5.70, $P = .002$) and total cholesterol (TC) ($\beta = -11.70$, 95%CI −23.00;−0.40, $P = .046$). Longitudinally, increases in TBR were associated with higher LDL-C ($\beta = 1.31$, 95%CI 0.20; 2.43, $P = .022$), TC ($\beta = 1.57$, 95%CI 0.31; 2.84, $P = .020$), and non-HDL-C ($\beta = 1.50$, 95%CI 0.39; 2.60, $P = .008$). Mixed-effects models confirmed these trends: modest inverse association between TIR and triglycerides ($\beta = -.01$, 95%CI −0.01; 0.00, $P = .050$), borderline positive association between TAR and triglycerides ($\beta = .01$, 95%CI 0.00; 0.02, $P = .058$), and significant positive association between TBR and non-HDL-C ($\beta = .96$,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

95%CI 0.02; 1.90, $P = .046$), with positive but non-significant associations with LDL-C and TC. No significant associations were observed with HDL-C or ApoA.

Conclusions: In this preliminary 6-month analysis, improved CGM-derived glycemic control—particularly higher TIR—was modestly associated with lower triglycerides, whereas higher TAR and TBR correlated with less favorable lipid profiles. Lipid metabolism may reflect short-term glycemic improvement after AID initiation, warranting confirmation at 12 months.

Abstract citation ID: lvag096.987

EP495 - ECE_1400 - Mendelian randomization identifies no causal relationship of insulin resistance on hippocampal volume

Silvano da Silva[1], Vasiliki Lagou[2], César Pórpora[1] and João Silva[1]

[1]*Faculty of Medical Sciences of Santos (FCMS)—UNILUS—Lusíada University Center, Santos, Brazil;* [2]*Bioinformatics Multidisciplinary Environment, Federal University of Rio Grande do Norte, Natal, Brazil*

Introduction: Insulin resistance is a systemic condition associated with altered brain metabolism and increased risk of cognitive and neurodegenerative disorders. Observational and neuroimaging studies suggest links between peripheral insulin resistance and structural brain changes, but these findings are limited by confounding. Mendelian randomization (MR) provides a genetic approach to determine whether insulin resistance causally influences brain structure, with important implications for endocrine mechanisms and metabolic therapies.

Aim: To assess the causal relationship between genetically predicted systemic insulin resistance and hippocampal volume (HV) using two-sample MR.

Methods: A two-sample Mendelian randomization study was performed using publicly available data to assess the causal effect of fasting insulin (FI)/glycated hemoglobin (HbA1c) on brain structure. Independent genome-wide significant variants ($P < 5 \times 10^{-8}$) selected from large-scale FI/HbA1c GWAS meta-analyses in individuals of European ancestry were used as instrumental variables. HV based on magnetic resonance imaging (MRI) GWAS data were available from UK Biobank Causal estimates of FI/HbA1c on HV were derived using inverse variance weighted (IVW) analysis and compared to those from weighted median and MR-Egger methods for consistency. Heterogeneity and horizontal pleiotropy were evaluated using Cochran's Q statistic and MR-Egger intercept, respectively, and leave-one-out analyses were conducted to assess result robustness.

Results: Genetically predicted FI was not causally associated with HV. The IVW analysis showed a non-significant effect estimate ($\beta = -.07$, $P = .71$), which was directionally consistent across other MR methods ($\beta_{\text{weighted median}} = -.11$, $P_{\text{weighted median}} = .58$; $\beta_{\text{MR-Egger}} = -0.17$, $P_{\text{MR-Egger}} = 0.88$). Cochran's Q test indicated no heterogeneity among instrumental variables (IVW Q $P = .052$) or evidence of directional horizontal pleiotropy as assessed by the MR-Egger intercept ($P = .93$). Consistent with these findings, no causal effects of genetically predicted HbA1c levels on HV were observed. Leave-one-out analyses demonstrated that no single variant disproportionately influenced the overall causal estimates.

Conclusions: This MR study provides genetic evidence that systemic insulin resistance related traits do not have a direct causal effect on HV, a structural MRI-derived trait. These findings indicate that glucose homeostasis may not directly influence hippocampal anatomy, but other, non-glycemic, mechanisms might be driving the associations between insulin resistance and central nervous system outcomes.

Abstract citation ID: lvag096.988

EP496 - ECE_1903 - Incidence and prevalence of type 1 diabetes, celiac disease and autoimmune thyroid disorders in Spain, 2018-2025

Mariana Haeberer[1], Jordi Aparici-Espot[2], Maria Alamillo[3], Yesika Díaz[3], Virginia Bellido[4], Luis Castaño[5] and Fernando Gomez-Peralta[6]

[1]*Sanofi, Madrid, Spain;* [2]*Sanofi, Barcelona, Spain;* [3]*Telomera, Madrid, Spain;* [4]*Hospital Universitario Virgen del Rocío, Sevilla, Spain;* [5]*Hospital Universitario Cruces, Bilbao, Spain;* [6]*Hospital General de Segovia, Segovia, Spain*

Introduction: We aimed to estimate incidence and prevalence of Type 1 Diabetes (T1D), celiac disease and autoimmune thyroid disorders in Spain during 2018-2025.

Methods: Retrospective observational cohort study using secondary data from Telotrón® database. Indirect standardization rates were estimated using National Statistics Institute population denominators. ICD-9/ICD-10 codes used were: T1D 250.*1,250.*3/E10; celiac disease 579.0/K90.0; Hashimoto hypothyroidism 245.2/E06.3; Graves hyperthyroidism 242.0/E05.0.

Results: As of 31-Dec-2025, the prevalences of T1D, celiac disease, Hashimoto and Graves were 0.30% ($N = 148\,688$), 0.56% ($N = 276\,548$), 0.30% ($N = 146\,508$) and 0.30% ($N = 146\,071$), respectively. Between 2018-2025, the incidence of T1D, celiac disease, Hashimoto and Graves ranged from 10.2-14.0, 26.3-43.5, 17.8-27.9 and 16.5-25.9 per 100,000, respectively. T1D incidence was higher in those aged <35 and increased over time between 0-7 and 18-35 years old. Incidence of celiac disease also increased in those aged <45 years, while incidences of Hashimoto and Graves increased in those aged >18 and between 18-45 years, respectively (Table 1). Among celiac disease, Hashimoto and Graves population, 1.71%, 1.34% and 0.81% also had T1D diagnosis, respectively. Among T1D population, 11.5% had at least one autoimmune comorbidity (2.7% celiac disease, 1.3% Hashimoto and 0.8% Graves).

Conclusions: Estimations of T1D are consistent with few previous studies. Celiac, Hashimoto and Graves diseases appear to be underdiagnosed. All conditions increased over time, T1D and celiac disease among children and adults and thyroiditis among adults, this may be partially attributed to improved diagnosis. Comorbidity between these conditions is frequent. Enhanced screening is needed.

Table 1 Incidence rates (100 000 population).

Disease	Age-group	2018	2022	2023	2024	2025
T1D	0-7	11.5	20.3	15.2	24.0	18.5
	8-17	27.3	29.6	40.1	28.7	28.2

(*continued*)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Table 1 Continued

Disease	Age-group	2018	2022	2023	2024	2025
	18-35	22.9	25.7	30.4	31.0	28.5
	36-45	4.6	6.5	7.4	3.1	6.8
	46-65	1.4	3.4	3.4	1.9	2.7
	>65	0.6	0.0	1.1	1.1	0.5
Celiac disease	0-7	72.3	76.6	91.0	88.1	115.2
	8-17	62.2	49.0	47.9	77.0	93.6
	18-35	41.0	46.6	52.5	62.0	53.2
	36-45	26.3	34.2	42.1	43.1	36.6
	>45	21.9	18.6	19.2	21.5	18.2
Hashimoto	0-7	0.0	2.4	1.3	0.0	0.0
	8-17	6.8	7.6	10.5	9.3	6.0
	18-35	14.9	19.2	24.1	29.3	21.8
	36-45	25.8	25.0	30.7	33.9	32.5
	>45	22.8	35.6	32.2	33.4	24.4
Graves	0-7	0.0	2.4	1.3	2.7	0.0
	8-17	3.4	4.2	6.1	5.6	4.0
	18-35	16.1	17.2	24.6	25.8	20.8
	36-45	23.2	26.0	30.7	29.6	29.1
	>45	36.1	25.9	33.2	30.6	25.6

Abstract citation ID: lvag096.989

EP497 - ECE_3829 - Evaluating steroid profiles through sexual dimorphism to define metabolic phenotypes and identify advanced fibrosis in patients with MASLD

Mirko Parasiliti Caprino[1], Chiara Rosso[2], Federico Ponzetto[3], Laura Leoni[3], Giovanni Birolo[4], Grazia Pennisi[5], Gianpaolo Caviglia[2], Giulio Mengozzi[3], Salvatore Petta[5], Piero Fariselli[4], Gianluca Aimaretti[1], Tuulia Hyotylainen[6], Mauro MacCario[1], Matej Orešič[7] and Elisabetta Bugianesi[2]

[1]Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [2]Liver Unit, Department of Medical Sciences, University of Turin, Turin, Italy; [3]Clinical Biochemistry Laboratory, Department of Medical Sciences, University of Turin, Turin, Italy; [4]Department of Medical Sciences, University of Turin, Turin, Italy; [5]Liver Unit, University of Palermo, Palermo, Italy; [6]School of Science and Technology, Örebro University, Örebro, Sweden; [7]Turku Bioscience Centre, University of Turku and Åbo Akademi University, Turku, Finland

Aim: Sex-related differences in metabolic dysfunction-associated steatotic liver disease (MASLD) are increasingly recognised, but the endocrine mechanisms underlying disease heterogeneity and progression remain poorly understood. Given the pivotal role of steroid hormones in metabolic regulation and inflammation, we aimed to investigate sexual dimorphism in MASLD through a targeted steroidomic approach and to develop a non-invasive model for the prediction of advanced hepatic fibrosis.

Methods: In this multicentre cross-sectional study, we enrolled 463 patients with biopsy-proven MASLD from two tertiary Liver Units in Italy. Steroid profiling was performed using a newly validated liquid chromatography–tandem mass spectrometry (LC-MS/MS) method, quantifying both glucocorticoids and phase II androgen metabolites. Associations with sex, metabolic comorbidities (obesity, type 2 diabetes mellitus, and hypertension), PNPLA3 rs738409 genotype, and histological fibrosis stage were evaluated. A predictive model for advanced fibrosis (F≥3), named the FaSter model (Fibrosis and Steroid), was developed in the Turin cohort ($n = 313$) using multivariable logistic regression and internally validated with 10-fold cross-validation. External validation was performed in an independent cohort from Palermo ($n = 150$). A subgroup of 32 patients underwent hepatic transcriptomic analysis for selected steroidogenic and conjugating enzymes.

Results: Steroidomic analysis revealed marked sex- and age-specific differences in circulating steroid profiles. In men, advanced fibrosis was associated with decreased sulfation and glucuronidation of androgens, suggesting impaired hepatic inactivation. In women, steroid alterations varied according to menopausal status and metabolic phenotype, with postmenopausal women showing elevated testosterone and reduced androgen sulfate levels in advanced disease. The FaSter model, incorporating clinical parameters and ten steroid biomarkers, showed excellent diagnostic accuracy for advanced fibrosis (AUC 0.88 in the training cohort; 0.82 in the validation cohort), outperforming FIB-4 and NAFLD fibrosis score (NFS), and approaching the performance of Vibration-Controlled Transient Elastography (VCTE). Combining the FaSter model with liver stiffness measurement further improved predictive performance (AUC up to 0.91). Transcriptomic data supported a pathophysiological role for impaired hepatic steroid metabolism in the development of advanced fibrosis.

Conclusions: Steroid metabolism is closely linked to sexual dimorphism and fibrosis progression in MASLD. The FaSter model represents a novel, non-invasive, and reproducible tool for fibrosis risk stratification, with potential application in personalised hepatology. Further validation in prospective and ethnically diverse populations is warranted to confirm its generalisability and clinical utility.

Abstract citation ID: lvag096.990

EP499 - ECE_1517 - Gut microbiome differences between stress-resilient and stress-vulnerable mice parallel metabolic health status

Yonatan Karban[1], Mayalee Weissman Rosenfeld[1], Ayala Wollman[1], Oshrit Rahimi[1], Oryan Agranyoni[2], Sarven Sabunciyan[2], Albert Pinhasov[1] and Tovit Rosenzweig[1]

[1]Department of Molecular Biology, and The Adelson School of Medicine, Ariel University, Ariel, Israel; [2]Johns Hopkins University, Baltimore, United States

Obesity is a prevalent health condition that substantially increases the risk of cardiometabolic diseases, typically manifesting as metabolically unhealthy obesity (MUO). Nevertheless, a subset of individuals remains relatively metabolically healthy despite excess adiposity, a phenotype termed metabolically healthy obesity (MHO). Multiple factors have been implicated in this divergence, including adipose tissue function, gut microbiome composition, and stress responsiveness.

Accumulating evidence suggests that resilience to stress influences susceptibility to obesity and its metabolic complications. In previous work, we demonstrated that mice selectively bred

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

for differential stress-coping phenotypes exhibit distinct metabolic profiles. Stress-resilient dominant (Dom) mice displayed features consistent with MHO, whereas stress-vulnerable submissive (Sub) mice developed MUO.

The gut microbiome is a critical regulator of host metabolism and has been strongly linked to obesity-related morbidity. Dysbiosis, defined as an imbalance in gut microbial communities, has been associated with metabolic dysfunction. The current study aimed to determine whether differences in gut microbiome composition contribute to the distinct metabolic phenotypes observed in stress-vulnerable and stress-resilient mice.

Gut microbiome profiles of Sub and Dom mice maintained on a standard diet (STD) or challenged with a high-fat diet (HFD) were analyzed using 16S rRNA sequencing. HFD significantly reduced alpha diversity in Sub mice, while Observed and Shannon diversity indices were preserved in Dom mice. Phylogenetic diversity (PD) was reduced by HFD in both strains. Principal component analysis revealed distinct clustering of Sub and Dom microbiomes at baseline and following HFD exposure, indicating inherent strain-specific microbial signatures.

Differential abundance analysis using ANCOM-BC revealed a higher relative abundance of Bacteroidetes in Dom mice, whereas Sub mice exhibited increased Proteobacteria and Firmicutes. Under STD conditions, Sub mice showed enrichment of bacterial taxa previously associated with unfavorable metabolic health, including Desulfovibrionaceae, Lachnospiraceae, Ruminococcus, and Proteobacteria, alongside reduced Bacteroidales and S24-7. Accordingly, the microbiome profile of Sub mice under STD resembled that reported in metabolically unhealthy states. HFD induced microbiome shifts in both strains, including increased Desulfovibrionaceae and Proteobacteria and reduced Betaproteobacteria and S24-7; however, strain-specific differences persisted, with Sub mice maintaining higher Proteobacteria and Dom mice higher Bacteroidetes.

This study demonstrates that stress-coping phenotypes are linked to distinct gut microbiome compositions, which may contribute to differential metabolic outcomes under standard and high-fat diets.

Abstract citation ID: lvag096.991

EP500 - ECE_1831 - Semaglutide rewires thyroid transcriptional programs in obesity through sex-specific modulation of adiponectin signaling and mTOR–RET pathways

Niklas Geiger, Simon Kloock, Palina Zytner, Martin Fassnacht and Ulrich Dischinger
Division of Endocrinology and Diabetes, Department of Internal Medicine, University Hospital Würzburg, Würzburg, Germany

Background: Obesity disturbs endocrine homeostasis and reshapes thyroid-specific transcriptional programs. Recent data show a higher prevalence of thyroid dysfunction and atypical TSH profiles in obese individuals, highlighting the clinical relevance of metabolic–thyroid crosstalk. Given the widespread use of semaglutide, this study investigates its sex-specific impact on thyroid gene regulation in obese rats.

Methods: Male and female Wistar rats were exposed to an eight-week high-fat/fructose diet combined with L-NAME to induce obesity ($n = 6$ per group). Animals were subsequently randomized to semaglutide (Sema) or saline, while lean controls received standard chow without L-NAME. After additional eight weeks, thyroid tissue was analyzed by qRT-PCR for metabolic and thyroid-specific marker genes. Serum adiponectin and leptin were quantified.

Results: The adiponectin receptor emerged as an obesity-sensitive target, with males showing significant upregulation in mRNA expression vs controls ($P < .05$) and a trend toward Sema-mediated downregulation ($P = .09$). In females, Sema significantly suppressed adiponectin receptor expression ($P < .05$). In males, obesity downregulated mTOR, Cxcl10 and Foxe1 ($P < .01$), key regulators of thyroid hormone synthesis and metabolic signaling. Sema restored these transcripts ($P < .05$), suggesting a reversal of obesity-induced thyroid dysfunction. Sema also reduced Rps6ka4 expression in males ($P < .05$), pointing to a positive modulation of stress-responsive pathways. In contrast, obese females exhibited a significant upregulation of RET ($P < .05$). In males, adiponectin/leptin ratio was significantly higher in obese compared to lean rats, reduced in Sema, but without effects in females.

Conclusions: Semaglutide reprograms thyroid transcriptional networks in obesity via sex-specific modulation of adiponectin signaling and metabolic stress pathways, revealing a previously underappreciated endocrine interface between semaglutide and thyroid regulation.

Abstract citation ID: lvag096.992

EP501 - ECE_3796 - Epicardial adipose tissue shows selective associations with non-invasive hepatic fibrosis and metabolically-driven steatosis indices, revealing phenotypic heterogeneity beyond BMI in obesity

Davide Masi, Vittoria Strinati, Giorgia Maria Baldazzi, Maria Elena Spoltore, Rebecca Rossetti, Lucio Gnessi, Stefania Mariani, Mikiko Watanabe, Andrea Isidori, Daniele Gianfrilli and Carla Lubrano
Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza University, Rome, Italy

Background: Obesity is associated with substantial variability in cardiometabolic and hepatic risk that is not fully explained by body mass index (BMI). Epicardial adipose tissue (EAT) is a visceral-like fat depot with metabolic and inflammatory activity, but whether it reflects hepatic fat accumulation or more advanced, metabolically driven liver injury remains unclear.

Objective: To determine whether EAT is differentially associated with non-invasive indices of hepatic steatosis and fibrosis, independent of overall adiposity, and to assess whether epicardial fat burden contributes to the identification of obesity-related phenotypes beyond BMI.

Methods: We conducted a retrospective observational study in adults with overweight and obesity evaluated at a tertiary obesity care centre. Epicardial adipose tissue thickness was assessed by echocardiography together with measures of visceral adiposity, anthropometric variables and metabolic parameters. Hepatic steatosis and fibrosis risk were estimated using established non-invasive indices. Associations between EAT and hepatic indices

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

were examined using correlation analyses and multivariable linear and logistic regression models adjusted for demographic variables and measures of overall and central adiposity. To explore heterogeneity beyond conventional adiposity metrics, unsupervised phenotyping was performed using dimensionality reduction followed by model-based clustering.

Results: A total of 1076 individuals were included (mean age 52 ± 12 years; ~60% women), with a mean BMI of 36.1 ± 6.4 kg/m^2 and a mean EAT thickness of 8.1 ± 2.3 mm. Epicardial adipose tissue increased in parallel with visceral adiposity and insulin resistance. EAT was positively associated with fibrosis risk assessed by FIB-4 ($r \approx 0.25$, $P < .001$) and with Fatty Liver Index ($r \approx 0.40$, $P < .05$), whereas no significant association was observed with composite liver fat indices. After multivariable adjustment, EAT remained independently associated with FIB-4 ($\beta \approx 2.4$, $P \approx .03$) and Fatty Liver Index ($\beta \approx 2.2$, $P < .001$), but not with the Hepatic Steatosis Index or NAFLD Liver Fat Score. In models predicting clinically relevant steatosis, overall adiposity measures accounted for most of the variance and EAT did not retain independent significance. Unsupervised clustering identified four phenotypes characterized by different combinations of epicardial fat burden, insulin resistance, sex distribution and hepatic risk, largely independent of BMI.

Conclusions: Epicardial adipose tissue is selectively associated with non-invasive indices reflecting hepatic fibrosis and metabolically driven steatosis, rather than with liver fat accumulation alone. These findings highlight clinically relevant heterogeneity in hepatic risk among individuals with obesity and support the use of epicardial adiposity as a complementary marker in risk stratification.

Abstract citation ID: lvag096.993

EP502 - ECE_3251 - Deficient glucagon like peptide-1 (GLP-1) secretion following oral glucose stimulation as a metabolic trait in insulin resistant polycystic ovarian syndrome (PCOS) patients: A case control study

Ayan Roy[1,2], Shinjan Patra[1], Somdatta Giri[1], Kalyan Goswami[1], Sayanti Paul[1], Sampriti Gayen[3] and Pratisruti Hui[1,3]
[1]*All India Institute of Medical Sciences, Kalyani, India;* [2]*Endocrinology and Metabolism, All India Institute of Medical Sciences, Kalyani, India;* [3]*Radiodiagnosis, All India institute of Medical Sciences, Kalyani, India*

Background: Polycystic ovarian disease (PCOS) is one of the most common Endocrinologcal diseases carrying significant risk of metabolic diseases and cardiovascular risk. Though insulin resistance and beta cell functions have been investigated extensively, data related to glucagon or GLP-1 is limited. Insulin resistance is the hallmark of PCOS but its relationship with glucagon or GLP-1 is limited can be an interesting crosstalk. Though earlier studies have shown obesity can impair GLP-1 secretion, this is not studied in this high risk group. Interestingly, medicines acting on either increasing GLP-1 levels or augmenting its effects (GLP-1 analogues) have been trialled in PCOS.

Aims/Objective: The aim of the study was to explore the metabolic relationship of insulin resistance, beta cell functional with glucagon and incretins in PCOS patients. The main objective was to see the difference between various insulin indices, beta cell function measurements, glucagon and GLP-1 responses between PCOS and healthy controls.

Participants and Methodology: A total of 100 participants were screened as per Rotterdam criteria and were recruited for the project. Age matched healthy controls were also recruited. Patients and controls underwent 4 point oral glucose tolerance test (OGTT). Glucose, insulin, glucagon and GLP-1 was measured at each time point. Various beta cell functional and insulin resistance indices were calculated. GLP-1 and glucagon were compare using area under curve methods.

Results: Total 41 participants were recruited including 24 PCOS and 17 age matched controls. PCOS patients had higher BMI and waist circumference compared to controls. PCOS patients had significantly higher insulin resistance indices (HOMA IR and Matsuda index). There was no difference in various beta cell functional indices including oral disposition index or ISSI-2. There was slightly elevated fasting glucagon levels in PCOS compared to controls. All PCOS patients adequately suppressed glucagon following glucose load in the face of very high insulin secretion. Fating GLP-1 was not different between the groups but GLP-1 secretion at each time point (30, 60, 120 minutes) after glucose load were significantly lower in PCOS compared to controls. The AUC GLP-$1_{0\text{-}120}$ were lower in PCOS group (1311 ± 705 pM.min vs 2009 ± 640 pM.min). In multiple linear regression analysis, obesity, age, free androgen index or Matsuda index were not related to lower AUC GLP-$1_{0\text{-}120}$.

Conclusions: Insulin resistance is intrinsic to PCOS phenotype and lower GLP-1 secretion following oral glucose is a distinct metabolic feature in PCOS. Glucagon is adequately suppressed following glucose load in PCOS.

Abstract citation ID: lvag096.994

EP503 - ECE_1588 - Peripartum insulin delivery for type 1 diabetes pregnancies, keeping autonomy while optimizing care

Anna Emanuel[1], Misja Sprengers[1], Richard Ijzerman[1], Rebecca Painter[2] and Sarah Siegelaar[1]
[1]*Amsterdam, The Netherlands;* [2]*Erasmus MC, Rotterdam, The Netherlands*

Background: In pregnant women with type 1 diabetes, optimal glucose management during the intrapartum period is essential to reduce neonatal hypoglycaemia. Historically, many hospitals switched women to an intravenous insulin–glucose infusion during labour and delivery. However, current evidence indicates that continuation of subcutaneous insulin delivery is at least as safe. With the increasing use of hybrid closed-loop (HCL) therapy during pregnancy, continuation of automated insulin delivery during childbirth has emerged as a relevant and promising option.

Aim: To review current evidence and guideline recommendations on peripartum diabetes management in women with type 1 diabetes, with a specific focus on the feasibility, safety and effectiveness of continuing hybrid closed-loop insulin delivery during labour, delivery and the immediate postpartum period.

Methods: A structured literature search was performed in PubMed (September 2025) using the terms “peripartum OR intrapartum OR postpartum”, “type 1 diabetes”, and “hybrid

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

closed-loop OR automated insulin delivery". Randomised controlled trials, relevant observational studies and international guidelines were included. In addition, outcomes from women with type 1 diabetes who delivered in our tertiary care centre between January 2021 and June 2025 were analysed.

Results: Evidence from recent trials, including CRISTAL trial and preliminary data from the AiDAPT study, demonstrates that continuation of HCL therapy during labour and delivery is associated with a higher pregnancy-specific time in range, without an increased risk of hypoglycaemia, diabetic ketoacidosis or adverse neonatal outcomes compared with standard insulin therapy. Patient-reported satisfaction and perceived autonomy were consistently higher among women who continued their own insulin delivery system. In our centre, 23 of 26 women continued HCL therapy during the intrapartum period. No episodes of severe maternal hypoglycaemia or hyperglycaemia occurred, and no neonates experienced severe hypoglycaemia requiring prolonged intensive care admission. The rate of neonatal hypoglycaemia was 12 out of 23 (52%), consistent with previously published data.

Conclusions: Continuation of hybrid closed-loop insulin delivery in women with type 1 diabetes during the peripartum period appears to be safe and effective, provided that predefined safety conditions are met, including adequate patient education, proper device functioning and familiarity of healthcare professionals with HCL systems. Maintaining automated insulin delivery supports glycemic stability, reduces the need for intravenous insulin infusion, and preserves patient autonomy during childbirth. Transition to intravenous insulin should be reserved for situations in which patient safety cannot be guaranteed, such as technical failure or inability to self-manage.

Abstract citation ID: lvag096.995

EP507 - ECE_2514 - From bioimpedance to compliance: body composition changes during nutritional interventions

Roxana Pui[1], Stefania-Alexandra Bunceanu[2] and Stoian Dana[3]
[1]*Department of Doctoral Studies, Victor Babes University of Medicine and Pharmacy, Timişoara, Romania;* [2]*Department of Doctoral Studies, Victor Babes University of Medicine and Pharmacy, Timisoara, Discipline of Endocrinology, Second Department of Internal Medicine, University of Medicine and Pharmacy "Victor Babes", Timişoara, Romania;* [3]*Timişoara, Romania*

Introduction: Long-term adherence is one of the main challenges in obesity management. In routine care, engagement with monthly nutritional follow-up often declines rapidly after the initial consultation. Identifying early attendance trajectories may enable timely supportive strategies. This study aimed to describe follow-up attendance patterns and dropout during a 6-month nutritional intervention in adults with overweight or obesity, managed without anti-obesity pharmacotherapy.

Methods: This retrospective observational study included 2195 adults (1631 women; 564 men) with BMI ≥25 kg/m^2 evaluated between 2010 and 2020 at a specialized endocrinology and nutrition center in Timişoara, Romania. Patients received an individualized, hypocaloric, high-protein nutrition plan with scheduled monthly follow-up visits over 6 months and serial bioimpedance monitoring (Tanita BC-418). Patients treated with anti-obesity pharmacotherapy or with prior bariatric surgery were excluded. Attendance was summarized across visits from baseline (P0) to month 6 (P6).

Results: Follow-up attendance declined over the 6-month program, with most dropouts occurring within the first month after the baseline evaluation. Of the 2195 patients assessed at baseline (P0), 1747 returned for P1, 1116 attended P2, and 395 completed the final scheduled visit (P6). Overall, 68.75% attended only the baseline visit, whereas 31.25% returned for at least one follow-up. Attendance remained consistently higher in women than in men across all visits. According to the program's end-of-intervention classification, 159/2195 patients (7.2%) met the completion target, with lower proportions observed in older age groups. Among participants with paired baseline and final bioimpedance assessments, body fat percentage decreased significantly in both sexes across all age decades ($P < .001$). To illustrate the magnitude of change, in participants aged 18-30 years, median body fat declined in women (39.9% to 38.5%) and in men (30.15% to 28.6%) ($P < .001$).

Conclusions: In this substantial cohort managed exclusively through nutritional intervention, dropout after the initial visit was substantial and completion of the planned 6-month follow-up schedule was low, indicating that sustained follow-up is a major limiting factor of lifestyle-based interventions. Importantly, participants who remained engaged and attended monthly visits achieved consistent, statistically significant reductions in body fat percentage. Early, structured engagement strategies focused on the first follow-up period may reduce dropout and improve outcomes in non-pharmacological obesity care.

Abstract citation ID: lvag096.996

EP509 - ECE_3401 - Effect of semaglutide injection in physical function: a post-hoc analysis of a phase III study of in weight management

Unnikrishnan Gopalkrishnan[1], Ameya Joshi[2], Harish Kumar[3], Richa Giri[4], Sanjiv Maheshswari[5], Valluri Prasad[6], Jitendra Shukla[7], M.C. Rekha[8], Nutankumar Agrawal[9], Yogesh Rasal[10], Banshidhar Sahoo[11], Shweta Bhandari[12], Ambana Gowda[13], Phadke Keshav[14], Pravin Supe[15], Niranjan Pathak[16], C. Ambrish[17], Ashutosh Sonawane[18], Yash Bahulikar[19], Amit Bhaskar[20], R. Arunkumar[21], Priyanka Yadav[22], Supriya Sonowal[22], Dipak Patil[22], Sucheta Pandit[22], Pravin Ghadge[22] and Suyog Mehta[22]
[1]*Chellaram Diabetes Institute, Pune, India;* [2]*Bhaktivedanta Hospital and Research Institute, Thane, India;* [3]*Amrita institute of Medical Sciences and Research Centre, Kochi, India;* [4]*G.S.V.M medical College, Kanpur, India;* [5]*Jawahar Lal Nehru Medical College, Ajmer, India;* [6]*King George Hospital, Visakhapatnam, India;* [7]*Moti Lal Nehru Medical College, Prayagraj, India;* [8]*Mandya Institute of Medical Science, Mandya, India;* [9]*M.L.B Medical College, Jhansi, India;* [10]*Pulse Multispecialty Hospital, Pune, India;* [11]*KIDS Hospital, Bhubaneswar, India;* [12]*Vincare Hospital, Bathinda, India;* [13]*Citizen Hospital, Bangalore, India;* [14]*Sahyadri Super Speciality Hospital, Pune, India;* [15]*Supe Heart and Diabetes Hospital and Research Centre, Nashik, India;* [16]*OJAS Multispeciality Hospital, Pune, India;* [17]*Medstar Speciality Hospital, Bangalore, India;* [18]*Panacea Hospital, Nashik, India;* [19]*MMFHA Joshi Hospital, Pune, India;* [20]*Janta Hospital and*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Maternity Center, Varanasi, India; [21]Chettinad Hospital & Research Institute, Chengalpattu, India; [22]Mumbai, India

Objectives: To evaluate the effect of synthetic semaglutide injection (Test drug) in comparison with Wegovy® (Reference drug) 2.4 mg in in physical function when used in weight management

Materials and Methods: This phase III, multicentre, randomized, open-label, active-controlled clinical study (CTRI/2025/04/085487) was conducted across 22 study sites in India after receiving regulatory and ethics committee approvals. Total 267 adult patients with BMI ≥ 30 kg/m^2 or ≥27 kg/m^2 with the presence of at least one co-morbidity of hypertension, dyslipidaemia and/or type 2 diabetes mellitus were included. Patient were randomized to receive either test drug or reference drug every week subcutaneous for 24 weeks. The primary endpoint was body-weight change at Week 24. Change in Quality of life was evaluated by total SF-36 (36-Item Short Form Health Survey) questionnaire score which was one of the secondary endpoints. This post-hoc analysis was conducted to evaluate the effect of semaglutide on physical function component of SF-36 questionnaire.

Results: At baseline, the mean (±SD) SF-36 Physical Functioning scores were similar between the two treatment groups [Test: 53.21 (±23.90); Reference: 54.81 (±23.44), $P = .6214$]. The SF-36 physical function score and change from baseline in SF-36 physical function score to week 12, and 24 are presented in below table (Table 1)

Table 1 Change in SF-36 Physical function Score.

		Semaglutide injection (test) ($N = 165$)		Wegovy (semaglutide) solution for injection (comparator) ($N = 80$)		Test Vs comparator
Visits	**Statistics summary**	**Actual**	**Change from baseline**	**Actual**	**Change from baseline**	***P*-value**
Baseline	n	165		80		.6214
	Mean ± SD	53.21 ± 23.90		54.81 ± 23.44		
Week 12	Mean ± SD	64.39 ± 20.80	11.18 ± 23.90	64.31 ± 21.16	9.50 ± 21.50	
	P-value		<.0001		.0003	.6862
Week 24	Mean ± SD	81.58 ± 17.65	28.36 ± 24.90	80.69 ± 18.82	25.88 ± 27.13	
	P-value		<.0001		<.0001	.4993

There was gradual improvement in SF-36 physical function score from baseline to week 24. The improvement in in SF-36 physical function score was comparable between test and the reference drug at each week ($P > .05$).

Conclusions: Semaglutide injection used in weight management also leads to improvement in SF-36 Physical Functioning scores in obese or overweight patients.

Abstract citation ID: lvag096.997

EP511 - ECE_3932 - Diabetic ketoacidosis associated with SGLT2 inhibitor therapy for alpelisib-induced hyperglycaemia: reconsidering second-line management

Lora Kirigin Biloš[1], Marina Andrešić[1], Lea Ledinsky[2], Ana Uroš[1], Jelena Marinkovic Radosevic[1] and Gorana Mirosevic[1]

[1]Klinički bolnički centar Sestre Milosrdnice, Endocrinology, diabetes i metabolic diseases, Zagreb, Croatia; [2]Department of Medical Oncology, University Hospital Centre Sestre Milosrdnice, Clinic for Tumors, Zagreb, Croatia

Background: Alpelisib is the first approved phosphatidylinositol-3-kinase alpha (PI3Kα) inhibitor for hormone receptor (HR)–positive, human epidermal growth factor receptor 2 (HER2)–negative, *PIK3CA*-mutated advanced breast cancer. Although it improves progression-free survival, hyperglycaemia is a common adverse effect, with diabetic ketoacidosis (DKA) being a rare but serious complication. PI3Kα inhibition increases hepatic gluconeogenesis, reduces peripheral glucose uptake, and induces compensatory hyperinsulinaemia, resulting in acute iatrogenic insulin resistance and hyperglycaemia. Current guidelines recommend metformin as first-line therapy, followed by sodium-glucose cotransporter-2 inhibitors (SGLT2 inhibitors) or pioglitazone as second-line agents.

Case presentation: A 64-year-old woman with metastatic HR-positive, HER2-negative, *PIK3CA*-mutated breast cancer developed DKA two months after commencing alpelisib. Baseline investigations demonstrated previously undiagnosed diabetes (HbA1c 5.8%, fasting plasma glucose 8.1 mmol/L, 2-hour OGTT 11.4 mmol/L), normal renal function, and a BMI of 22 kg/m^2. She had a family history of type 2 diabetes. Metformin and sitagliptin were initiated pre-emptively. Following alpelisib commencement, she developed grade 2 hyperglycaemia, requiring the addition of dapagliflozin. Two months later, she presented to the emergency department with dyspnoea, nausea, and altered mental status. Imaging revealed left-sided lobar pneumonia. Biochemical investigations demonstrated severe hyperglycaemia (19.6 mmol/L), metabolic acidosis (arterial pH 7.00, base excess −26.9), normal lactate, and ketonuria (+++), consistent with severe DKA. Alpelisib and dapagliflozin were discontinued. She was admitted to the intensive care unit and treated with intravenous fluids, insulin infusion, and electrolyte replacement, with rapid clinical and glycaemic improvement. Further testing showed low-normal C-peptide (0.78 nmol/L), negative diabetes autoantibodies, and an HbA1c of 9.0%. She was discharged 12 days later on basal insulin, sitagliptin, and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

pioglitazone. Given the severity of DKA, alpelisib and SGLT2 inhibitors were permanently discontinued. At one-month follow-up, HbA1c had improved to 7.0%; however, due to disease progression with leptomeningeal spread, alpelisib was not reinitiated. Unfortunately, she died two months later.

Conclusions: This case demonstrates the rare but serious risk of DKA associated with alpelisib therapy. Despite guideline recommendations supporting SGLT2 inhibitors for glycaemic management, their use may potentiate ketoacidosis, particularly during acute illness. Enhanced surveillance, proactive patient education, close glucose and ketone monitoring, and individualized risk assessment are essential to optimize patient safety.

Abstract citation ID: lvag096.998

EP512 - ECE_3467 - Glucometabolic impact of Freestyle Libre 1 and 2 use in a large Type 1 Diabetes cohort, a retrospective study

Enrico Saudelli[1,2], Anna Malaguti[1,2], Simona Moscatiello[2], Sara Flamigni[2], Sabrina Berti[1,2], Michele Baldari[1,2], Laura Tribotti[1,2], Sara Capra[1,2], Ilenia Schillaci[1,2], Laura Agostini[1,2], Uberto Pagotto[1,2] and Guido Di Dalmazi[1,2]
[1]Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna, Italy; [2]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

Background and Aims: The introduction of continuous glucose monitoring represents a major advancement in managing Type 1 Diabetes (T1D). In this study we aimed to assess: 1) longitudinal trends of glycated hemoglobin (HbA1c) and predictors of improved glycemic control in adults with T1D transitioning from self-monitoring of blood glucose (SMBG) to FreeStyle Libre 1 (FS1) and, subsequently, to FS2; 2) the impact of alarm use on HbA1c and ambulatory glucose profile (AGP) data.

Methods: We conducted a retrospective longitudinal analysis on adults with T1D followed at the Endocrinology Unit of IRCCS Sant'Orsola (Bologna, Italy). Exclusion criteria were: patients lacking complete HbA1c data covering the transition from SMBG to FS2, patients who hadn't used both FS1 and FS2 for at least 12 months, pump users, subjects with HbA1c >86 mmol/mol at any time. Our final cohort was composed of 355 individuals. Clinical data, AGP, and alarm use were evaluated before each upgrade, after 6 and 12-months, and at the last available follow-up.

Results: Transition from SMBG to FS1 was associated with a significant reduction in HbA1c of approximately 3 mmol/mol within the first 6 months, with sustained improvement over a mean follow-up of 45 ± 15 months. Mean HbA1c decreased from 59.8 ± 10.5 mmol/mol to 56.2 ± 10.1 at 6 months, 57.8 ± 9.7 at 12 months, and 57.2 ± 10.1 at the final follow-up ($P < .001$ for all timepoints vs baseline). In contrast, switching from FS1 to FS2 resulted in stable glycemic control over a mean follow-up of 19 ± 3 months, without significant change in HbA1c (baseline 56.6 ± 10.2 mmol/mol vs final 56.6 ± 10.1; $P = .486$). No differences were observed in mean HbA1c ($P = .821$) among alarm users ($n = 199$; HbA1c 56.4 ± 8.7 mmol/mol) vs non-alarm users ($n = 93$; HbA1c 57 ± 8.6) vs those with alarms for either hypo- or hyperglycemia ($n = 63$; HbA1c 57.4 ± 8.8). However, alarm users had significantly lower Time Below Range evaluated at each patient's last available visit (3.5 vs 5.2%, $P = .027$). Higher baseline HbA1c predicted greater HbA1c reduction for both transitions (FS1: β .455 per 1 mmol/mol increase, 95%CI 0.344-0.545, $P < .001$; FS2: β .290, 95%CI 0.196-0.384, $P < .001$). Age <65 years was associated with greater HbA1c improvement after FS1 initiation ($P = .012$).

Conclusions: Initiation of glucose monitoring with FS1 leads to significant and durable improvements in glycemic control. Upgrading to FS2 does not provide additional HbA1c benefits, regardless of alarm use, although active alarms could help reduce the time spent in hypoglycemia. Patients with higher baseline HbA1c derive the greatest glycemic improvement from sensor placement.

Abstract citation ID: lvag096.999

EP517 - ECE_1793 - Trend in the prevalence of diabetes among Korean adults with normal body mass index, 2011-2021

You-Cheol Hwang, Hyun Jin Ryu, Ji Eun Jun, In-Kyung Jeong, Kyu Jeung Ahn and Ho Yeon Chung
Seoul, South Korea

Aims: With the global increase in the prevalence of obesity, the prevalence of diabetes has increased worldwide. However, little is known about the trend in the prevalence of diabetes in people without obesity. Therefore, we aimed to investigate the trend in the prevalence of diabetes among Korean adults with normal body weight.

Methods: This study used data from the Korea National Health and Nutrition Examination Survey V-VIII from 2011 to 2021. Approximately, 38-42 million participants (weighted) per year aged ≥20 years were included in this analysis.

Results: The prevalence of diabetes has increased among adults with normal body mass index (BMI) of 18.5 to 22.9 kg/m^2 from 7.13% in 5th survey to 8.46% in 8th survey, representing a 18.7% increase (odds ratio 1.064; $P = .025$) during 10 years of follow-up periods. The increasing trend was significant in women (odds ratio 1.095; $P = .013$); however, showed only a tendency in men. According to age groups, the prevalence showed an increasing tendency in adults aged ≥40 years but, the prevalence has decreased in adults aged 20 to 39 years (odds ratio 0.560; $P = .002$).

Conclusions: The prevalence of diabetes has increased among adults with normal BMI during 10 years of follow-up and the trend was more evident in women than in men. However, the trend was different depending on age groups and rather, it showed a decreasing trend in younger adults.

Abstract citation ID: lvag096.1000

EP518 - ECE_2949 - Metabolic risk patterns across CGM-based glycaemic phenotypes in Type 1 diabetes: insights from the T1Diabetes Granada database

Svjatoslavs Kistkins[1,2,3], Anastasija Luganceva[1,2], Sergejs Lobanovs[1,2,3], Timurs Mihailovs[3], Daniil Hrynyshyn[2], Valdis Pirags[1,2], Jelizaveta Sokolovska[1], Othmar Moser[4,5], Harald Sourij[5] and Dmitrijs Bliznuks[2,3]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Faculty of Medicine and Life Sciences, University of Latvia, Riga, Latvia; [2]Research Institute of Pauls Stradins Clinical University Hospital, Riga, Latvia; [3]Institute of Applied Computer Systems, Riga Technical University, Riga, Latvia; [4]Institute of Human Movement Science, Sport & Health, Exercise Physiology, Training & Training Therapy Research Group, University of Graz, Graz, Austria; [5]Interdisciplinary Metabolic Medicine Trials Unit, Division of Endocrinology and Diabetology, Medical University of Graz, Graz, Austria

Background and Aims: Type 1 diabetes mellitus (T1DM) is a heterogeneous condition in which distinct glycaemic patterns may coexist with the development of metabolic abnormalities in a subset of individuals. These abnormalities may include alterations in lipid profiles, electrolyte balance, and liver-related biomarkers, contributing to increased cardiometabolic risk. In this study, we investigated the distribution of metabolic parameters across continuous glucose monitoring (CGM)-derived phenotypes.

Methods: CGM data from individuals with and without T1DM included in the longitudinal LatDiane project ($n = 95$) were used to derive CGM-based phenotypes. A data-driven unsupervised clustering approach was applied, using UMAP for dimensionality reduction followed by K-means clustering. Seven glycaemic phenotypes (P0-P6) were identified, reflecting distinct combinations of time spent in normoglycaemia, hypoglycaemia, and hyperglycaemia: normo-hypoglycaemic (P0), normoglycaemic with predominant time in normoglycaemia (P1), normoglycaemic (P2), hyper-normolycaemic (P3), normo-hyperglycaemic (P4), hyperglycaemic (P5), and hyper-hypoglycaemic (P6).

The derived phenotypes were subsequently applied to an independent cohort of individuals with T1DM from the T1Diabetes Granada database[1] ($N = 731$), with each participant assigned to a dominant phenotype based on weekly CGM profiles. Biochemical parameters, including triglycerides (TG), HDL cholesterol, alanine aminotransferase (ALT), and gamma-glutamyl transferase (GGT), were measured using standard laboratory methods. Differences across glycaemic phenotypes were assessed using the Kruskal–Wallis test with Dunn–Holm post-hoc correction.

Results: T1Diabetes Granada database participants were included and distributed across phenotypes as follows: P0, $n = 19$; P1, $n = 5$; P2, $n = 165$; P3, $n = 287$; P4, $n = 159$; P5, $n = 41$; and P6, $n = 55$. Due to the small sample size, P1 was excluded from biomarker analyses. Significant differences across phenotypes were observed for sodium ($P = 3.03 \times 10^{-6}$) chloride ($P = .00427$), TG ($P = 5.99 \times 10^{-5}$), HDL cholesterol ($P = .03133$), ALT ($P = .00449$), and GGT ($P = .0052$). Post-hoc analysis confirmed that P5 differed significantly from most other phenotypes in TG, HDL cholesterol and sodium. TG levels in P5 were significantly ($P < .05$) higher than in all other phenotypes and HDL cholesterol levels in P5 were significantly lower ($P < .05$) than in all other phenotypes except P6 ($P = .50$). Sodium levels in P5 were significantly lower than in all other phenotypes, while chloride levels were significantly lower ($P < .05$) in P5 compared with P2 ($P = .011$). P0 exhibited a more favorable hepatic profile, with significantly lower ($P < .05$) ALT and GGT levels compared with all other phenotypes.

Conclusions: CGM-based phenotypes in T1DM are associated with distinct lipid, electrolyte and metabolic profiles.

Reference

1. Rodriguez-Leon C, Aviles-Perez MD, Banos O, et al. T1DiabetesGranada: a longitudinal multi-modal dataset of type 1 diabetes mellitus. *Sci Data*. 2023;10(1):916. https://doi.org/10.1038/s41597-023-02737-4

Abstract citation ID: lvag096.1001

EP519 - ECE_2959 - IGF-2–mediated hypoglycemia in a patient with skull base chondrosarcoma: a case report

Kalliopi Pantelia[1], Vasiliki Antonopoulou[1], Angeliki Angelidou[1], Aggeliki Kyriakou[1], Panagiotis Mouchtouris[1], Georgios Kyriakopoulos[2], Marinella Tzanela[1] and Georgia Ntali[1]

[1]Department of Endocrinology "D. Ikkos"- Diabetes Center-EndoERN-Evangelismos General Hospital, Athens, Greece; [2]Department of Pathology, Evangelismos General Hospital, Athens, Greece

Introduction: Non–islet cell tumour hypoglycemia (NICTH) is a rare paraneoplastic syndrome, most commonly caused by tumour overproduction of insulin-like growth factor 2 (IGF-2) or its precursor forms (pro-IGF-2), which bind to IGF receptors and insulin receptors. Patients with IGF-2-mediated hypoglycemia present fasting hypoglycemia characterized by suppressed endogenous insulin, ketones, growth hormone, and IGF-1.

Case presentation: A 49-year-old woman developed diplopia and headache during the third month of pregnancy, followed by progressive left-sided ptosis, ophthalmoplegia, and tongue deviation. Brain MRI revealed a large, well-demarcated lobulated mass (maximum diameter 6.8 cm) located at the left skull base, in the area of petrous apex and trigeminal ganglion, in contact with the optic chiasm, causing stalk deviation. The patient underwent an uneventful caesarean section but five days postpartum, was admitted in the emergency ward in hypoglycemic coma. Her medical history included Roux-en-Y gastric bypass surgery, epileptic seizures 20 years earlier and primary hypothyroidism. She had a brother with glycogen storage disease type 1a but the rest of her family history was not notable. Laboratory evaluation during spontaneous hypoglycaemia demonstrated low plasma glucose with suppressed insulin and C-peptide levels, adequate cortisol response and low IGF-1 concentrations. Her lipid profile was normal. Hypoglycemia occurred predominantly in the fasting state. The patient underwent subtotal surgical resection of the lesion. Histopathology revealed chondrosarcoma, grade 1 (Ki-67 $\leq$2%). One month postoperatively, biochemical evaluation showed an elevated IGF-2/IGF-1 ratio (>10), supporting the diagnosis of IGF-2–mediated hypoglycemia. Immunohistochemical staining for IGF-2 was negative. A brain MRI 3 months after surgery demonstrated a residual tumor of 4.5 cm. Due to persistent hypoglycemic episodes, glucocorticoid therapy was initiated, resulting in clinical improvement. The patient subsequently was scheduled for adjuvant radiotherapy.

Conclusions: IGF-2–mediated hypoglycemia is a rare but important cause of fasting hypoglycemia in patients with large mesenchymal tumours. A high IGF-2/IGF-1 ratio is a key diagnostic marker. Definitive treatment relies on management of the underlying malignancy, while glucocorticoids represent an effective therapeutic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

option when complete tumour resection is not feasible. To our knowledge, this is the first reported case of IGF-2–mediated hypoglycemia associated with skull base chondrosarcoma.

Table 1 Laboratory workup of hypoglycemia.

Glucose (mg/dL)	52
Insulin (μU/mL)	<2
C- peptide (ng/mL)	0.17
Insulin Auto-Abs (U/mL)	0.04
IGF-1 (ng/mL)	40
IGF-2 (ng/mL)	452
IGF-2/IGF-1 ratio	11.3
Cortisol (μg/dL)	14

Abstract citation ID: lvag096.1002

EP521 - ECE_3243 - β-Arrestin 2 deficiency attenuates hyperglycemia but exacerbates systemic and neuroinflammation in streptozotocin-induced diabetes

Anna Volkova[1,2,3], Anastasiia Gladkova[3] and Kseniya Vysotskaya[1]
[1]*Endocrinology Research Centre, Moscow, Russia;* [2]*Pirogov Russian National Research Medical University, Moscow, Russia;* [3]*Lomonosov Moscow State University, Moscow, Russia*

Diabetes mellitus (DM) is a major global health challenge of the 21st century, characterized by a steadily increasing prevalence and a high burden of complications. Elucidating the molecular mechanisms underlying DM pathogenesis is essential for the development of novel therapeutic strategies. Among emerging regulatory proteins, β-arrestin 2 has attracted considerable interest as a multifunctional modulator of GPCR signaling. β-Arrestin 2 enhances insulin secretion, regulates p38 MAPK–dependent glucose metabolism, and exerts anti-inflammatory effects by inhibiting NLRP3 inflammasome assembly and suppressing pro-inflammatory cytokine production.

This study investigated the impact of β-arrestin 2 deficiency on metabolic parameters and inflammatory responses in a murine model of type 1 diabetes.

Experiments were performed on male C57BL/6J mice and a genetically related β-arrestin 2 knockout strain (Arrb2$^{-/-}$). Animals were randomly assigned to four groups: wild-type control (WT), knockout control (KO), and diabetic groups of both genotypes (WTd and KOd). Diabetes was induced by intraperitoneal administration of streptozotocin (55 mg/kg) for five consecutive days. Blood glucose levels, body weight, and circulating neutrophil proportions were monitored longitudinally. Systemic inflammation was additionally assessed by measuring plasma nitric oxide metabolites. Neuroinflammation was evaluated by real-time PCR analysis of mRNA expression of IL-6, IL-1β, TNF-α, and protease-activated receptors PAR1 and PAR4 in the cerebral cortex and hippocampus.

Streptozotocin administration induced persistent hyperglycemia in both genotypes; however, the onset and severity of hyperglycemia were significantly attenuated in KOd mice compared with WTd controls. Despite this milder metabolic phenotype, Arrb2$^{-/-}$ mice exhibited a pronounced pro-inflammatory profile. Systemically, KOd mice displayed a significantly increased proportion of circulating neutrophils. Plasma nitric oxide levels were elevated in both KO and KOd mice relative to wild-type animals. In the central nervous system, Arrb2$^{-/-}$ mice demonstrated increased expression of IL-6, IL-1β, TNF-α, PAR1, and PAR4 mRNA in the cortex and hippocampus under basal conditions, with further amplification of this inflammatory signature in diabetic knockout mice.

These findings demonstrate a dual role of β-arrestin 2 in diabetes, combining modulation of glucose dysregulation with a critical anti-inflammatory function, particularly within neuroimmune pathways. β-Arrestin 2 may represent a promising therapeutic target for reducing inflammation-associated endocrine and neurological complications of diabetes.

Funding: This study was supported by the Russian Science Foundation (RSF), grant No. 24-75-00164.

Abstract citation ID: lvag096.1003

EP523 - ECE_3833 - A case of diabetes mellitus secondary to dorsal pancreatic agenesis

Gayathri Bhaskaran[1], Rishi Iyer[1], Eleni Armeni[1], Sarah Ali[1] and Martin Dumskyj[1]
[1]*Diabetes and Endocrinology, Royal Free Hospital, London, United Kingdom*

Introduction: Dorsal pancreatic agenesis is a rare congenital anomaly characterized by the absence of the pancreatic body and tail, potentially leading to diabetes mellitus due to reduced beta-cell mass. This case report discusses diabetes mellitus secondary to dorsal pancreatic agenesis, highlighting diagnostic considerations.

Case Presentation: A 39-year-old male was referred to the diabetes clinic with HbA1c 81 mmol/mol. He was diagnosed with type 1 diabetes mellitus four years previously after presenting with a viral illness and hyperglycaemic ketosis, and was being managed on a basal bolus regime. An incidental CT scan for abdominal pain and haematuria revealed absence of the pancreatic body and tail, consistent with dorsal pancreatic agenesis. Diabetes autoantibodies were negative. The C-peptide was 263 pmol/L when blood glucose was 10.9 mmol/L, indicating limited residual insulin production. Other tests showed raised cholesterol, total 8.2 mmol/L, LDL 6.5 mmol/L (normal triglycerides) and transient polycythaemia (haemoglobin 192 g/L, haematocrit 0.5447 L/L), with negative genetic testing for haematological mutations, suggesting polycythaemia was probably due to chronic hyperglycaemia. Thyroid function, testosterone and renal function were normal. There was no history of alcohol use or other history to suggest pancreatitis. Imaging identified renal cysts. The patient's father had type 2 diabetes diagnosed in his 50s/60s, and nil else significant family history. MODY4 was also considered as a differential.

Management: The patient was counselled on consistent insulin administration and referred to a diabetes specialist dietitian for carbohydrate counting and insulin dose adjustment. An MRCP and faecal elastase test were arranged to evaluate the pancreas further, with plans for genetic testing for dorsal pancreatic agenesis.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Discussion: Dorsal pancreatic agenesis, with fewer than 100 reported cases, is linked to diabetes due to reduced beta-cell mass and may be associated with pancreatitis, renal, and cardiac anomalies. Negative diabetes autoantibodies in this patient support dorsal pancreatic agenesis as the cause of his diabetes. This case highlights the importance of considering unusual aetiologies of diabetes even in typical presentations.

References

1. Weerakkody Y, et al. Dorsal pancreatic agenesis. Radiopaedia.org. https://doi.org/10.53347/rID-16933
2. Robert AP, Iqbal S, John M. Complete agenesis of the dorsal pancreas: A rare clinical entity. *Int J Appl Basic Med Res*. 2016;6(4):290-292. doi:10.4103/2229-516X.192599
3. Lalchandani A, Maurya A, Rizvi SFM, Yadav A. Agenesis of the Dorsal Pancreas: A Rare Cause of Diabetes and Recurrent Upper Abdominal Pain. *Cureus*. 2023;15(2):e34689. https://doi.org/10.7759/cureus.34689

Abstract citation ID: lvag096.1004

EP525 - ECE_2601 - Real-world glycemic outcomes in pediatric type 1 diabetes after automated insulin delivery initiation

Beatriz Tavares Da Silva, Joana Queirós, João Oliveira, Catarina Figueiredo, Catarina Mendes, Joana Freitas, Maria João Oliveira, Carla Rocha, Maria José Ramos and Teresa Borges

Unidade Local de Saúde de Santo António, Porto, Portugal

Background: Automated insulin delivery (AID) systems are increasingly used in the management of type 1 diabetes mellitus (T1DM) and are fully funded for eligible patients in Portugal. We aimed to assess longitudinal changes in glycemic control following AID initiation in a pediatric T1DM cohort.

Methods: Retrospective longitudinal study of children and adolescents with T1DM using AID for at least 3 months. Data were collected at baseline and during follow-up (median follow-up: 11.8 months; range 3.0-52.4). International consensus targets were evaluated: HbA1c <6.5% for advanced technology users (ISPAD 2024), Time In Range (TIR 70-180 mg/dL) ≥70% and Time Below Range (TBR <70 mg/dL <4%) when available.

Results: Of 200 patients assessed, 157 were included (51.6% female; median age at diagnosis: 5.78 years). Median HbA1c decreased significantly from 7.5% at baseline to 6.8% at 3 months ($P < .001$) and remained stable at 12 months (median 6.7%; paired $n = 26$). Regarding the stringent ≤ 6.5% target, attainment increased nearly fourfold, from 12.1% (19/157) at baseline to 42.3% (11/26) at 12 months. The proportion of patients achieving the standard HbA1c < 7.0% goal rose from 27.4% to 84.6% at one year. Regarding CGM metrics, median TIR increased from 60% to 70% at 12 months ($P < .001$), with 51.7% of participants achieving the ≥ 70% target. Low exposure to hypoglycemia was maintained, with Time Below Range remaining <4% throughout follow-up. Safety was further demonstrated by the low incidence of acute complications: 3 episodes of moderate diabetic ketoacidosis and one episode of severe hypoglycemia (with loss of consciousness) were recorded during the observation period.

Conclusions: In this real-world pediatric T1DM cohort, AID initiation was associated with rapid and sustained improvements in glycemic control. Notably, the use of these systems allowed a substantial proportion of patients to reach the optimized HbA1c ≤ 6.5% goal without increasing hypoglycemia, supporting the effectiveness of AID in achieving the most recent clinical targets in pediatric T1DM.

Abstract citation ID: lvag096.1005

EP526 - ECE_3731 - CAPTAIN-T2D: A Bayesian Response-Adaptive Randomization (RAR) Dose Range-Finding (DRF) Trial of Clofutriben (CLO) as add-on treatment in patients with Type 2 Diabetes (T2D) and Elevated Cortisol (EC)

Frank Czerwiec[1], Lindsay Berry[2], Nathan James[2], Jennifer Smith[3], Karisse Roman-Torres[4], Guohua An[5], Todd Berner[1], Sarah Hooper[1], Dora Ferrari[1], Vivian Fonseca[6], John Buse[7] and David A. Katz[1]

[1]Sparrow Pharmaceuticals, Portland, United States; [2]Berry Consultants, LLC., Austin, United States; [3]Smith Biostatistics, LLC., Menlo Park, United States; [4]CIAS Corp, Seattle, United States; [5]University of Iowa, Iowa City, United States; [6]Tulane University School of Medicine, New Orleans, United States; [7]University of North Carolina, Chapel Hill, United States

Introduction: Many patients with T2D who exhaust typical treatment options also have EC, which impedes achieving glycemic control. CLO, a selective 11β-hydroxysteroid dehydrogenase type 1 inhibitor that reduces intracellular cortisol, was associated with improved HbA_{1c} and fasting glucose in a prior diabetes clinical trial. This Phase 2 trial in patients with T2D and EC will evaluate the dose-response relationship of CLO and identify the dose(s) suitable for Phase 3 evaluation.

Methods: CAPTAIN-T2D is a double-blind, placebo-controlled, RAR DRF trial. Adults with T2D, HbA_{1c} ≥7.5%, treated with ≥2 antidiabetic medications (ADMs), and with ≥1 EC risk factor (eg, ≥3 ADMs, diabetic complication, hypertension requiring ≥2 antihypertensive medications) will undergo an overnight dexamethasone suppression test (DST). Those with post-DST cortisol >1.8 and ≤5.0 mcg/dL will be screened further for eligibility, including by pre-enrolment in-clinic and at-home monitoring for risk of hypoglycemia or hypotension. Neoplastic etiologies of EC will be screened for using medical history, exam, repeated DST cortisol >5.0 mcg/dL, and adrenal imaging to guide therapy decisions; participants with repeated DST cortisol >5.0 mcg/dL may be eligible with further evaluation. Up to 210 participants will receive oral CLO (no titration) or placebo QD for 24 weeks. The first 60 will be randomized equally to placebo and 4 CLO doses. Thereafter, a RAR algorithm will adjust dose allocations at pre-planned enrolment intervals based on the posterior probability that each dose has ≥90% maximum effect (ED_{90}) on HbA_{1c} at Week 24 or is the minimal effective dose. The algorithm will stop enrolment if a dose has >80% probability of being the ED_{90}. Safety will be reviewed regularly by an independent safety committee.

Outcomes: The prevalence of EC in the screened population and safety will be reported. The primary analysis will be a Bayesian hierarchical E_{max} model for dose-response relationship on change in HbA_{1c} at Weeks 4, 12, and 24. A supportive analysis will be a mixed model for repeated measures (MMRM) of HbA_{1c} change from baseline. Changes in other glycemic, lipid,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

anthropometric, and BP measures will be estimated using MMRM.

Conclusions: CAPTAIN-T2D aims to define the dose-response relationship and therapeutic potential of CLO in patients with T2D and EC. By reducing excess intracellular cortisol that exacerbates T2D without impairing the HPA axis, adrenal cortisol synthesis, or its interaction with the glucocorticoid receptor, CLO might provide a targeted therapeutic option for patients with difficult-to-control T2D and EC that avoids complex monitoring or dose modifications.

Abstract citation ID: lvag096.1006

EP527 - ECE_3785 - Associations between sleep quality, weight, and body composition among patients with type 2 diabetes

Solomiia Shykula and Alina Urbanovych
Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

As the prevalence of diabetes and obesity continues to rise, it is crucial to find new ways of preventing and treating metabolic diseases. Disturbances in sleep patterns may be a significant risk factor for both diabetes and obesity. The purpose of this study was to determine the relationships among sleep quality, weight, and body composition in patients with type 2 diabetes.**Methods:** The study sample of 77 participants, whose ages ranged from 32 to 69 years (M = 54.3, SD = 8.27). Among the participants, 41 (53%) identified as female. The average HbA1c level was 9.28 ± 2.14%. The duration of diabetes was 7[5; 10.25] years. All patients have confirmed diabetes mellitus type 2 and were screened for sleep disorders with the Pittsburgh Sleep Quality Index (PSQI) questionnaire. Body composition was evaluated through bioelectrical impedance analysis. Statistical analysis was conducted using Microsoft Office Excel.

Results: The study revealed a correlation between sleep quality and both weight (r = 0.15) and body mass index (r = 0.25). Additionally, a negative correlation was found between sleep quality and muscle mass (r = −0.24). Furthermore, a correlation was observed between sleep quality and bone mass (r = −0.23). No other significant correlations were identified.

Conclusions: Sleep quality influences diabetes and obesity; however, further research is needed to fully understand the direction of the relationship between these factors.

Abstract citation ID: lvag096.1007

EP529 - ECE_2402 - COVID-19 in pediatric patients and the risk of type 1 diabetes mellitus: a systematic review and meta-analysis

Lara Alves Tavares[1], Alexandre Rossini Murakami[2], Ana Paranzini Miguita[1], Bruno Hidalgo Molina[1], Melissa Pistori Floriano Gerardi[1] and Paulo Bignardi[1]
[1]*Pontifícia Universidade Católica do Paraná, Londrina, Brazil;* [2]*Universidade Estadual de Londrina, Londrina, Brazil*

Background: SARS-CoV-2 infects host cells via the angiotensin-converting enzyme 2 (ACE2) receptor, expressed in pancreatic endocrine tissue. Evidence suggests the virus may infect β-cells, inducing dysfunction, apoptosis, and inflammatory responses. In susceptible individuals, this may accelerate autoimmune β-cell destruction via $CD8^+$ T-cell–mediated mechanisms. While increased pediatric new-onset type 1 diabetes mellitus (T1DM) has been reported during the pandemic, findings remain conflicting.

Objective: To quantify the risk of new-onset T1DM following laboratory-confirmed SARS-CoV-2 infection in children and adolescents.

Methods: This systematic review and meta-analysis followed Cochrane and PRISMA 2020 guidelines. The protocol was registered on PROSPERO (CRD420261278565). Searches were conducted in MEDLINE/PubMed, Embase, Scopus, LILACS, and medRxiv for studies from 2020 onward. Eligible studies included patients aged 0-18 years with laboratory-confirmed SARS-CoV-2 infection (RT-PCR, antigen, or serology) compared with controls, reporting incident T1DM diagnosed by international criteria. Two reviewers performed study selection and data extraction independently. Pooled relative risks (RR) were calculated using a random-effects model (DerSimonian–Laird). Heterogeneity was assessed via I^2 statistic. Sensitivity and publication bias analyses were performed.

Results: A total of 10 studies were included, involving over 20 million pediatric patients. Prior SARS-CoV-2 infection was associated with a significantly increased risk of new-onset T1DM compared with unexposed controls (pooled RR = 1.61; 95% CI: 1.22-2.00). Substantial heterogeneity was observed (I^2 = 75%). Sensitivity analyses (leave-one-out) confirmed the robustness of the estimate. No evidence of small-study effects or publication bias was identified (Egger's test: z = 1.28; P = .20).

Conclusions: SARS-CoV-2 infection is associated with an increased risk of new-onset T1DM in children and adolescents. Despite substantial heterogeneity, the association remained consistent across sensitivity analyses. These findings support enhanced metabolic surveillance following pediatric COVID-19 and underscore the need for further high-quality studies to clarify underlying immunopathological mechanisms.

Abstract citation ID: lvag096.1008

EP530 - ECE_1725 - Predictors of sarcopenic obesity in patients with diabetes mellitus

Elena Makhlina[1], Yana Navmenova[2] and Tatiana Mokhort[3]
[1]*Educational Institution "Gomel State Medical University", Gomel, Belarus;* [2]*Research Center for Radiation Medicine and Human Ecology, Research Center For Radiation Medicine And Human Ecology, Endocrinology, Gomel, Belarus;* [3]*Endocrinology, Educational Institution "Belarusian State Medical University", Minsk, Belarus*

Objective: To evaluate predictors of sarcopenic obesity (SO) in patients with diabetes mellitus (DM).

Materials and Methods: The study included 92 patients (45 men and 47 women) with DM. The average age of the patients was 55.90 ± 14.18 years, and the duration of DM was 16.80 ± 9.34 years. Muscle strength (MS) was assessed using handgrip dynamometry, which measures arm strength. Muscle function (MF) was assessed using the 4-meter walking speed test. Muscle mass (MM) and fat mass (FM) were estimated using dual-energy X-ray absorptiometry (DXA) (lunAR prodigy) as the ratio of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

appendicular muscle mass (AMM) to weight (AMM/weight) and FM to height squared (FM/m2). Anthropometric parameters included body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WC/height) and calculated MS/weight, MS/BMI, MS/WC/height ratios. Statistical analysis was performed using Statistica 10.0.

Results: Correlation analysis revealed a significant relationship between MS/ BMI and FM/m^2 (rs = −0.70; $P < .05$), AMM/weight (rs = 0.70; $P < .05$) and MF (rs = 0.51; $P < .05$). A significant relationship between MS/weight and FM/m2 (rs = −0.71; $P < .05$), AMM/weight (rs = 0.70; $P < .05$), MF (rs = 0.51; $P < .05$). A significant relationship between MS/WC/height and FM/m2 (rs = −0.76; $P < .05$), AMM/weight (rs = 0.69; $P < .05$), MF (rs = 0.57; $P < .05$). Using the ROC analysis, the cutoff value of MS/WC/height corresponding to SO was less than 39.54 kg/cm/cm (AUS 0.826; $P < .001$; sensitivity 100.00% [95% CI 71.5;100.0], specificity 61.76% [95% CI 43.6;77.8], Youden index 0.61; $P = .001$). The cutoff value of MS/BMI for diagnosing SO was less than 0.690 kg/kg/m^2 (AUS 0.844; $P < .001$; sensitivity 100.00% [95% CI 71.5; 100.0], specificity 68.57% [95% CI 50.7;83.1], Youden index 0.68; $P = .001$). The MS/weight cutoff value corresponding to SO was less than 0.214 kg/kg (AUS 0.852; $P < .001$; sensitivity 100.00% [95% CI 75.1; 100.0], specificity 77.14% [95% CI 59.9; 89.6], Youden Index 0.77; $P = .001$).

Conclusions: We propose using MS/WC/height, MS/BMI, or MS/weight as predictors of SO, as a strong correlation between these parameters and MF, MM, and FM has been demonstrated. A MS/weight cutoff value of <0.214 kg/kg is the most sensitive and specific predictor of SO in patients with DM.

Abstract citation ID: lvag096.1009

EP531 - ECE_1992 - Subclinical HFpEF in diabetes: the role of NT-proBNP, BMI and inflammatory activation

Anastasiia Sokolova[1,2]
[1]*Diabetology, Institute of Endocrinology and Metabolism of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine;* [2]*Institute of Endocrinology and Metabolism of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine*

Background: Heart failure with preserved ejection fraction (HFpEF) is the most prevalent heart failure phenotype in patients with type 2 diabetes mellitus (T2DM) and is increasingly considered an immune-metabolic disorder driven by obesity, chronic low-grade inflammation, and metabolic stress. Subclinical HFpEF frequently remains unrecognized due to preserved left ventricular ejection fraction and absence of overt symptoms. Identification of early biomarkers reflecting myocardial stress and inflammatory activation is essential for timely risk stratification. NT-proBNP is a well-established marker of heart failure; however, its role in detecting subclinical HFpEF and its association with inflammatory pathways in T2DM remains insufficiently characterized.

Aim: To evaluate the associations between NT-proBNP levels, body mass index (BMI), and IL-17A–mediated inflammatory activation in patients with T2DM without clinically overt heart failure.

Methods: This cross-sectional observational study included 57 patients with type 2 diabetes mellitus and preserved left ventricular ejection fraction, without clinical signs or history of heart failure. All participants underwent comprehensive clinical and anthropometric assessment. Laboratory evaluation included measurement of serum NT-proBNP and IL-17A concentrations using standardized immunoassays. Transthoracic echocardiography was performed with a focus on left ventricular systolic and diastolic function. Patients were stratified according to NT-proBNP levels. Associations between NT-proBNP, BMI, inflammatory markers, and echocardiographic parameters were analyzed using correlation and comparative statistical methods.

Results: Elevated NT-proBNP levels were identified in 78% of patients with T2DM despite preserved ejection fraction and absence of overt heart failure. Patients with elevated NT-proBNP demonstrated a significantly higher BMI compared with those with normal NT-proBNP values (30.1 vs 27.2 kg/m^2), indicating a greater burden of adiposity. NT-proBNP concentrations showed a positive association with IL-17A levels, suggesting a link between myocardial stress and Th17-related inflammatory activation. In addition, higher NT-proBNP levels were associated with echocardiographic features consistent with early diastolic dysfunction, while left ventricular ejection fraction remained within the preserved range across the cohort.

Conclusions: Subclinical HFpEF is highly prevalent among patients with type 2 diabetes mellitus and is characterized by elevated NT-proBNP levels in the absence of clinical heart failure. The associations of NT-proBNP with increased BMI and IL-17A-driven inflammatory activation support the concept of HFpEF as an immune-metabolic disorder in T2DM. Combined assessment of NT-proBNP, adiposity, and inflammatory biomarkers may improve early identification of patients at risk for HFpEF and inform preventive strategies in diabetes management.

Abstract citation ID: lvag096.1010

EP535 - ECE_3274 - Clinical profile of severe hypoglycaemia in adults with type 1 diabetes: real-world data from emergency care

Aida Elhadri-Egea, Víctor Siles-Guerrero, Rosa Natalia García Pérez and Martín López de la Torre-Casares
Hospital Universitario Virgen de las Nieves, Granada, Spain

Introduction: Severe hypoglycaemia remains a major complication in type 1 diabetes mellitus (T1DM) and continues to be associated with significant clinical consequences, including emergency care utilisation and impaired quality of life. This persists despite advances in diabetes education, glucose monitoring technologies, and insulin delivery systems. Real-world descriptive data are essential to better characterise patients presenting with severe hypoglycaemia and to identify common clinical features associated with persistent vulnerability.

Objective: To describe the clinical characteristics of adults with T1DM requiring emergency care for severe hypoglycaemia in a real-world setting.

Methods: A retrospective, observational, descriptive study was conducted including 66 adult patients with T1DM who required pre-hospital emergency assistance for severe hypoglycaemia between 2018 and 2022 in a tertiary hospital. Collected variables included demographic data, diabetes-related characteristics, history of severe hypoglycaemia, hypoglycaemia awareness

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

status, nocturnal occurrence of events, and recurrence after the index episode during follow-up. Data were analysed using descriptive statistics.

Results: The median age of the cohort was 42.5 years, and 65.2% of patients were male. A history of previous severe hypoglycaemia was documented in 54.5% of cases, indicating frequent prior exposure to severe events. Hypoglycaemia unawareness was reported in 43.9%, reflecting impaired recognition of early symptoms. Nocturnal hypoglycaemia was experienced by 53.0% of patients, highlighting the relevance of events occurring during periods of reduced monitoring. Following the index episode, 22.7% of patients presented at least one new severe hypoglycaemic event requiring emergency intervention during follow-up. These clinical features tended to cluster in patients with long-standing T1DM, suggesting a persistent vulnerability profile rather than isolated episodes.

Conclusions: n this cohort of 66 adults with T1DM, severe hypoglycaemia frequently occurred in the context of prior severe episodes, impaired hypoglycaemia awareness, and nocturnal occurrence, with a substantial proportion of patients experiencing recurrence after the index event. These real-world descriptive findings underscore the importance of focused post-event clinical reassessment following severe hypoglycaemia, with particular attention to awareness status and nocturnal risk, to reduce recurrent emergency episodes.

Abstract citation ID: lvag096.1011

EP542 - ECE_1523 - Clinical and immunological profile of latent autoimmune diabetes in youth

Nataliia Pashkovska and Iryna Tsaryk
Bukovinian State Medical University, Chernivtsi, Ukraine

Background: Latent autoimmune diabetes in youth (LADY) is underdiagnosed form of autoimmune diabetes mellitus (DM) that combines features of type 1 (T1DM) and type 2 (T2DM) diabetes. In contrast to classical T1DM, LADY is characterized by a slowly progressive autoimmune destruction of pancreatic β-cells, leading to a gradual loss of insulin secretion, and usually manifests before the age of 30 years.

The objective: of the study was to determine the clinical and immunological characteristics of patients with LADY compared with LADA and classical T1DM.

Methods: Under our observation were 106 patients with autoimmune diabetes, who were divided into three clinical groups according to the phenotype of the disease: 40 (37.7%) had classical T1DM, 36 (34%)—LADA, 30 (28.3%)—LADY. We study complaints, history, objective examination data, laboratory tests (blood glucose and glycated hemoglobin, C-peptide, levels of antiGAD and IA-2 ab). The diagnosis of LADY was established based on a comprehensive assessment of clinical, laboratory and immunological data.

Results: Patients with LADY had a mean age of onset of 20 years, as like as classical T1DM patients, mild hyperglycemia, no ketoacidosis at diagnosis, and a high frequency of positive autoantibodies (GAD65 in almost all, IA-2 in half). The level of C-peptide in patients with LADY was 0.62 [0.29; 0.82] (ng/mL)—more than 6 times higher compared to classical T1DM ($P = .000$), indicating slower destruction of β-cells, but almost the same like in LADA group without intergroup difference. Compared to patients with LADA, patients with LADY had a younger age of onset, lower BMI, more often a multiple positive antibody profile and progressed more quickly to insulin dependence. Most patients with LADY had normal weight and no pronounced insulin resistance. Approximately a quarter of patients with LADY were initially misdiagnosed with T2DM due to the similarity of clinical manifestations. Further laboratory examination allowed to clarify the diagnosis. Treatment at the initial stage was mainly based on oral therapy (mainly metformin) with a gradual transition to insulin therapy in case of worsening control and a decrease in C-peptide. Patients who were immediately diagnosed with T1DM began basal-bolus insulin therapy with low daily doses of insulin, which was sometimes accompanied by hypoglycemia and weight gain.

Conclusions: LADY is a separate clinical and immunological variant of autoimmune DM with a young age of onset, preserved β-cell function, a high frequency of autoantibodies and rapid progression to insulin dependence, which requires early comprehensive examination and individualized treatment.

Abstract citation ID: lvag096.1012

EP544 - ECE_1466 - Ten-year change in insulin injection technique knowledge and self-reported practices after the "Diabetes school" educational program implementation in Armenia: repeated cross-sectional survey

Karineh Sharian[1,2,3], Meri Danielyan[1], Gayane Bayburdyan[1], Lusine Arakelyan[1], Arthur Melkonyan[1], Naira Zohrabyan[1], Sona Hakobyan[1], Irina Muradyan[1], Shogher Grigoryan[1], Vrej Issa[1] and Yelena Aghajanova[1]
[1]Yerevan State Medical University after M. Heratsi, Endocrinology Clinic of "Muratsan" University Hospital Complex, Yerevan, Armenia; [2]American University of Armenia, Turpanjian College of Health Sciences, Yerevan, Armenia; [3]Noncommunicable Diseases, National Center for Disease Control and Prevention, Yerevan, Armenia

Background: Correct insulin injection technique is essential for safe and effective diabetes care. Armenia scaled up structured diabetes education ("Diabetes school"), but long-term changes in patients' injection-technique knowledge and related practices have not been described.

Methods: We conducted a repeated cross-sectional study comparing two independent samples of insulin-treated people with type 1 and type 2 diabetes surveyed in 2015 (paper) and 2025 (paper and electronic). Patients were recruited at Endocrinology Clinic of "Muratsan" university hospital complex in Yerevan; 2015's participants were enrolled during routine visits from January to July 2015 and were trained in insulin therapy techniques by a nurse, while the 2025 sample included patients who had previously attended the "Diabetes school". A questionnaire (based on existing injection-technique tools) captured demographics, self-reported practices, and knowledge; evidence-based responses were scored as 1 to generate a total knowledge score. Group comparisons and multivariable linear regression (gender, age, diabetes type, HbA1c, insulin therapy duration) were used.

Results: Valid total score data were available for 199 participants (2015) and 198 participants (2025). Mean total score (calculated from the score distributions) increased from 12.9 (SD 2.5) in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

2015 to 15.0 (SD 2.4) in 2025 (mean difference 2.15 points). Marked improvements were observed in key safety-related practices: holding the needle for at least 10 seconds rose from 28.6% (2015) to 66.2% (2025), while "immediate" needle removal fell from 38.7% to 0.5%. Mixing different insulin types in one syringe decreased from 54.3% to 0.5%. Syringe/needle disposal in a special container increased from 8.6% to 38.6%. The proportion reporting shaking long-acting insulin decreased from 88.3% to 28.1%. In 2025 regression, higher scores were associated with older age (B 0.755, $P = .043$) and were lower in type 2 vs type 1 diabetes (B −1.977, $P < .001$) and with longer insulin-therapy duration (B −0.362, $P = .021$); in 2015 predictors were not statistically significant.

Conclusions: Across a decade, insulin injection technique knowledge and several high-impact self-reported practices improved substantially in Armenia. Remaining gaps (safe disposal and other technique elements) support continued reinforcement within diabetes education, with attention to groups at risk of lower knowledge (type 2 diabetes and longer insulin exposure). Education in diabetes school remains the main method of informing patients about the correct technique of insulin therapy.

Abstract citation ID: lvag096.1013

EP545 - ECE_2695 - Development of personalized postprandial glucose prediction models using machine learning: integrating clinical, metabolic, and nutritional variables

Doohwa Kim[1,2,3], Hajin Park[1,2], Kyeongjun Lee[4], Jinmi Kim[2,5] and Sang Soo Kim[1,2,3]

[1]Division of Endocrinology and Metabolism, Pusan National University Hospital, Busan, South Korea; [2]Biomedical Research Institute, Pusan National University Hospital, Busan, South Korea; [3]Department of Internal Medicine, Pusan National University School of Medicine, Yangsan, South Korea; [4]Department of Mathematics and Big Data Science, Kumoh National Institute of Technology, Gumi, South Korea; [5]Department of Biostatistics, Clinical Trial Center, Biomedical Research Institute, Pusan National University Hospital, Busan, South Korea

Background & Objectives: Personalized dietary management is crucial for preventing and managing metabolic disorders, including diabetes. Individual glycemic responses to food vary greatly, despite the existence of basic dietary guidelines. This study aimed to develop and validate machine learning (ML) models to predict personalized postprandial glucose responses (PPGR), specifically focusing on the incremental Area Under the Curve (iAUC), peak glucose (Peak), and glucose slope (Slope) after meals.

Methods: We analyzed 5361 meal records from 274 subjects collected at Pusan National University Hospital. The dataset integrated 3 categories of features: 14 clinical variables, 8 nutritional variables, and 17 glucose metabolism variables (derived from CGM and insulin assays, eg, disposition index). Additionally, 30 derived variables were generated to account for nutrient ratios, interactions, and glucose-mitigating factors. Four ML algorithms—Random Forest, XGBoost (XGB), LightGBM (LGB), and CatBoost—were employed, with hyperparameter tuning performed using FLAML. Model performance was evaluated using 5-fold cross-validation on an 80/20 train-test split. We also compared models with and without glucose metabolism variables.

Results: In our evaluation, LGB and XGB consistently emerged as the top-performing models, showing not only superior predictive accuracy but also high stability across all target variables. Our analysis demonstrated distinct determinants for each PPGR metric. For iAUC and Peak prediction, factors such as meal start time, carbohydrate intake, and the fiber-to-carbohydrate ratio were identified as primary predictors. The oral disposition index (oDI) and postprandial glucose at 30 minutes (oglu30) showed high feature importance among metabolic variables. Interestingly, lipid-related variables acted mainly as secondary mitigating factors. For the slope prediction, carbohydrate-fiber interactions and HbA1c were dominant drivers. When we excluded metabolic variables to reflect a more practical, non-invasive clinical setting, basic clinical features such as fasting glucose and HDL-cholesterol showed increased importance, though predictive accuracy was slightly lower. In addition, using an ensemble approach that integrates multiple models resulted in a notable improvement in recall compared to using a single model.

Conclusions: This study shows that machine learning models can effectively predict key aspects of postprandial glycemic response by using detailed nutritional and clinical information. We found that while carbohydrate and fiber dynamics alongside meal timing are universally critical, the inclusion of specific glucose metabolism markers significantly enhances prediction precision. Our ensemble modeling provided a strong basis for developing personalized precision nutrition platforms.

Abstract citation ID: lvag096.1014

EP546 - ECE_1252 - Mechanistic pathways linking maternal diabetes to offspring obesity and metabolic syndrome: quantitative synthesis of impact

Fawziya Alyafei, Ashraf Soliman, Ahmed Elawwa, Noora Alhemaidi, Nada Alaaraj, Noor Hamed and Shayma Ahmed

Hamad Medical Center, Pediatric Endocrinology, Doha, Qatar

Background: Children born to mothers with diabetes—both gestational and pregestational—are at increased risk for obesity and metabolic syndrome later in life. This association is mediated by a complex interplay of prenatal and postnatal mechanisms, which have been increasingly elucidated through clinical and experimental research. Understanding the relative impact of each mechanism is critical for early identification and risk stratification of vulnerable offspring.

Objective: To systematically evaluate and quantify the mechanisms by which maternal diabetes predisposes offspring to obesity and metabolic syndrome, and to determine their relative contributions based on published data.

Methods: A comprehensive review was conducted of 40 studies published between 2000 and 2024 that addressed the biological and developmental mechanisms linking maternal diabetes to obesity and metabolic disorders in offspring. Mechanisms were grouped into five main categories: fetal programming via hyperglycemia and insulin exposure, altered adipose tissue development, endocrine and hormonal alterations, epigenetic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

imprinting, and postnatal influences including feeding behavior and microbiome changes. Quantitative synthesis and impact estimates were derived by pooling reported effect sizes or proportions across studies.

Results: Among the five categories of mechanisms identified, fetal programming emerged as the most impactful, accounting for approximately 30% of the total mechanistic contribution. This includes intrauterine hyperglycemia leading to beta-cell hyperplasia, hyperinsulinemia, and permanent alterations in energy regulation. Altered adipose tissue development contributed an estimated 25%, associated with increased fetal adiposity and adipocyte hyperplasia. Hormonal disruptions—including impaired leptin and adiponectin signaling—were responsible for approximately 20% of the effect, followed by epigenetic mechanisms such as DNA methylation of metabolic genes (15%). Postnatal factors, including altered infant feeding patterns, taste preferences, and gut microbiome dysbiosis, were estimated to contribute 10% to the total impact. These proportions reflect data synthesized from observational birth cohort studies, epigenomic analyses, and animal models.

Conclusions: The predisposition to obesity and metabolic syndrome in offspring of diabetic mothers arises from a multifactorial process rooted in both prenatal and postnatal exposures. Quantitative analysis reveals that fetal programming and adipose tissue development are the predominant mechanisms, but endocrine, epigenetic, and environmental factors also play significant roles. These findings underscore the need for mechanistic-based risk assessments in clinical practice to guide early interventions in at-risk children

Abstract citation ID: lvag096.1015

EP550 - ECE_3432 - Impact of nutritional status on bone mineral density in hospitalized patients with eating disorders

Rosa Natalia García Pérez, Víctor Siles-Guerrero, Aida Elhadri-Egea and Araceli Munoz-Garach
Hospital Universitario Virgen De Las Nieves, Granada, Spain

Introduction: Eating disorders (EDs), particularly anorexia nervosa, are associated with a significant impairment of bone health as a result of prolonged malnutrition and disease-related hormonal disturbances. This study evaluates the association between nutritional status, body composition parameters, and bone mineral density (BMD) in patients hospitalized for EDs.

Materials and Methods: A total of 12 women older than 16 years with severe EDs and a body mass index (BMI) ≤ 14 were included. All patients were admitted to the Eating Disorders Inpatient Unit of Virgen de las Nieves University Hospital between 2020 and 2024. Anthropometric, biochemical, body composition, and bone densitometry variables (Z-score) were collected. A descriptive and correlational statistical analysis was performed.

Results: Ninety-three percent of the patients presented some degree of bone alteration, including osteopenia or osteoporosis. Patients with lower BMD values showed reduced body cell mass (BCM), poorer nutritional index, and lower phase angle (PA) values, along with a higher degree of dehydration. Clinically relevant differences were observed between patients with osteopenia and those without bone disease in terms of BCM (17.6 ± 1.2 kg vs 19.9 ± 1.0 kg), fat mass (FM) (5.0 ± 2.1 kg vs 7.5 ± 0.8 kg), PA (4.6 ± 0.4 vs 4.8 ± 0.2), and skeletal muscle index (SMI) (6.3 ± 3.3 kg/m^2 vs 6.4 ± 1.2 kg/m^2). In densitometric assessment, lumbar spine Z-scores were -3.36 ± 0.79 in patients with osteoporosis, -1.83 ± 0.29 in those with osteopenia, and -0.3 ± 0.99 in patients without bone pathology. Clinically relevant correlations were identified between total body Z-score and SMI ($r = 0.89$), nutritional status ($r = 0.94$), and BCM ($r = 0.58$). Negative associations were also observed with body fat and hydration status. Although not all associations reached statistical significance, the observed patterns demonstrate clear clinical relevance for a multidisciplinary management approach.

Conclusions: Alterations in bone health are highly prevalent in patients with severe eating disorders. Variables such as muscle mass, hydration status, nutritional status, and body composition show clinically meaningful associations with bone mineral density. Early identification of these factors may be key to preventing bone deterioration in this patient population.

Abstract citation ID: lvag096.1016

EP551 - ECE_1112 - Amylin as a metabolic marker of latent autoimmune diabetes

Iryna Tsaryk[1] and Nataliia Pashkovska[2]
[1]*Bukovinian State Medical University, Chernivtsi, Ukraine;* [2]*Clinical Immunology, Allergology and Endocrinology, Bukovinian State Medical University, Chernivtsi, Ukraine*

Background: Amylin is thought to play a role in the development of diabetes mellitus (DM), hypertension, hyperlipidemia, and other problems in non-PCOS patients. If these findings can be extrapolated to women with PCOS, hyperamylinemia may contribute to their high risk for developing DM and its comorbidities.

The objective of the study was to determine the features of the level of amylinemia in fertile women with different types of DM.

Methods: A study of 60 patients was carried out as well as 15 individuals of control group. The patients were divided into four groups by the types of DM (15 patients in each group—classical T1DM, LADA, LADY, T2DM). The LADA group included patients with LADA1 and LADA2 phenotype (7 and 8 respectively). We study complaints, history, objective examination data, laboratory tests (blood glucose and glycated hemoglobin, C-peptide, antiGAD and serum amylin).

Results: In patients with classical T1DM the level of amylinemia did not change compared to control, whereas in T2DM it was 13.3 times significantly higher compared to the control and 7.6 times higher than in classical T1DM ($P < .05$). In LADA the amylin content was 8.6 times higher than in control and 4.9 times higher compared to classical T1DM ($P < .05$). In LADY group the amylin content was 5.3 times higher than in control and 3 times higher compared to classical T1DM, but 38% lower than in LADA patients ($P < .05$). In patients with LADA1, the serum level of amylin was 5.2 times higher relative to the control ($P < .01$), 3 times higher than in classical T1DM ($P < .05$), but 2.5 times as low as in T2DM ($P < .05$) and practically the same as in LADY group. In LADA2 the above indicator exceeded that in the control group by 12.8 times, in the group of classical T1DM—by 7.3 times, LADY—by 2.4 times, and in patients with LADA1—by 2.4 times ($P < .05$). In patients with LADY, an interdependence was found between the content

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

of amylin and insulin (r = 0.348; $P < .05$), HbA1c (r = 0.418; $P < .05$).

Conclusions: Serum amylin level significantly increase in fertile women with LADA (especially in LADA2), LADY and T2DM, which indicates the role of hyperamylinemia in the development and progression of this types of diabetes. Because amylin receptors are present in the ovarian tissue, amylin may play a role in ovarian dysfunction in PCOS. Future studies are needed to determine the role that amylin plays in metabolic abnormalities and ovarian dysfunction in PCOS.

Abstract citation ID: lvag096.1017

EP553 - ECE_2761 - Interaction between type 1 diabetes mellitus and gender-affirming hormone therapy: impact on glycemic control and clinical decision-making. A case series

Kevin David Díaz Gorrín, Selena Rodriguez Fernandez, Javier Panizo Fra, Paula Pérez, Elena Rodríguez Sosa, Patricia León González, Óliver Quintero Rodríguez, Itziar Aznar Ondoño, Juan Ignacio Márquez De La Rosa, Laura Mesa Suárez and Patricia Cabrera García
Endocrinology and Nutrition, Hospital Universitario de Canarias, San Cristóbal de La Laguna, Spain

Objectives: To analyze the interaction between type 1 diabetes mellitus (T1DM) and gender-affirming hormone therapy (GAHT), assessing its impact on glycemic control and on clinical decision-making related to GAHT, gender-affirming surgery, and therapeutic management of T1DM.

Material and Methods: Retrospective descriptive study of a case series of transgender individuals with T1DM followed in a specialized gender identity clinic. Five patients with longitudinal follow-up were included (four trans women and one trans man). Demographic and clinical variables, transition-related data, glycemic control parameters (HbA1c and basic continuous glucose monitoring metrics), and use of diabetes technology were collected. The temporal relationship between GAHT initiation, glycemic control, and clinical decision-making was analyzed using descriptive methods.

Results: Mean age was 28.4 years (range 19-41), with a mean age at T1DM diagnosis of 11.6 years. Four patients were receiving GAHT, initiated at a mean age of 19.8 years. Mean baseline HbA1c was 8.7%, increasing to 9.0% at 6 months and 8.9% at 12 months. T1DM did not influence the indication, initiation, or intensity of GAHT in any case. However, in two patients, gender-affirming surgery (vaginoplasty) was postponed due to the need for preoperative optimization of glycemic control. Only one patient was treated with continuous subcutaneous insulin infusion (CSII); this patient showed a clinically relevant improvement in glycemic control after pump initiation, with HbA1c decreasing from 8.2% to 6.1% at 6 months. In the remaining four cases, CSII was not initiated: in three patients due to poor treatment adherence and difficulties attending nursing follow-up (currently awaiting pump initiation), and in one patient due to adequate glycemic control without advanced technology. No systematic deterioration in glycemic control attributable to GAHT initiation was observed.

Conclusions: In this case series, T1DM did not represent a barrier to access to or intensity of GAHT. Glycemic control did influence the planning of gender-affirming surgery, requiring prior metabolic optimization in some cases. GAHT was not associated with a systematic worsening of glycemic control. The improvement observed in the single patient using insulin pump therapy suggests that access to diabetes technology, together with adequate adherence, may play a key role in metabolic control among transgender individuals with T1DM.

Abstract citation ID: lvag096.1018

EP554 - ECE_3268 - Keeping an ear out for diabetes—to hear what is seen

Mukhopadhyay Babulayeb[1,2], Mari-Anne Scott[1] and Ross Cairns[1]
[1]*University Hospital Hairmyres, NHS Lanarkshire, Diabetes Clinic, Diabetes and Endocrinology, Glasgow, United Kingdom;* [2]*East Kilbride, Diabetes & Endocrinology, East Kilbride, United Kingdom*

The NHS Right Care Pathway for Diabetes outlines some key criteria for diagnostic uncertainty in patients with new onset diabetes. However there are no validated criteria for diagnosis of monogenic diabetes, although disease probability scoring systems are available. In the UK 90% patients with monogenic diabetes are mistakenly diagnosed with type 1 or type 2 diabetes at first.[1] We describe two young patients with a rare form of monogenic diabetes, misdiagnosed initially; we suggest features that should trigger appropriate diagnostic testing.

Patient 1: A 34 year old female, with history of gestational diabetes, presented with osmotic symptoms, HbA1c 83 mmol/mol and mild ketosis, she was commenced on gliclazide. Her BMI was 27, she had a strong maternal family history of deafness. She was found to have mild sensorineural deafness, Her genetic testing for monogenic causes confirmed MT-TL1 m.3243A>G pathogenic mutation, associated with maternally inherited diabetes and deafness (MIDD). She remains well controlled on metformin monotherapy.

Patient 2: A 33 year old male, with sensorineural hearing loss since aged 4, and cardiac conduction abnormalities (WPW syndrome), presented with osmotic symptoms and HbA1c 89 mmol/mol. His BMI was 16, and he was commenced on insulin as type 1 diabetes was suspected. His type 1 Diabetes autoantibodies were negative, C-peptide levels were high, there was a strong family history of diabetes and deafness. His MODY probability score was 15% and genetic testing confirmed MT-TL1 m.3243A>G pathogenic variant. His insulin was discontinued, his HbA1c is 47 mmol/mol on sulphonylurea monotherapy.

MIDD is a monogenic mitochondrial disorder, most commonly caused by the m.3243A>G variant of the *MT-TL1* gene, presenting with diabetes, and sensorineural hearing loss. It may also be associated with a range of other abnormalities[2]—phenotype is variable depending on the level of heteroplasmy. This disorder is under recognised and often mis-diagnosed as type 2 or type 1 diabetes. The genetic diagnosis is important for counselling (maternal transmission), identification of other affected family members and screening for associated complications like cardiomyopathy, deafness and neurological problems. The presence of sensorineural deafness in a patient or kindred with diabetes should prompt one to consider this diagnosis.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

References

1. Maturity onset diabetes of the young (MODY). Accessed January 13, 2026. https://www.diabetes.org.uk/about-diabetes/other-types-of-diabetes/mody.
2. Kyriakidou A, Hadjivassiliou M, Papapostolou A, Picolos MK. Maternally inherited diabetes and deafness (MIDD)—atypical clinical diabetes features leading to the diagnosis. *JCEM Case Rep*. 2023;1(3):luad047. https://doi.org/10.1210/jcemcr/luad047

Abstract citation ID: lvag096.1019

EP558 - ECE_2046 - Impact of caloric restriction with or without time-restricted eating on ambulatory blood pressure, renin, and aldosterone: exploratory analysis of a randomised controlled trial

You Jin Chang[1,2], Laurent Turner[1,2], Xiao Tong Teong[1,2], Lijun Zhao[1,2], Athena Variji[1,2], Morag Young[3,4], Gary Wittert[1,2], Leonie Heilbronn[1,2] and Amy Hutchison[1,2]
[1]*South Australian Health and Medical Research Institute, Adelaide, Australia;* [2]*School of Medicine, Adelaide University, Adelaide, Australia;* [3]*Baker Heart and Diabetes Institute, Melbourne, Australia;* [4]*Baker Department of Cardiometabolic Health, University of Melbourne, Melbourne, Australia*

Background: Time-Restricted Eating (TRE), in which food intake is limited to a 6- to10-hour window, and caloric restriction (CR) independently improve cardiovascular risk factors. Whether combining TRE with CR provides additional cardiovascular benefits is unknown. Furthermore, blood pressure (BP) and its regulators, renin and aldosterone, exhibit circadian variation, but remains unclear whether the meal timing affects these rhythms.

Aim: This study examined whether early (eCR) or delayed (dCR) CR differentially impacted BP and its regulators compared with un-restricted CR, in adults at-risk of hypertension.

Methods: This study included 114 adults (mean ± SD; age 59 ± 9 years; BMI 32.1 ± 4.6 kg/m^2; 80% female), with overweight/obesity and elevated fasting glucose. Participants were stratified by sex and fasting blood glucose (≤6.0 mmol/L; >6.0 mmol/L) and randomised (1:1:1) to a 30% energy restricted diet with all foods provided, as either eCR (eating between 0800-1600), dCR (1200-2000), or un-restricted CR for eight weeks. A 24-hour ambulatory BP monitor was worn from ~0800, including overnight sleep (~0000 to ~0730), and blood samples were collected every four hours during a 26-hour ward visit at baseline and week 8. Linear mixed models analysed day- and night-time systolic (SBP) and diastolic (DBP) BP, nocturnal SBP dipping, SBP average real variability, and plasma renin and aldosterone, adjusting for stratification factors, age, antihypertensive medication classifications, and BMI. Sensitivity analyses by dipping status (dipper ≥10%, non-dipper <10%) were conducted for nighttime BP. The cosinoRmixedeffects R package was used to analyse the MESOR (Midline Statistic Of Rhythm), amplitude, and acrophase of SBP, DBP, renin, and aldosterone. Participants with <70% successful BP readings ($n = 16$) or who withdrew ($n = 3$) were excluded.

Results: Daytime and nighttime SBP and DBP and fasting renin were significantly reduced ($P < .05$) after eight weeks, with no changes in other parameters. There were no significant interactions between study group and week or weight for any parameter ($P > .05$). Sensitivity analyses showed nighttime SBP and DBP reductions over time in both dippers and non-dippers ($P < .05$), with no differences between groups. For circadian analysis, the MESOR of SBP, DBP, renin, and aldosterone were significantly reduced within all groups. Only the DBP MESOR significantly decreased between groups. Amplitude and acrophase did not significantly change between groups in any parameter.

Conclusions: Early, or delayed CR are potential strategies to CR to improve BP vs CR alone. However, over eight weeks, neither provided additional benefits for BP measures.

Abstract citation ID: lvag096.1020

EP559 - ECE_2082 - Effects of a multidisciplinary lifestyle program on muscle strength and body composition in children with excess weight

Nicoletta Gianni[1], Maria Rea[1], Danilo Fintini[1], Francesco D'aniello[1], Alessia Aureli[1], Elena Madonna[1], Gabriele Scozia[1], Valentina Russo[1], Stefano Cianfarani[1], Deny Menghini[1] and Melania Manco[1,2]
[1]*Ospedale Pediatrico Bambino Gesù, Roma, Italy;* [2]*Bambino Gesù Children's Hospital Capital, Rome, Italy*

Introduction: Sarcopenic obesity, marked by high fat mass and reduced fat-free mass, is increasingly recognized in children and may predispose them to metabolic and functional complications. This study assessed whether an intensive lifestyle intervention could improve early sarcopenic traits in pediatric patients with overweight or obesity.

Methods: Within the RESILIENT Project at Bambino Gesù Children's Hospital, children aged 6-12 years underwent an Intensive Health Behavior and Lifestyle Treatment (IHBLT) combining nutritional counseling and Adapted Physical Activity. Anthropometric measures (weight, BMI-SDS, waist circumference, waist-to-height ratio), body composition (fat mass, fat-free mass, total body water via bioelectrical impedance), and muscle strength (handgrip test) were evaluated at baseline (T0), 2 months (T1), and 5 months (T2). Associations between handgrip strength (absolute and relative), body composition, and age were explored.

Results: BMI-SDS, waist indices, and fat mass decreased, while fat-free mass and total body water increased. Absolute handgrip strength improved in both hands (dominant: 14.31 ± 3.95 to 15.12 ± 3.77 kg; non-dominant: 13.76 ± 3.37 to 14.38 ± 3.41 kg). The proportion of children above the 50th percentile for relative strength rose from 17.6% to 39.2%. Strength correlated positively with age, weight, and fat-free mass, and inversely with fat mass. Normalized strength declined with age and adiposity, suggesting early sarcopenic patterns.

Conclusions: Multidisciplinary lifestyle intervention enhances body composition and muscle strength in children with excess weight. Early strategies are essential to counteract sarcopenic obesity.

Abstract citation ID: lvag096.1021

EP560 - ECE_2371 - Muscle function in adults with class III obesity receiving liraglutide vs tirzepatide

Maria Evangelia Koloutsou[1], Maria Yavropoulou[1], Maria Mateniadou[1], Evanthia Kassi[2], Kyriaki Cholidou[3], Georgia Argyrakopoulou[4], Evrydiki Kravvariti[5], Nikolaos Tentolouris[5] and Alexander Kokkinos[5]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Laiko University Hospital, Medical School, National and Kapodistrian University of Athens, First Department of Propaedeutic Internal Medicine, Joint Academic Rheumatology Program, Endocrinology Unit, Athens, Greece; [2]First Department of Propaedeutic Internal Medicine, Endocrinology Unit, Laikon General Hospital, Athens, Greece; [3]1st Respiratory Medicine Department, Sotiria Chest Disease Hospital, Athens, Greece; [4]Diabetes and Obesity Unit, Athens Medical Center, Athens, Greece; [5]First Department of Propaedeutic Internal Medicine, Laikon General Hospital, Athens, Greece

Introduction: GLP-1 receptor agonists and the dual GIP/GLP-1 receptor agonist, tirzepatide, induce substantial weight loss. However, concern exists that rapid weight reduction may adversely affect skeletal muscle and increase the risk of sarcopenia, while data on muscle strength and physical performance remain scarce. This prospective observational study compared the 3-month effects of liraglutide vs tirzepatide on screening tools for sarcopenia in adults with class III obesity.

Methods: Adults with a BMI >40 kg/m^2 without diabetes received liraglutide ($n = 14$, administered once daily starting at 0.6 mg with weekly dose escalation of 0.6 mg to the target dose of 3 mg) or tirzepatide ($n = 15$, administered once weekly starting at 2.5 mg with monthly dose escalation of 2.5 mg to the target dose of 7.5 mg), over a 3-month follow-up period. Demographic and anthropometric data were collected, body composition was assessed by bioelectrical impedance analysis, and sarcopenia-related functional tests (handgrip strength, gait speed, and chair-stand test) were evaluated at baseline and at 3 months. Statistical analysis was performed using SPSS version 26.

Results: At baseline, no participant met diagnostic criteria for sarcopenia. The mean age was 47 years, mean body weight 129 kg, and mean BMI 44 kg/m^2. At 3 months, weight loss was similar between the liraglutide and tirzepatide group (11.5 vs 11.9 kg, $P = .83$), as was percentage weight loss (10% vs 9%, $P = .75$). Reductions in fat percentage (−2.3% vs −2.6%, $P = .76$), fat mass (−7.3 vs −7.6 kg, $P = .86$), and fat-free mass (−4.2 vs −3.9 kg, $P = .79$) were comparable. Between-group differences were not significant for either handgrip strength (+2.0 vs −0.2 kg, $P = .29$) or chair-stand test (−2.9 vs −1.7 sec, $P = .21$), with the latter improving in both groups, and a statistically significant increase in gait speed observed in the liraglutide group compared with tirzepatide (+0.2 vs +0.0 m/s, $P = .01$).

Conclusions: Despite concerns that pharmacologically induced weight loss with incretin-based therapies may exacerbate sarcopenia, real-world data from adults with class III obesity demonstrated preserved muscle function after 3 months of treatment with liraglutide 3 mg once daily or tirzepatide 7.5 mg once weekly, despite a concomitant reduction in muscle mass.

The study protocol was prospectively registered at ClinicalTrials.gov (NCT07094568).

Abstract citation ID: lvag096.1022

EP561 - ECE_2786 - Skeletal muscle function in men with obesity-related functional hypogonadism

Alicja Stańska[1], Krzysztof Kusy[2], Joanna Gorwa[3], Monika Ciekot-Sołtysiak[2], Maja Maćkowiak-Tadyszak[2], Aleksandra Derwich-Rudowicz[1], Marek Ruchala[1] and Nadia Sawicka-Gutaj[1]

[1]Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznań, Poland; [2]Poznań, Poland; [3]Department of Biomechanics, Poznan University of Physical Education, Poznań, Poland

Introduction: Obesity and its complications—metabolic, hormonal, and sexual dysfunction have become a serious public health concern. Not only is obesity a risk factor for functional hypogonadism in men, but functional hypogonadism causes increased fat accumulation and reduced muscle mass, creating a vicious circle.

Aim: The aim of the study was to compare hormonal parameters and muscle function between men with obesity-related hypogonadism, eugonadal obese men, and healthy controls.

Methods: Men aged 18-60 years, with diagnosed functional hypogonadism (a serum testosterone level 8-12 nmol/L and sexual dysfunction) and obesity (BMI ≥ 30 kg/m^2), were prospectively enrolled in the study. Eugonadal men with obesity and healthy controls (HCs) were also included. Each participant filled the International Physical Activity Questionnaire (IPAQ) and the WHOQOL-BREF questionnaire for quality of life. Hormonal parameters (total testosterone, LH, FSH, SHBG, and prolactin concentration) and biochemical parameters were assessed. Physical capacity was measured using a cardiopulmonary exercise test (CPET) and grip strength with a hand dynamometer.

Results: A total of 107 participants were included in the analysis (hypogonadal obese $n = 51$, eugonadal obese $n = 17$, and healthy controls $n = 39$). In hypogonadal group, mean age was 36.37 years, median BMI 32.29 kg/m^2, and median total testosterone 9.26 nmol/L. The most pronounced difference was observed in quality of life, revealing a median gradient pattern (HCs (93), hypogonadal obese (83), and eugonadal obese (71)). Although the total time spent sitting did not differ significantly between the HCs and hypogonadal group, participants with hypogonadism spent less time participating in vigorous and moderate physical activity ($P = .021$ and $P = .002$, respectively). There were also significant differences in physical capacity between healthy controls and obese participants (VO2 max/kg: 33.13 ± 6.07, 23.75 ± 5.81, and 21.35 ± 5.76 ml/min/kg in HCs, eugonadal obese, and hypogonadal obese, respectively) and relative strength (1.54 ± 0.10 vs 1.43 ± 0.10 and 1.41 ± 0.11 kg/kg), with healthy controls demonstrating markedly superior performance compared to obesity groups.

Conclusions: In the hypogonadal group, we observed a typical clinical picture of sarcopenic obesity, which may have significant functional and metabolic consequences. Reduced muscle strength and lower physical capacity may further reduce patients' motivation for regular physical activity and hinder effectivity of non-pharmacological treatment. These findings underscore the need for a comprehensive therapeutic approach and for optimizing the management of obesity-related hypogonadism, especially regarding quality of life and physical performance.

Abstract citation ID: lvag096.1023

EP562 - ECE_2924 - Reduced weight loss response to semaglutide in patients with hypothyroidism: a real-world study

Patricia Oriol Ocejo, Jersy Cardenas, Victor Pérez de Arenaza Pozo, Alvaro Fernandez Sanchez, Blanca Timón, Beatriz Baraia Etxaburu Astigarraga, Cristina Luengo Alvarez de Buergo and Clotilde Vazquez Martinez

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Endocrinology, Fundación Jiménez Díaz University Hospital, Madrid, Spain

Background: Currently, limited data are available evaluating whether the weight-loss response to glucagon-like peptide-1 receptor agonists (GLP-1 RA) differs between patients with hypothyroidism and euthyroid individuals. Given the key role of thyroid hormones in body energy metabolism, hypothyroidism could potentially influence the effectiveness of obesity pharmacotherapy. The aim of this study was to assess whether hypothyroidism is associated with a reduced weight-loss response to semaglutide in real-world clinical practice.

Methods: A retrospective observational study was conducted including patients prescribed semaglutide between May and August 2024 in two specialised obesity clinics from two public hospitals in Madrid. All patients participated in a structured lifestyle modification programme. Patients with type 2 diabetes mellitus ($n = 32$), type 1 diabetes mellitus ($n = 2$), or incomplete data ($n = 121$) were excluded. A total of 123 patients were included in the final analysis, of whom 23 (18.7%) had a diagnosis of hypothyroidism. Weight loss during follow-up was the primary outcome. Multivariable linear regression analysis was performed, including 18 baseline demographic, anthropometric, analytical, comorbidity-related and treatment-related variables.

Results: After a mean follow-up of 6.5 ± 1.2 months, the mean achieved semaglutide dose was 1.31 ± 0.74 mg/week. Mean weight loss in the overall cohort was -5.7 ± 0.3 kg (95% CI −6.3 to −5.1). Weight loss was significantly greater in euthyroid patients compared with those with hypothyroidism: -6.3 ± 6.1 kg (95% CI −7.5 to −5.1) vs -3.2 ± 3.9 kg (95% CI −4.9 to −1.5), with a mean difference of −3.0 kg (95% CI −5.7 to −0.4; $P = .025$). No significant changes in thyroid-stimulating hormone (TSH) levels were observed in either group during follow-up. In the multivariable model, higher baseline body mass index (β −.28, $P = .02$), prediabetes (β −3.20, $P = .02$), and GLP-1–naïve status (β −2.96, $P = .02$) were associated with greater weight loss, whereas hypothyroidism (β +3.10, $P = .041$) was independently associated with reduced weight loss.

Conclusions: In this real-world cohort, hypothyroidism was independently associated with a reduced weight-loss response to semaglutide. These findings indicate that thyroid status may represent an important modulator of the effectiveness of GLP-1 receptor agonist therapy. Consideration of thyroid function may be relevant when evaluating suboptimal response to obesity pharmacotherapy.

Abstract citation ID: lvag096.1024

EP563 - ECE_3136 - Exploring MASLD-associated features in women with PCOS: a subset analysis from a broader gut microbiota-focused study

Bojana Mićić[1], Sofija Ignjatović[1], Miloš Vratarić[1], Ivana Bozic-Antic[2,3,4], Uroš Gašić[1], Jelena Brkljačić[1], Mark Davids[5], Amir Bahmani[5], Max Nieuwdorp[5], Jelica Bjekic MacUt[6], Ana Djordjevic[1], Nataša Veličković[1] and Danijela Vojnović Milutinović[1]

[1]*Institute for Biological Research "Siniša Stanković"—National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia;* [2]*Department of Endocrinology, Euromedik General Hospital, Belgrade, Serbia;* [3]*Department of Endocrinology, Faculty of Stomatology, University Business Academy, Novi Sad, Serbia;* [4]*Euromedik General Hospital, Belgrade, Serbia;* [5]*AmsterdamUMC, University of Amsterdam, Amsterdam, The Netherlands;* [6]*Department of Endocrinology, UMC Bežanijska kosa, Faculty of Medicine, University of Belgrade, Belgrade, Serbia*

Introduction: Metabolic dysfunction–associated steatotic liver disease (MASLD) is highly prevalent worldwide and frequently coexists with endocrine and metabolic disorders. Polycystic ovary syndrome (PCOS), often characterized by insulin resistance and metabolic dysregulation, has been associated with an increased risk of MASLD. However, the extent to which this association defines a distinct metabolic phenotype within PCOS remains to be explored. Within a broader multi-omics clinical study of MASLD patients from Serbia, we identified a subset of women with PCOS and investigated whether MASLD is associated with distinct metabolic, hormonal or gut microbiota features within an age-matched PCOS patients.

Patients and Methods: Exploratory subset analysis included age-matched women with PCOS stratified by ultrasound-defined MASLD (non-MASLD group, $n = 9$ and MASLD group, $n = 5$). Anthropometric, metabolic and hormonal parameters were assessed using routine clinical methods. Gut microbiota composition was analysed based on 16S rRNA gene sequencing, using diversity metrics and genus-level comparisons, while fecal short-chain fatty acids (SCFA) were measured as functional readouts of gut microbial activity. Given the small sample size and distributional characteristics of several variables, non-parametric statistical methods were applied.

Results: Age-matched PCOS women with and without MASLD showed largely overlapping anthropometric, lipid, hepatic, and hormonal profiles. Among parameters of glucose metabolism, only HbA1c was modestly higher in women with MASLD, indicating mild sustained metabolic alteration associated with MASLD within PCOS. Beta diversity analysis indicated higher heterogeneity in MASLD-PCOS women, although without clear group separation. At the genus level, MASLD-PCOS women more frequently exhibited higher abundance of taxa commonly associated with metabolic disturbances (*Rothia*, *Streptococcus*, *Lachnoclostridium*). Fecal SCFA concentrations and composition did not differ between groups, suggesting that, in our cohort, these microbial metabolites do not show an apparent association with MASLD in PCOS.

Conclusions: Within an age-matched women with PCOS, MASLD was not associated with a distinct metabolic or functional microbial signature, but rather with higher gut microbiota heterogeneity and consistent directional shifts at the genus level. Higher HbA1c, suggesting modest variation in cumulative glycaemic exposure, may reflect early metabolic divergence associated with the MASLD–PCOS phenotype.

Abstract citation ID: lvag096.1025

EP564 - ECE_3229 - Post-bariatric hypoglycaemia—a case series from a large surgical bariatric centre

Aparna Chaudhary, Stephanie Miles and Foteini Kavvoura

Diabetes and Endocrinology, Royal Berkshire Hospital, Reading, United Kingdom

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Post-bariatric hypoglycaemia (PBH) is a post-operative complication attributed to exaggerated post-prandial hyperinsulinaemia. It is defined by Whipple's triad: hypoglycaemic symptoms, low glucose levels, and symptom resolution with euglycemia. PBH typically occurs 1-4 hours post-prandially and develops 1-3 years post-operatively.

Methods: We audited patients referred between 2019 and 2025 with symptoms of PBH against 2024 Society for Endocrinology guidelines. Cases were identified from clinician worklists. Electronic records were reviewed for clinical characteristics, method of diagnosis, and interventions.

Results: Of 21 patients referred with typical symptoms, 19 were diagnosed with PBH.

Cohort characteristics:

Median age at presentation	43 years
Sex	Female 18/19 (95%)
Type of surgery	Roux-en-Y 13/19 (68%) Sleeve gastrectomy 3/19 (16%) Mini gastric bypass 3/19 (16%)
Median time from surgery to presentation	26 months
Pre-existing diabetes	4/19 (21%)
Median BMI at presentation	26.4
Median excess weight loss	82%

Mixed meal test (MMT) was performed in 16/19 patients, capillary blood glucose (CBG) in 15/19, venous glucose in 13/19 and continuous glucose monitoring (CGM) in 11/19. The median number of confirmatory tests was 3.

Rates of glucose detection <3.0 mmol/L were: MMT 44% (7/16), CBG 73% (11/15), venous glucose 38% (5/13), and CGM 90% (10/11).

All patients received information on controlled portions of carbohydrates; 79% were reviewed by a dietician (15/19).

Pharmacotherapy was used in 68% (13/19). Acarbose was used first line in all patients (13/13). GLP-1 analogues were used second line (7/13); diazoxide was used four times, verapamil and octreotide twice, and tirzepatide once. Six patients on GLP-1 analogues reported symptomatic improvement (86%).

Transoral outlet reduction was performed in three patients (16%), all remained symptomatic; two patients (67%) returned to GLP-1 analogues with improvement of symptoms.

Six patients achieved symptom resolution and were discharged (32%), two patients were lost to follow-up, and 11 patients are receiving ongoing appointments (58%). Two patients needed hospitalisation due to hypoglycaemia.

Conclusions: This cohort confirmed suggested PBH risk factors include female sex and higher weight loss post-surgery. The diagnostic challenges are reflected in the number of confirmatory tests required.

Dietary advice, dietician review and acarbose use complied with audit standards. Octreotide, pasireotide and diazoxide use is limited by convenience, funding restrictions, and tolerability. GLP-1 analogues are accessible and well tolerated; 86% of patients reported an improvement in symptoms, highlighting the importance to further consider their role in management. PBH remains challenging to manage in a considerable proportion of patients.

Abstract citation ID: lvag096.1026

EP565 - ECE_3436 - Correlation between weight loss and reduction in waist circumference in weight management with semaglutide injection: post-hoc analysis of phase 3 study

Unnikrishnan Gopalkrishnan[1], Ameya Joshi[2], Harish Kumar[3], Richa Giri[4], Sanjiv Maheshswari[5], Valluri Prasad[6], Jitendra Shukla[7], M.C. Rekha[8], Nutankumar Agrawal[9], Yogesh Rasal[10], Banshidhar Sahoo[11], Shweta Bhandari[12], Ambana Gowda[13], Phadke Keshav[14], Pravin Supe[15], Niranjan Pathak[16], C. Ambrish[17], Ashutosh Sonawane[18], Yash Bahulikar[19], Amit Bhaskar[20], R. Arunkumar[21], Priyanka Yadav[22], Supriya Sonowal[22], Dipak Patil[22], Sucheta Pandit[22], Pravin Ghadge[22] and Suyog Mehta[22]

[1]Chellaram Diabetes Institute, Pune, India; [2]Bhaktivedanta Hospital and Research Institute, Thane, India; [3]Amrita institute of Medical Sciences and Research Centre, Kochi, India; [4]G.S.V.M medical College, Kanpur, India; [5]Jawahar Lal Nehru Medical College, Ajmer, India; [6]King George Hospital, Visakhapatnam, India; [7]Moti Lal Nehru Medical College, Prayagraj, India; [8]Mandya Institute of Medical Science, Mandya, India; [9]M.L.B Medical College, Jhansi, India; [10]Pulse Multispecialty Hospital, Pune, India; [11]KIDS Hospital, Bhubaneswar, India; [12]Vincare Hospital, Bathinda, India; [13]Citizen Hospital, Bangalore, India; [14]Sahyadri Super Speciality Hospital, Pune, India; [15]Supe Heart and Diabetes Hospital and Research Centre, Nashik, India; [16]OJAS Multispeciality Hospital, Pune, India; [17]Medstar Speciality Hospital, Bangalore, India; [18]Panacea Hospital, Nashik, India; [19]MMFHA Joshi Hospital, Pune, India; [20]Janta Hospital and Maternity Center, Varanasi, India; [21]Chettinad Hospital & Research Institute, Chengalpattu, India; [22]Mumbai, India

Objectives: To evaluate the correlation between weight loss and reduction in waist circumference in patients treated with Semaglutide injection for weight management

Materials and Methods: This phase III, multicentre, randomized, open-label, active-controlled clinical study (CTRI/2025/04/085487) was conducted across 22 study sites in India after receiving regulatory and ethics committee approvals. Total 267 adult patients with BMI $\geq$ 30 kg/m^2 or $\geq$ 27 kg/m^2 with the presence of at least one co-morbidity of hypertension, dyslipidaemia and/or type 2 diabetes mellitus were included. Patients were randomized to either test arm to receive synthetic semaglutide injection or reference arm to receive Wegovy® every week subcutaneously for 24 weeks. The primary endpoint was change in body-weight from baseline to week 24. Secondary endpoints included change in BMI, waist circumference, SF-36, and glycaemic measures in diabetic and non-diabetic patients. Safety assessments included incidence of TEAEs and anti-drug/neutralizing antibody. This post-hoc analysis was conducted to evaluate the correlation between weight loss and reduction in waist circumference.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: The Pearson's correlation coefficient between decrease in weight loss and decrease in waist circumference was 0.2753 with *P* value = .0003 in test arm. The Pearson's correlation coefficient between decrease in weight loss and decrease in waist circumference was 0.2753 with *P* value = .0134 in reference arm. There is positive co-relation between weight loss and reduction in waist circumference in both test and reference arm indicating greater reduction in weight is associated with more decrease in waist circumference. The correlation between weight loss and reduction in waist circumference was statistically significant in both test and reference arm. The statistical significance observed in the Pearson correlation analysis in both the arms supports the robustness of this association.

Conclusions: This post-hoc analysis demonstrated that there is greater reduction in weight is associated with grated reduction in waist circumference demonstrating favourable effect in central adiposity along with overall weight reduction

Abstract citation ID: lvag096.1027

EP571 - ECE_2552 - The evolution and management of type V familial hypertriglyceridemia during pregnancy

Fatma Ben Abdessalem, Taieb Ach, Imen Halloul, Wiem Saafi, Hamza Fekih, Ghada Saad and Yosra Hasni
Endocrinology, Hôpital Farhat Hached, Sousse, Tunisia

Introduction: Pregnancy triggers profound metabolic adaptations characterized by hormonal shifts that can increase lipid levels by up to fourfold. While often physiological, this rise poses significant risks for patients with pre-existing dyslipidemia. We present a case of severe hypertriglyceridemia further complicated by the onset of gestational diabetes. This report highlights the clinical challenges of managing extreme lipid elevations to prevent life-threatening maternal and fetal complications.

Observation: We report the case of a 31-year-old primigravida referred at 25 weeks of gestation following a pathological oral glucose tolerance test. Her medical history includes familial mixed hypertriglyceridemia, diagnosed at age 19 after an acute pancreatitis episode (triglycerides: 23.4 mmol/L; total cholesterol: 8 mmol/L). Fenofibrate therapy was discontinued at the start of pregnancy. Clinical examination was unremarkable, specifically showing no eruptive xanthomas or hypertension. Upon admission, lipase levels were normal, but labs revealed severe hypercholesterolemia (18.41 mmol/L) and hypertriglyceridemia (14.12 mmol/L). Following a strict low-fat diet and omega-3 supplementation (3 g/day), levels adjusted to 16.11 mmol/L and 13.11 mmol/L by week 27. While glycemia was controlled via lifestyle changes, third-trimester ultrasound suggested a trend toward fetal macrosomia.

Conclusion: Hypertriglyceridemia was exacerbated by pregnancy, gestational diabetes, and glucose provocations, with acute pancreatitis remaining the primary risk. Furthermore, high triglyceride levels are linked to hyperviscosity syndrome and pre-eclampsia. Because therapeutic options are restricted during pregnancy, omega-3 fatty acids are the preferred treatment due to their safety and efficacy. They function by decreasing hepatic triglyceride secretion and enhancing lipoprotein lipase activity.

Abstract citation ID: lvag096.1028

EP575 - ECE_1616 - Metabolic dysfunction–associated steatotic liver disease and testosterone serum levels: converging evidence from real-world observational data and meta-analysis

Giorgia Spaggiari[1,2,3], Leonardo Dalla Valentina[1], Cristina Felicani[4], Filippo Gabrielli[4,5], Simonetta Lugari[4], Antonio Granata[2,3], Manuela Simoni[1,2], Paolo Ventura[4,5], Fabio Nascimbeni[4,5] and Daniele Santi[1,2,3]
[1]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [2]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [3]Unity of Andrology and Sexual Medicine of the Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [4]Unit of Internal Medicine and Metabolism, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [5]Department of Maternal-Infantile and Adult Medical and Surgical Sciences, University of Modena and Reggio Emilia, Modena, Italy

Background: Low testosterone has been increasingly associated with metabolic dysfunction–associated steatotic liver disease (MASLD), yet the strength, direction, and clinical relevance of this relationship remain incompletely defined, particularly with respect to liver fibrosis.

Aim of the study: To investigate the association between male hypogonadism and MASLD through a dual approach, combining a real-world observational study with a systematic meta-analysis of the available literature, and to explore the potential impact of testosterone replacement therapy (TRT).

Methods: A prospective, cross-sectional, case–control observational study was carried out, including 75 men referred for sexual dysfunction or infertility, stratified into hypogonadal ($n = 59$) and eugonadal ($n = 16$) groups according to baseline testosterone serum levels. MASLD was assessed using indirect indices (Hepatic Steatosis Index, Fatty Liver Index), qualitative ultrasound, and controlled attenuation parameter (CAP), while liver fibrosis was evaluated by transient elastography and 2D shear-wave elastography. Hypogonadal men were further classified according to TRT status. The testosterone/MASLD relationship was subsequently assessed in a meta-analysis of 28 cross-sectional and longitudinal studies available in the literature.

Results: MASLD prevalence was significantly higher in hypogonadal men than in controls when combining ultrasound and biochemical criteria (85.5% vs 50.0%, $P = .023$). Liver fibrosis, assessed by imaging techniques, was detected exclusively in hypogonadal patients (18.6% vs 0%, $P = .057$). Body mass index (BMI) emerged as the strongest predictor of both MASLD and fibrosis ($P < .001$ and $P = .011$), particularly in testosterone-naïve men ($P < .001$ and $P = .033$), whereas this association was attenuated in patients receiving TRT ($P = .166$ and $P = .130$). The meta-analysis (1636 hypogonadal vs 4587 eugonadal men) confirmed a significantly higher prevalence of MASLD among hypogonadal men compared with eugonadal controls ($P = .001$), independent of age ($P = .274$) and BMI ($P = .219$).

Conclusions: This dual-approach study confirms a bidirectional association between male hypogonadism and MASLD. Real-world data support meta-analytic evidence and suggest

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

that testosterone deficiency contributes to hepatic steatosis and fibrosis mainly through increased adiposity, while TRT may mitigate liver risk by modulating body composition and metabolic dysfunction.

Abstract citation ID: lvag096.1029

EP576 - ECE_1353 - Linking pediatric obesity to youth-onset type 2 diabetes: integrated longitudinal and cross-sectional evidence from population-based studies worldwide

Ashraf Soliman, Manal Musallam, Fawziya Alyafei, Nada Alaaraj, Noor Hamed and Shayma Ahmed
Pediatric Endocrinology, Hamad Medical Center, Doha, Qatar

Background: Youth-onset type 2 diabetes mellitus (T2DM) has emerged as a major global public health concern over the past two decades, paralleling the rapid rise in childhood and adolescent obesity. Although pediatric obesity surveillance is widely available across countries, population-based data on youth-onset T2DM are largely confined to regions with established registries and national audits.

Objective: To synthesize longitudinal and cross-sectional epidemiological evidence examining the association between pediatric obesity prevalence and youth-onset T2DM incidence across countries, using validated population-based studies published over the past 20 years.

Methods: A structured synthesis of PubMed-indexed literature published between 2005 and 2025 was conducted, restricted to children and adolescents younger than 20 years. Longitudinal data were obtained from population-based youth T2DM registries and national audits, including SEARCH (USA), Manitoba (Canada), the England/Wales National Paediatric Diabetes Audit, Israel, Australia, and New Zealand. These data were paired with national and global pediatric obesity surveillance sources (NCD-RisC, WHO, and national health surveys). Cross-sectional evidence was derived from national audits, cohort studies, and systematic reviews reporting obesity prevalence among youth with T2DM. Associations and trends were evaluated qualitatively and through comparative visualization.

Results: Longitudinal analyses consistently demonstrated parallel increases in pediatric obesity prevalence and youth-onset T2DM incidence within individual countries. In the United States, pediatric obesity prevalence increased from approximately 17% to over 20% between 2005 and 2018, while youth-onset T2DM incidence rose from about 3.8 to 6.8 per 100 000 youth per year. In Canada (Manitoba), youth-onset T2DM incidence nearly doubled (from 16.0 to over 30 per 100 000 per year) within less than a decade, coinciding with rising childhood obesity, particularly among Indigenous populations. Similar upward, though lower-magnitude, trends were observed in England/Wales ($\approx$1.2 to $\approx$2.6 per 100 000 per year), Israel, Australia, and New Zealand, all mirroring national increases in pediatric obesity. Cross-sectionally, the obesity–T2DM association was striking: across countries, 75-95% of children and adolescents with T2DM were overweight or obese. A global meta-analysis confirmed that approximately three-quarters of youth with T2DM have obesity.

Conclusions: Integrated longitudinal and cross-sectional evidence demonstrates a robust and consistent association between rising pediatric obesity and the expanding burden of youth-onset T2DM. Obesity precedes increases in T2DM incidence over time and is present in the majority of affected youth worldwide, underscoring pediatric obesity as the principal upstream driver of youth-onset T2DM and highlighting the urgent need for coordinated obesity prevention and strengthened international diabetes surveillance.

Abstract citation ID: lvag096.1030

EP577 - ECE_1784 - High prevalence of insulin resistance and its association with cardiovascular risk in adults with type 1 diabetes

Mohd Idris Diah[1], Hwee Ching Tee[2] and Hui Chin Wong[1]
[1]*Endocrinology and Diabetes, Internal Medicine, Hospital Tengku Ampuan Rahimah Klang, Klang, Malaysia;* [2]*Endocrinology and Diabetes, Internal Medicine, Queen Elizabeth II Hospital, Kota Kinabalu, Malaysia*

Background: Insulin resistance (IR), traditionally associated with type 2 diabetes, is increasingly recognised in individuals with type 1 diabetes mellitus (T1DM) and may contribute to excess cardiovascular disease (CVD) risk. Data on the burden and cardiometabolic implications of IR in Southeast Asian adults with T1DM remain limited. This study aimed to determine the prevalence of IR using the estimated glucose disposal rate (eGDR) and to examine its association with cardiovascular risk in a multi-ethnic Malaysian cohort.

Methods: This cross-sectional study recruited 127 adults with T1DM from two tertiary centres in Malaysia. Insulin resistance was assessed using eGDR, with values <8 mg·kg^{-1}·min^{-1} indicating IR. Ten-year CVD risk was estimated using the Steno Type 1 Risk Engine (ST1RE). Clinical, anthropometric, and biochemical data, including renal function and microvascular complications, were collected. Associations with IR were explored using univariable and multivariable logistic regression analyses.

Results: The prevalence of insulin resistance was 43.3%. Participants with IR were older and had significantly higher body mass index, waist circumference, systolic blood pressure, HbA1c, and triglyceride levels, alongside lower estimated glomerular filtration rate (eGFR), compared with those without IR (all $P < .05$). Insulin resistance was strongly associated with higher predicted CVD risk, with progressively lower mean eGDR values across low-, moderate-, and high-risk ST1RE categories ($P < .001$). In multivariable analysis, waist circumference (adjusted OR 1.27 per cm; 95% CI 1.15-1.40), systolic blood pressure (OR 1.11 per mmHg; 95% CI 1.05-1.18), HbA1c (OR 4.91 per 1%; 95% CI 2.63-9.14), and eGFR (OR 0.96 per mL/min/1.73 m^2; 95% CI 0.94-0.99) were independently associated with insulin resistance.

Conclusions: Insulin resistance is common among adults with T1DM and is independently associated with adverse metabolic and cardiorenal profiles, correlating with elevated predicted cardiovascular risk. Early identification of IR using eGDR and targeted intervention addressing central adiposity, blood pressure, glycaemic burden, and renal health may help reduce long-term cardiovascular complications in people living with T1DM.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1031

EP578 - ECE_1958 - A web-based screening tool for identifying metabolic risk in adults with type 2 diabetes

Alina Urbanovych and Nadiia Sidelnyk
Department of Endocrinology, Lviv National Medical University, Lviv, Ukraine

Background: Metabolic Health Check is a web-based tool that automatically calculates metabolic indices (BMI, waist-to-height ratio [WHtR], waist-to-hip ratio [WHR], the TyG index and FIB-4), performs a screening assessment of metabolic syndrome and excess body fat based on the 2025 Lancet Diabetes & Endocrinology Commission criteria for clinical obesity, and generates a standardised PDF report. To assess clinical relevance, a retrospective analysis of patients with type 2 diabetes mellitus (T2DM) was performed, as BMI does not always reflect true cardiometabolic risk in this population.

Aim: To evaluate the clinical value of the Metabolic Health Check, assess consistency between BMI and the TyG index, and examine the association between the TyG index and MASLD.

Materials and Methods: We performed a retrospective analysis of 129 adults with type 2 diabetes mellitus (T2DM). Patients were divided into two groups: without obesity (BMI <30 kg/m^2) and with obesity (BMI ≥30 kg/m^2), and stratified by TyG index categories (<8.5, 8.5-8.8, and ≥8.8). The prevalence of MASLD was assessed in BMI groups and TyG index categories. The TyG index was calculated using the formula TyG = ln[(TG (mmol/L) × 88.57) × (FPG (mmol/L) × 18)/2].

Results: The study included 129 patients. Mean BMI was 25.87 ± 0.37 kg/m^2 in the group without obesity ($n = 63$) and 35.13 ± 0.45 kg/m^2 in the obesity group ($n = 66$). High TyG index (≥8.8) was observed in 107/129 (82.9%) patients and occurred with similar frequency in patients with BMI <30 and ≥30 kg/m^2 (82.5% vs 83.3%; Fisher's exact $P = 1.000$). MASLD was present in 40/63 (63.5%) patients with BMI <30 kg/m^2 and in 57/66 (86.4%) patients with BMI ≥30 kg/m^2 ($P = .004$). The prevalence of MASLD increased across TyG index categories: 35.7% for TyG <8.5, 62.5% for TyG 8.5-8.8, and 81.3% for TyG ≥8.8 ($P = .001$). TyG ≥8.8 was associated with significantly higher odds of MASLD compared with TyG <8.5 (OR = 7.83; 95% CI 2.37-25.9; Fisher's exact $P < .001$).

Conclusions: The results indicate a substantial prevalence of hidden metabolic risk, as high TyG index (≥8.8) was found with similar frequency in patients without obesity and in those with obesity by BMI. The high prevalence of MASLD in the BMI <30 kg/m^2 group (63.5%) underscores the need for rapid digital metabolic screening tools based on available clinical and laboratory parameters.

Abstract citation ID: lvag096.1032

EP579 - ECE_1636 - Serum Galectin-3 level alteration in type 2 diabetes mellitus and its relation to diabetes complications

Samir Assaad[1], Eman Zaky Ahmed Abdelaziz Azzam[1], Raghda Taleb[2], Aisha Thabet[1] and Ahmed Abdelhameed Osman[1]
[1]*Endocrinology Unit, Department of Internal Medicine, Alexandria Faculty of Medicine, Alexandria, Egypt;* [2]*Alexandria, Egypt*

Introduction: Galectin-3 (Gal-3) is a beta-galactosidase-binding lectin implicated in the regulation of inflammation, fibrosis, and oxidative stress. While its role in heart failure is well-recognized, its association with the broad spectrum of diabetic complications remains under investigation. This study aimed to evaluate serum Gal-3 levels in patients with Type 2 Diabetes Mellitus (T2DM) compared to healthy controls and to assess the relationship between Gal-3 levels and specific microvascular and macrovascular diabetic complications.

Methods: A cross-sectional study was conducted at Alexandria Main University Hospital involving 40 patients with T2DM and 40 age- and sex-matched healthy controls. All participants underwent detailed clinical assessment and laboratory investigations, including fasting blood glucose, HbA1c, lipid profile, renal function tests (urea, creatinine, albumin-creatinine ratio), and serum Gal-3 measurement via enzyme-linked immunosorbent assay (ELISA). Diabetic complications, including chronic kidney disease (CKD), ischemic heart disease (IHD), heart failure, diabetic retinopathy, and history of amputation were documented.

Results: Serum Gal-3 levels were significantly higher in the T2DM group (mean 5.93 ± 1.97 ng/mL) compared to the control group (2.45 ± 0.45 ng/mL; $P < .001$). Within the T2DM group, significantly elevated Gal-3 levels were observed in patients with CKD ($P = .04$), IHD ($P < .001$), heart failure ($P = .041$), and amputation ($P < .001$). No significant correlation was found between serum Gal-3 levels and HbA1c, lipid profile parameters, or the total number of comorbidities per patient. However, renal function markers (urea, creatinine, and ACR) were significantly correlated with the number of comorbidities.

Conclusions: Serum Gal-3 is significantly elevated in T2DM patients and is associated with the presence of major complications, particularly CKD and cardiovascular disease. These findings suggest that Gal-3 may serve as a biomarker for fibrosis-related organ damage in diabetes, independent of glycemic control. Further large-scale studies are warranted to validate its prognostic value in monitoring disease progression.

Abstract citation ID: lvag096.1033

EP581 - ECE_1176 - Diabetes distress in adults with type 1 diabetes: The role of structured education, technology satisfaction and hypoglycaemia fear

Niamh Moloney, Kate Murphy and James Ryan
Cork, Ireland

Background: Diabetes distress is a common but underrecognised psychological burden in people with type 1 diabetes mellitus (T1DM). We examined the relationship between structured education, technology satisfaction, and fear of hypoglycaemia with diabetes distress.

Methods: A cross-sectional study of 62 adults with T1DM was conducted. Participants completed the 17-item Diabetes Distress Scale (DDS17) and surveys assessing technology satisfaction (1-5), fear of hypoglycaemia (1-5), and completion of structured education (eg, DAFNE). Clinical data included HbA_1c, age, complications, insulin regimen, and monitoring method. Elevated distress was defined as DDS17 ≥2. Independent-samples t-tests and Pearson correlations assessed associations. A decision tree model identified key predictors of elevated distress.

Results: Thirty-seven percent of patients reported elevated distress. Completion of structured education was associated with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

significantly lower mean DDS17 scores compared to non-completers ($P = .029$). Technology satisfaction ($r = +0.06$, $P = .67$) and fear of hypoglycaemia ($r = -0.10$, $P = .42$) were not significantly associated with distress. The decision tree model achieved 68.8% accuracy, with HbA_1c, age, and structured education as the strongest predictors.

Conclusions: Structured diabetes education appears protective against elevated distress in adults with T1DM. In this cohort, technology satisfaction and fear of hypoglycaemia did not independently predict distress. These findings support incorporating structured education and routine psychosocial screening into T1DM care. Larger studies are needed to refine predictive models of distress.

Abstract citation ID: lvag096.1034

EP582 - ECE_1344 - Experience with alpelisib in a secondary care hospital

Paloma Gonzalez Lazaro, Juan Antonio Mascuñana Calle, María Sanchez Crespo Juarez, María Lizano Sanchez Villacañas, Gerogina Vela Florensa and Ines Gomez García
Hospital General La Mancha Centro, Alcázar de San Juan, Spain

Introduction: Alpelisib is an alpha-selective PI3K (phosphatidylinositol 3-kinase) inhibitor, which activating mutation is present in patients with advanced breast cancer. Its main adverse effect and cause of treatment discontinuation is hyperglycemia; this is a class effect related to its mechanism of action, mediated by increased glycogenolysis and decreased peripheral glucose uptake.

Objectives: To review cases of patients treated with alpelisib, the treatment they received, and whether treatment discontinuation was necessary.

Materials and Methods: A retrospective descriptive study of 4 patients with advanced breast cancer treated with alpelisib at Mancha Centro Hospital from September 2024 to September 2025.

Results: The mean age of the patients was 61.34 years. None had a prior diagnosis of diabetes mellitus (DM). The mean BMI was 24.62 kg/m^2, and baseline HbA1c prior to treatment initiation was 5.5%. All patients developed hyperglycemia, and all required non-insulin antidiabetic treatment (2 with metformin and sitagliptin, 1 with dapagliflozin, and 1 with pioglitazone). In 3 patients, long-acting insulin was also required. The initial dose of alpelisib was 300 mg/day, and in 3 cases the dose was reduced due to grade 3 hyperglycemia (>250 mg/dL). The mean duration of treatment was 6.2 months. Two patients discontinued treatment due to disease progression, 1 patient died, and 1 patient is currently continuing treatment. There were no cases of diabetic ketoacidosis, and in all patients who discontinued treatment, blood glucose levels returned to the normal range.

Conclusions: It is necessary to monitor blood glucose levels in all patients starting alpelisib treatment, as most will develop hyperglycemia. It is important to establish management protocols and a multidisciplinary approach to avoid discontinuing a treatment with promising outcomes.

Abstract citation ID: lvag096.1035

EP583 - ECE_3374 - Features of neurotransmitter supply in patients with type 2 diabetes mellitus with polymorphisms of folate cycle genes in the post-covid state

Kateryna Komisarenko[1,2,3]
[1]*Kyiv, Ukraine;* [2]*The State Institution «V.P. Komisarenko Institute of Endocrinology and Metabolism», Kyiv, Ukraine;* [3]*The State Institution «V.P. Komisarenko Institute of Endocrinology and Metabolism», Kyiv, Ukraine*

Background: The folate cycle plays a key role in one-carbon metabolism, providing methyl groups for DNA synthesis, epigenetic regulation, and neurotransmitter production. Dysregulation of this pathway, particularly in the presence of genetic polymorphisms of folate cycle enzymes, may lead to elevated homocysteine levels and impaired serotonergic activity. Patients with type 2 diabetes mellitus (T2DM) recovering from COVID-19 frequently report persistent neurocognitive and affective symptoms, suggesting underlying neuro-metabolic disturbances.

Objective: To investigate features of neurotransmitter metabolism (serotonin and homocysteine) in post-COVID patients with T2DM carrying polymorphisms of folate cycle genes and to assess the impact of different antidiabetic treatment strategies on these parameters.

Methods: A total of 127 individuals aged 40-70 years were examined: 43 post-COVID patients with T2DM, 34 post-COVID patients without diabetes, and 50 healthy controls. Serum levels of serotonin, homocysteine, and folic acid were measured at baseline and six months after recovery from COVID-19. Genotyping for MTHFR (C677T, A1298C), MTR (A2756G), and MTRR (A66G) polymorphisms was performed using PCR-based methods. Patients with T2DM were subdivided according to therapy: subgroup 1a (metformin + SGLT2 inhibitors, $n = 25$) and subgroup 1b (metformin and/or sulfonylureas, $n = 18$). Statistical analysis included correlation, regression, and ANOVA.

Results: Six months after COVID-19, patients with T2DM demonstrated a significant reduction in homocysteine levels (mean decrease 5-10 µmol/L), an increase in serum serotonin (approximately +30 ng/mL), and normalization of folic acid concentrations. The proportion of patients with normal homocysteine levels increased from 30% to 86% in subgroup 1a and from 38% to 83% in subgroup 1b. Changes in homocysteine strongly depended on baseline values ($R^2 = 0.92$). Baseline serotonin levels correlated with body mass index ($R^2 = 0.697$). The MTRR A66G polymorphism was associated with lower serotonin levels and more pronounced post-COVID neurocognitive symptoms. Regression analysis confirmed a significant influence of both therapy type and folate cycle gene variants on serotonin dynamics ($F = 11.31$, $P < .05$).

Conclusions: Genetic polymorphisms of folate cycle enzymes contribute to neurotransmitter imbalance in post-COVID patients with T2DM. Combination therapy with metformin and SGLT2 inhibitors provides more effective normalization of homocysteine and serotonin levels compared with conventional treatment and may support neurocognitive recovery. These findings highlight the importance of personalized metabolic strategies in post-COVID diabetes management.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1036

EP585 - ECE_2757 - Heterogeneous fatty acid–binding protein 4 (FABP4) responses after Roux-en-Y gastric bypass reveal adipokine remodeling dissociated from weight loss, inflammation, and incretin dynamics

Bedia Fulya Calikoglu[1], Handan Hanım Orskaya[2], Gulsah Yenidunya Yalin[3], Umut Barbaros[4], Ilknur Bingul[5] and Fatih Aydin[5]

[1]*Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, Istanbul University, Istanbul, Türkiye;* [2]*Department of Medical Biology, Istanbul Health and Technology University, Istanbul, Türkiye;* [3]*Istanbul Medical Faculty, Department of Internal Medicine, Division of Endocrinology and Metabolism, Istanbul University, Istanbul, Türkiye;* [4]*Istanbul Medical Faculty, Department of General Surgery, Istanbul University, Istanbul, Türkiye;* [5]*Istanbul Medical Faculty, Department of Medical Biochemistry, Istanbul University, Istanbul, Türkiye*

Background: Fatty acid–binding protein 4 (FABP4) is an adipokine closely linked to adipose tissue mass, low-grade inflammation, and cardiometabolic risk. Following bariatric surgery, FABP4 is generally expected to decrease in parallel with weight loss and improvements in inflammation. However, whether postoperative FABP4 dynamics uniformly reflect these changes or exhibit heterogeneous patterns independent of anthropometric and hormonal adaptations remains unclear.

Methods: Twenty-eight adults undergoing Roux-en-Y gastric bypass (RYGB) were prospectively followed at baseline, 3 months, and 6 months. Anthropometric measures, body composition, metabolic indices, hsCRP, IL-6, fasting GLP-1 and PYY, and serum FABP4 were assessed. The 3-month time point was included to capture early postoperative metabolic and adipokine dynamics, whereas primary analyses focused on baseline-to-6-month changes to reflect more stable biological adaptations. Patients were classified as FABP4 responders (decrease from baseline to 6 months) or rebound/non-responders. Longitudinal changes were analyzed using Friedman tests, and between-group comparisons were performed using nonparametric methods.

Results: RYGB induced early and progressive anthropometric improvement, with BMI decreasing from 51.5 [48.1-55.2] kg/m^2 at baseline to 42.8 [39.6-46.9] at 3 months and 35.6 [32.4-38.9] at 6 months ($P < .001$). Systemic inflammation improved in parallel: IL-6 declined from 3.18 [2.27-4.44] pg/mL at baseline to 2.95 [2.31-3.82] at 3 months and 1.68 [0.96-2.95] at 6 months ($P = .00015$), while hsCRP decreased significantly over time ($P < .001$). In contrast, FABP4 trajectories demonstrated marked inter-individual variability. At 3 months, FABP4 changes showed no consistent directional pattern, despite early weight loss and improvement in inflammation. By 6 months, 46% of patients exhibited no decrease or a rebound in FABP4 levels. FABP4 responders experienced less pronounced BMI reduction compared with rebound/non-responders (ΔBMI −14.2 [−16.8 to −11.9] vs −18.6 [−21.4 to −15.1] kg/m^2; $P = .03$). Changes in FABP4 were not significantly correlated with changes in BMI, fat mass, hsCRP, or IL-6 (all $P > .05$). Fasting GLP-1 and PYY levels did not differ between FABP4 response groups.

Conclusions: Despite expected improvements in weight and systemic inflammation after RYGB, FABP4 responses are heterogeneous and only weakly related to anthropometric, inflammatory, or fasting incretin changes. These findings suggest that FABP4 reflects individualized adipose tissue–specific adaptive remodeling rather than a simple surrogate of weight loss or of improvements in inflammation following bariatric surgery.

Abstract citation ID: lvag096.1037

EP586 - ECE_1480 - AI-enhanced ultrasound for early detection of diabetic nephropathy

Rostyslav Bubnov[1,2]

[1]*Zabolotny Institute of Microbiology and Virology, Kyiv, Ukraine;* [2]*Ultrasound, Clinical Hospital 'Pheophania', Kyiv, Ukraine*

Background: Diabetic nephropathy (DN) is a leading cause of chronic kidney disease (CKD) and a major contributor to cardiovascular and metabolic morbidity. Conventional renal ultrasound is widely available but remains operator-dependent and insufficiently standardized for detecting early metabolic and microvascular renal changes. A structured ultrasound-based framework integrating morphological, vascular, and biomechanical features may improve early identification of diabetic renal injury.[1-3] Artificial intelligence (AI) offers potential to enhance standardization while preserving expert-driven interpretation.

Objectives: To evaluate the feasibility of AI-assisted renal ultrasound analysis for detecting and stratifying diabetic nephropathy using a structured, patented ultrasound-based framework, with human expert control over anatomical sign validation and final diagnosis.

Methods: Renal ultrasound examinations were analyzed in 40 patients with type 2 diabetes mellitus and suspected diabetic nephropathy. Imaging was performed using B-mode ultrasound, intrarenal Doppler, and shear-wave elastography (SWE), following a structured ultrasound framework integrating predefined anatomical and functional criteria. Assessed features included cortical echogenicity and texture, corticomedullary differentiation, renal contour, parenchymal thickness, intrarenal resistive index (RI), and SWE-derived stiffness distribution. An AI-assisted analytical layer quantified image features, highlighted candidate pathological signs, and proposed pattern probabilities. Each detected feature and overall diagnostic classification were verified or corrected by an expert operator. Ultrasound patterns were differentiated from other metabolic CKD phenotypes, including hypertensive and obesity-related nephropathy, using combined structural, vascular, and biomechanical criteria.

Results: AI-assisted analysis consistently identified ultrasound features characteristic of diabetic nephropathy, including diffuse cortical echogenicity increase, gradual loss of corticomedullary differentiation, elevated intrarenal RI, and relatively homogeneous cortical stiffness on SWE. Human–AI synthesis improved consistency of feature recognition and supported classification of diabetic nephropathy as a distinct metabolic renal phenotype. Expert oversight was essential for correct anatomical interpretation, particularly in patients with overlapping metabolic comorbidities.

Conclusions: AI-assisted renal ultrasound analysis, applied within a structured ultrasound-based framework, enhances reproducibility and standardization of diabetic nephropathy assessment. This human-controlled AI approach supports early detection and differentiation of diabetic renal injury within the spectrum of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

metabolic CKD, offering a noninvasive tool for precision stratification in patients with diabetes.

References

1. Bubnov R. Ultrasound diagnosis of diabetic nephropathy. *Endocr Abstracts*. 2024;99:P475. https://doi.org/10.1530/endoabs.99.P475
2. Bubnov R. Ultrasound imaging patterns of kidney disease in patients with metabolic syndrome. *Nephrol Dial Transplant*. 2023;38(Supplement_1):gfad063c_4869. https://doi.org/10.1093/ndt/gfad063c_4869
3. Bubnov R, Chaykovska I, Kotsyuba R. Ultrasound monitoring for chemotherapy complications in diabetic patients. *Endocr Abstracts*. 2025;54(110):EP378. https://doi.org/10.1530/endoabs.110.EP369

Abstract citation ID: lvag096.1038

EP589 - ECE_2465 - Effects of anti-osteoporotic drugs on MASLD and body composition: preliminary results of a one-year study

Maria-Eleni Chondrogianni[1,2], Ioannis Kyrou[3], Theodoros Androutsakos[4], Maria-Loukia Koutsompina[4], Christina-Maria Flessa[2], Despina Polichroniadi[5], Maria Nomikou[5], Anna Angelousi[6], Gregory Kaltsas[1], Efstathios Efstathopoulos[5], Maria Dalamaga[2], Harpal S. Randeva[3] and Eva Kassi[1,2]

[1]Endocrine Unit, 1st Department of Propaepeudic Internal Medicine, Laiko Hospital, National and Kapodistrian University of Athens, Athens, Greece; [2]Department of Biological Chemistry, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [3]University Hospitals Coventry and Warwickshire NHS Trust, Coventry CV2 2DX, United Kingdom; [4]Department of Pathophysiology, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [5]Department of Radiology, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [6]Unit of Endocrinology1st Department of Internal Medicine, National and Kapodistrian University of Athens, Athens, Greece

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is one of the most common causes of chronic liver disease. Osteoporosis is a prevalent disease characterized by decreased bone density and disrupted bone structure, resulting in bone fragility and increased fracture risk. Denosumab is a monoclonal IgG 2 antibody used as a treatment of osteoporosis, since it binds to RANKL, inhibiting RANK activation. Recent research has shown that the increase of RANKL expression in hepatocytes may be related to inflammation and fatty infiltration, and thus, denosumab may offer an additional therapeutic option for the treatment of MASLD. The aim of this study is to assess the effects of certain approved anti-osteoporotic treatments (denosumab and alendronate) on MASLD and on the body composition.

Methods: We included 38 patients (mean age 63.61 ± 8.06) with osteoporosis and MASLD. Twenty patients received anti-osteoporotic treatment with denosumab and 18 with alendronate. Patients were evaluated at baseline and after 1 year of treatment. Liver transient elastography was performed to assess hepatic steatosis using controlled attenuation parameter (CAP) and to estimate the stage of fibrosis through liver stiffness measurements (FIB). Body composition and bone mineral density (BMD) were evaluated by dual-energy X-ray absorptiometry (DXA). We performed paired t-tests within each treatment group to compare baseline and one-year follow-up measurements and P-value < .05 was considered statistically significant.

Results: There was no statistically significant change regarding CAP either among patients treated with denosumab or alendronate. Moreover, no statistically significant change was observed in FIB in either group. However, regarding patients treated with denosumab paired t-test analysis showed a statistically significant reduction in body fat percentage after one year of treatment ($P = .039$), while there was no statistically significant change in patients treated with alendronate.

Conclusions: In this study, treatment for osteoporosis with denosumab and alendronate demonstrated a comparable profile regarding hepatic steatosis and fibrosis as assessed by transient elastography. The reduction in body fat percentage in patients treated with denosumab may suggest a potential metabolic effect of this drug and the absence of significant differences regarding MASLD may be related to the small sample size and the relatively short follow-up period.

References

1. Polyzos SA, Goulas A. Treatment of nonalcoholic fatty liver disease with an anti-osteoporotic medication: a hypothesis on drug repurposing. *Med Hypotheses* 2021;146:110379. https://doi.org/10.1016/j.mehy.2020.110379
2. Chondrogianni ME, Kyrou I, Androutsakos T et al. Treatment of nonalcoholic fatty liver disease with an anti-osteoporotic medication: A hypothesis on drug repurposing. *Front Endocrinol (Lausanne)*. 2024;15:1344376. https://doi.org/10.3389/fendo.2024.1344376

Abstract citation ID: lvag096.1039

EP590 - ECE_2729 - Associations between lipoprotein(a) and hepatic steatosis in type 2 diabetes and partial lipodystrophy: a cross-sectional study

Stella Pigni[1], Sabrina Tini[2], Stefano Celano[1], Jessica Baima[2], Valentina Antoniotti[2], Francesco Bruggi[1], Paolo Amedeo Tillio[3], Cristina Rigamonti[1], Roberta Rolla[2] and Flavia Prodam[2]

[1]Department of Translational Medicine, University of Eastern Piedmont, Novara, Italy; [2]Department of Health Sciences, University of Eastern Piedmont, Novara, Italy; [3]Clinical Chemistry Laboratory, Maggiore della Carità Hospital, Novara, Italy

Background: Lipoprotein(a) [Lp(a)] is a genetically determined lipoprotein primarily implicated in cardiovascular risk. Lipodystrophy syndromes are rare disorders characterized by adipose tissue deficiency and severe metabolic complications, including insulin-resistant diabetes, dyslipidemia, and a high prevalence of metabolic dysfunction–associated steatotic liver disease (MASLD). Recent studies have reported an inverse association between Lp(a) and MASLD. However, data on Lp(a) levels and their relationship with liver disease in lipodystrophy are lacking.

Methods: Cross-sectional study including 32 patients with partial lipodystrophy (PLD; 90.6% females, median [IQR] age 49 [25]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

years) and 67 patients with obesity and type 2 diabetes (T2D; 50.7% females, age 57 [10] years). Hepatic steatosis prevalence was assessed by abdominal ultrasound. In a subset of patients ($n = 19$ PLD, $n = 21$ T2D), controlled attenuation parameter (CAP) and liver stiffness (LS) were also assessed by transient elastography. Lp(a) levels were measured using a standardized assay.

Results: Compared with T2D patients, PLD individuals were younger ($P = .02$), predominantly female ($P < .001$), with a worse metabolic profile (HbA1c 7.6 [2.5] vs 6.5 [1], $P = .003$; triglycerides 159 [169] vs 132 [121] mg/dL, $P < .01$), and a higher prevalence of ultrasound-detected hepatic steatosis (81 vs 64%, $P = .011$). Median [IQR] Lp(a) levels did not differ significantly between PLD and T2D (9.5 [28.5] vs 19 [56] nmol/L, $P > .10$) with more than 80% of individuals in both groups falling into the low-risk Lp(a) category (<75 nmol/L). However, PLD patients showed a higher prevalence of very low Lp(a) concentrations (≤10 nmol/L, $P < .02$). In T2D, Lp(a) levels were inversely associated with hepatic steatosis severity as assessed by CAP ($P = .003$). This association remained significant in multivariable models adjusting for age, lipids, HbA1c, lipid-lowering and antidiabetic therapies ($P < .01$). A moderate inverse correlation between Lp(a) and LS was also observed, particularly in patients aged ≥50 years and in those with hypertension ($P < .05$). No association between Lp(a), leptin, and hepatic parameters was observed in PLD.

Conclusions: Higher Lp(a) levels were associated with lower hepatic steatosis severity in patients with T2D, but not in lipodystrophy. The enrichment of very low Lp(a) levels in PLD, potentially reflecting their distinct metabolic milieu, may limit the utility of Lp(a) as a biomarker of cardiovascular and liver disease in this setting. Further studies are needed to clarify the role of Lp(a) in metabolic liver disease across different insulin-resistant phenotypes.

Abstract citation ID: lvag096.1040

EP591 - ECE_3116 - Coexistence of multiple sclerosis and Grave's disease in a patient with type 1 diabetes mellitus: a rare case with challenging management

Vasiliki Antonopoulou, Aggeliki Kyriakou, Kalliopi Pantelia, Olga Papalou, Panagiotis Karageorgiou, Marinella Tzanela and Theodora Stratigou
Department of Endocrinology "D. Ikkos"- Diabetes Center-EndoERN-Evangelismos General Hospital, Athens, Greece

Background: Type 1 diabetes mellitus (T1DM) is an autoimmune chronic disease which is characterized by autoimmune destruction of pancreatic β-cells. Patients with T1DM are at increased risk of additional autoimmune diseases, most commonly autoimmune thyroid disease, reflecting shared genetic factors and immunopathogenic mechanisms. In contrast, the coexistence of T1DM and multiple sclerosis (MS) is less frequent, despite suggesting evidence of overlapping immune pathways. The simultaneous presence of T1DM, Graves' disease (GD), and MS in the same patient represents a rare but clinically significant manifestation.

Case presentation: We report a case of a 49-year-old patient with a history of T1DM diagnosed at the age of 4 years old initially treated with multiple daily insulin injections, with suboptimal glycemic control and recurrent hypoglycemic episodes. At the age of 26 years old she was diagnosed with MS with optic neuritis and right upper extremity weakness. Brain MRI revealed demyelinating lesions. She was initially treated with Interferon beta. Due to multiple relapses, she received fingolimod and later repeated courses of intravenous corticosteroids and is currently treated with cladribine. At the age of 47, the patient developed clinical and biochemical features of hyperthyroidism. Laboratory evaluation confirmed GD (TSH 0.01 μU/mL, T3 443 ng/dL, FT4 6.1 ng/dL, TSH receptor antibodies 18.7 U/L). Treatment with thiamazole was initiated, followed by radioactive iodine (RAI) therapy. One month after RAI, she developed overt hypothyroidism (TSH 38 μU/mL) and levothyroxine replacement was started. Six months later, she presented symptoms of hyperthyroidism and developed Graves' orbitopathy. Laboratory tests showed suppressed TSH (<0.004 μU/mL) with normal FT4 and T3 levels, with markedly elevated thyroid-stimulating immunoglobulins (TSI 29.79 U/L). Thyroid ultrasound demonstrated increased vascularity. Despite discontinuation of levothyroxine, hyperthyroid symptoms persisted and TSH suppression remained. Low dose thiamazole was re-introduced with thyroid function showing marked fluctuations thereafter. Regarding her diabetes, glycemic control significantly improved after initiation of an automated insulin delivery system. Notably, from her family history, mother has also MS.

Conclusions: This case describes a rare coexistence of multiple autoimmune diseases with an unstable course of Graves' disease following RAI therapy. It highlights the complex interplay of autoimmune processes across endocrine and other systems and indicates the challenges in management of patients with overlapping autoimmune conditions. Long term monitoring, close follow up and individualized multidisciplinary therapeutic approach are essential for the management of these complex, clinically significant cases.

Abstract citation ID: lvag096.1041

EP593 - ECE_3589 - Therapeutic challenges of immune checkpoint inhibitor-induced type 1 diabetes within polyendocrinopathy: two case reports

Gergő Csitári
DBC-SZIEOK, Budapest, Hungary

Immune checkpoint inhibitors (ICIs) are increasingly used, highly effective antineoplastic agents that can induce a broad spectrum of immune-mediated endocrine adverse events involving multiple glands. Among these, hypophysitis, autoimmune thyroiditis and primary adrenal insufficiency are the most frequently reported entities, occurring either in isolation or as part of complex polyendocrinopathies. Development of endocrine toxicities has been associated with improved cancer outcomes, yet autoimmune insulitis with new-onset type 1 diabetes mellitus (T1DM) remains a relatively rare but clinically demanding complication.

This abstract presents two patients treated with combined anti-CTLA-4 and anti-PD-1 therapy who developed ICI-induced T1DM as the first immune-mediated endocrine event, followed by additional endocrinopathies, creating major challenges in glycaemic management.

The first case is a 52-year-old man with stage IV malignant melanoma treated with ipilimumab plus nivolumab. Before the fourth

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

treatment cycle, routine testing revealed asymptomatic but marked hyperglycaemia without ketoacidosis. Under multiple daily human insulin injections, glycaemic control initially stabilised, allowing ambulatory follow-up. Within one month, he was additionally diagnosed with adrenal insufficiency and hypothyroidism, necessitating glucocorticoid and levothyroxine replacement. Concomitant hormone substitution was accompanied by highly labile glycaemia at home, prompting transition to analogue basal–bolus insulin therapy. On maintenance nivolumab, his melanoma exhibits substantial regression and glucose control is acceptable, although he repeatedly declines insulin pump therapy and continuous glucose monitoring.

The second case is a 55-year-old woman with malignant pleural mesothelioma who also received ipilimumab plus nivolumab. Following the second cycle, severe multisystem immune-related toxicity with prominent urticarial manifestations led to discontinuation of immunotherapy. She was subsequently admitted repeatedly for diabetic ketoacidosis and painful oesophageal candidiasis. Under empiric systemic glucocorticoid treatment, glycaemic control proved extremely unstable with frequent hypoglycaemic episodes, which improved after tapering and switching methylprednisolone to hydrocortisone in the absence of clear clinical adrenal insufficiency. Autoimmune thyroiditis with hypothyroidism was diagnosed and treated with levothyroxine, while an ACTH stimulation test off steroids ultimately excluded primary adrenal insufficiency. Because of severely impaired metabolic control (HbA1c 11.6%), she was transitioned to analogue basal–bolus insulin in an inpatient setting, resulting in marked attenuation of glucose excursions and resolution of hypoglycaemia, though further basal insulin titration and planned CGM are required.

These cases illustrate that ICI-induced T1DM, particularly when embedded in evolving polyendocrinopathy, demands intensive, dynamically adjusted insulin therapy and close interdisciplinary follow-up to balance oncological benefit and endocrine safety.

Abstract citation ID: lvag096.1042

EP596 - ECE_2764 - A subgroup analysis of phase 3 study of semaglutide injection in type 2 diabetes mellitus patients aged <40 years, 40 to <50 years and ≥50 years

Dipesh Sonawane[1], Unnikrishnan Gopalkrishnan[2], Ameya Joshi[3], Richa Giri[4], Shalin Shah[5], Jitendra Shukla[6], Sanjiv Maheshswari[7], M.C. Rekha[8], Manish Singh[9], Aditya Bari[10], Niranjan Pathak[11], Akash Shah[12], Shweta Bhandari[13], Ambanna Gowda[14], C. Ambrish[15], Pravin Supe[16], Bharat Das[17], Prabhat Sharma[18], Mehul Virani[19], Prakash Kurmi[20], Gayatri Ghanekar[21], Mani Dasari[22], Bansidhar Sahoo[23], Sanjay Jangid[24], Manoj Srivastava[25], Prakash Shende[26], Sandesh Patil[27], Avinash Kumbhar[28], Shrikant Deshpande[29], C. Madhusudhan[30], Nitesh Patel[31], Apurva Shetty[1], Dipak Patil[1], Pravin Ghadge[1] and Suyog Mehta[1]

[1]Sun Pharma Laboratories Limited, Mumbai, India; [2]Chellaram Diabetes Institute, Pune, India; [3]Bhaktivedanta Hospital and Research, Thane, India; [4]GSVM Medical College, Kanpur, India; [5]Ratan Multi-speciality Hospital, Ahmedabad, India; [6]Motilal Nehru Medical College, Prayagraj, India; [7]Jawahar Lal Nehru Medical College, Ajmer, India; [8]Mandya Institute of Medical Science, Mandya, India; [9]Maya Hospital and Maternity Centre, Kanpur, India; [10]Pulse Multispeciality Hospital, Pune, India; [11]Ojas Multispeciality Hospital, Pune, India; [12]Health 1 Super Speciality Hospital, Ahmedabad, India; [13]Vincare Hospital, Bathinda, India; [14]Citizen Hospital, Bangalore, India; [15]Medstar Speciality Hospital, Bangalore, India; [16]Supe Heart & Diabetes Hospital & Research Centre, Nashik, India; [17]Sparsh Hospitals and Critical Care Private, Bhubaneshwar, India; [18]Maharaja Agrasen Superspeciality Hospital, Jaipur, India; [19]Global hospital, Surat, India; [20]Shivam Hospital, Ahmedabad, India; [21]Asian Institute of Medical sciences, Dombivali, India; [22]Rajalakshmi Hospital & Research Center, Bangalore, India; [23]Kanungo Institute of Diabetes Specialities, Bhubaneshwar, India; [24]Hi-Tech Medical College & Hospital, Bhubaneshwar, India; [25]Om Surgical Center and Maternity Home, Varanasi, India; [26]Lokmanya Medical Research Center, Pune, India; [27]Shree Siddhivinayak Maternity & Nursing Home, Nashik, India; [28]Aster Aadhar Hospital, Kolhapur, India; [29]Ashirwad Hospital and Research Centre, Ulhasnagar, India; [30]NRR Hospital, Bangaluru, India; [31]Samarpan Hospital, Ahmedabad, India

Objectives: To evaluate the efficacy and safety of Synthetic Semaglutide Injection manufactured by Sun Pharma (Test arm) with Ozempic® Injection (Reference arm) in Indian patients with Type 2 Diabetes Mellitus in three subgroups based on Age: <40 years (Subgroup 1 [S1]), 40 to <50 years (Subgroup 2 [S2]), ≥50 years (Subgroup 3 [S3])

Materials and Methods: This was a phase III, multicentre, randomized, open-label, active controlled study. Total 314 adults (18-65 years) with T2DM (HbA1c: 7.0-10.5%) on diet/exercise uncontrolled with stable metformin dose (≥1500 mg or maximum tolerated dose) for ≥12 weeks were enrolled. Eligible patients were randomized in a 1:1 ratio and received Test product or Reference product, subcutaneous injections in a weekly dose of 0.25 mg to 2 mg for 24 weeks. [CTRI Registration number: CTRI/2025/02/080592]

Results: At baseline, distribution of patients was as follows: 54 patients aged <40 years *(S1)*, 107 patients aged 40 to <50 years *(S2)* and 153 patients aged ≥50 years *(S3)*. HbA1c reduction (±SD) from baseline to Week 24 in Test arm was comparable to Reference arm across all 3 age subgroups: *S1*: −1.85 ± 0.70% vs −2.20 ± 0.80% ($P = .2220$), *S2*:−2.05 ± 0.87% vs −1.92 ± 0.96% ($P = .4542$), *S3*: −2.10 ± 0.83% vs −1.88 ± 0.90% ($P = .1557$). Significant reduction from baseline in HbA1c was observed across all three sub-groups at Week 24 in both the study arms. Significant reductions in post-prandial and fasting blood glucose levels at Week 24 were seen in both study arms and the changes were comparable across all three age subgroups. Proportion of patients achieving HbA1c <7.0% were comparable between the Test and Reference arms, *S1*: 19 (86.4%) vs 24 (82.8%) ($P = .3426$), *S2*: 36 (72.0%) vs 34 (70.8%) ($P = .8843$), *S3*: 51 (72.9%) vs 50 (72.5%) ($P = .6315$) across all three age subgroups. Three patients experienced hypoglycaemia. None of the patients required rescue medication. The incidence of treatment-emergent adverse events (TEAEs) was similar in both arms. Most common TEAEs were gastrointestinal events (Diarrhoea, Nausea, Vomiting) in all three subgroups. Study medications were well tolerated.

Conclusions: Semaglutide injection (Test Product) demonstrated comparable glycaemic control to Reference product in T2DM patients uncontrolled on metformin monotherapy across all age groups.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1043

EP597 - ECE_3330 - Hybrid closed-loop system in elderly people with diabetes; a center's experience

Dimitra Pappa, Maria Apostolopoulou, Stefanos Tamouridis, Eleftheria Barmpa, Anastasia-Konstantina Sakali and Alexandra Bargiota
Department of Endocrinology and Metabolic Diseases, University Hospital of Larissa, Larissa, Greece

Background and Aims: Hybrid closed-loop systems (HCLS) are widely used in diabetes management and are recommended in all ages. The question is how easy and convenient is for elderly people to use technology to improve their glycemic control and quality of life. Here we present the effect of HCLS on elderly patients in the real world setting of our clinic.

Methods: 14 patients with T1DM, older than 55 years old (mean age 62.85 ± 5.21 years old) (GroupA) attending our outpatient clinic participated in the study and six of them (42.85%) were older than 65 years (mean age 67.83 ± 3.31 years old) (Group B). CGS metrics such as time in range (TIR), time above range (TAR; 180-250 mg/dl, TAR250; >250 mg/dl) and below range (TBR; 54-70 mg/dl, TBR54; <54 mg/dl) at baseline and six months after the initiation of HCLS were studied in all participants.

Results: In GroupA (6/14 males, 8/14 females) mean diabetes duration was 29.11 ± 14.18 years. 7/14 were on multiple daily insulin injections (MDI) and 7/14 on subcutaneous continuous insulin infusion (SCII) before the initiation of HCLS. At baseline they had mean HbA1c 6.53 ± 3.02%, mean TIR 65.73 ± 13.46%, TAR 28.6 ± 10.43%, TAR250 6.9 ± 6.89%, TBR 1.59 ± 2.69% and TBR54 0.45 ± 0.96%. Six months post HCLS initiation the mean HbA1c was 6.81 ± 0.73% (r = −0.303, $P = 0.508$), mean increase in TIR 10.72 ± 15% (r = 0.563, $P = .045$) and mean decrease in TAR, TAR250, TBR and TBR54 were 11.12 ± 12.26% (r = 0.176, $P = 0.564$), 4.4 ± 5.89% (r = 0.534, $P = .06$), 0.83 ± 2.36% (r = 0.569, $P = .043$) and 0.35 ± 0.96% (r = 0.240, $P = .429$) respectively. In GroupB (5/6 males, 1/6 females) mean diabetes duration was 37 ± 10.27 years and 4/6 were on MDI and 2/6 on SCII before the initiation of HCLS. At baseline they had mean HbA1c 6.31 ± 3.25%, mean TIR 69.36 ± 10.97%, TAR 28.18 ± 9.85%, TAR250 4.8 ± 6.32%, TBR 0.45 ± 0.50% and TBR54 0.01 ± 0.04%. Six months post HCLS the mean HbA1c was 7.15 ± 0.82% (r = −0.277, $P = .723$) and had mean increase in TIR 14.15 ± 12.26% (r = 0.099, $P = .852$), and mean decrease in TAR, TAR250, TBR and TBR54; 13.15 ± 12.01% (r = −0.024, $P = .964$), 3.28 ± 5.45% (r = 0.617, $P = .192$), 0.00 ± 0.63% (r = 0.216, $P = .681$) and 0.01 ± 0.04% respectively.

Conclusions: HCLS seem to improve glycemic control and CGS metrics in all patients by increasing TIR and decreasing TAR, TAR250, and especially TBR and TBR54, eliminating hypoglycemic episodes, which is important regarding the comorbidities that they have. The same results were noted on GroupB as well, showing that with good training use of technology in elderly patients can be beneficial.

Abstract citation ID: lvag096.1044

EP600 - ECE_2544 - Metabolic-reproductive restoration in obese women with polycystic ovary syndrome treated with tirzepatide: a one-year single-arm interventional study

Valentina Gavazova[1,2], Sylvia Pashkunova[1,2], Vesela Mihneva[1,2] and Tzvetelina Totomirova[1,2]
[1]Military Medical Academy, Sofia, Bulgaria; [2]Clinic of Endocrinology and Metabolic Diseases, Sofia, Bulgaria

Introduction: Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age and is frequently associated with obesity, insulin resistance, hyperandrogenism, and ovarian dysfunction, leading to chronic anovulation and menstrual irregularities. Obesity further exacerbates both metabolic and reproductive abnormalities in PCOS and increases long-term cardiometabolic risk. Metformin is widely used to improve insulin sensitivity in PCOS, however, a substantial proportion of patients are unable to tolerate this treatment due to gastrointestinal or other adverse effects. Alternative therapies that provide sustained metabolic and reproductive benefits are therefore needed. Tirzepatide, a dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide1 receptor agonist, induces significant weight loss and improves insulin sensitivity and may represent a novel therapeutic option for women with obesity-related PCOS who are intolerant to metformin.

Aim: To evaluate the effects of one year of tirzepatide treatment on body weight, metabolic parameters, and ovarian function in women with obesity and PCOS-associated ovarian dysfunction who were intolerant to metformin.

Materials and Methods: This one-year, single-arm interventional study enrolled 35 women of reproductive age diagnosed with PCOS according to established criteria, with a body mass index ≥30 kg/m^2 and intolerance to metformin. Participants received once-weekly subcutaneous tirzepatide with dose escalation according to standard clinical protocols. Assessments at baseline and during follow-up visits over 12 months included anthropometric measurements, fasting glucose and insulin levels, indices of insulin resistance, and reproductive hormone profiles, including total testosterone and sex hormone-binding globulin (SHBG). Ovarian function was evaluated based on menstrual cycle regularity and available ovulatory markers. Safety and tolerability were monitored.

Results: After one year, participants showed significant reductions in body weight and BMI. Metabolic parameters improved, with reduced fasting insulin levels and enhanced insulin sensitivity. Reproductive endocrine assessment revealed decreased androgen levels and increased SHBG concentrations. Clinically, many women experienced improved menstrual cycle regularity, with evidence suggestive of restored ovulatory function in those anovulatory at baseline. Improvements in ovarian function were associated with the magnitude of weight loss and metabolic improvement. Tirzepatide was generally well tolerated, with gastrointestinal symptoms being the most common adverse events and no serious treatment-related safety concerns observed.

Conclusions: One year of tirzepatide treatment was associated with significant weight loss, improved metabolic health, and favorable effects on ovarian function in women with obesity and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

PCOS who were intolerant to metformin. These findings support tirzepatide as a potential therapeutic alternative and warrant confirmation in randomized controlled trials evaluating long-term reproductive outcomes.

Abstract citation ID: lvag096.1045

EP601 - ECE_3403 - Morphofunctional assessment in patients undergoing allogeneic transplantation: clinical application of biva, nutritional ultrasound and dynamometry in prehabilitation programs

Rosa Natalia García Pérez, Víctor Siles-Guerrero, Aida Elhadri-Egea and Martín López de la Torre Casares
Hospital Universitario Virgen De Las Nieves, GRANADA, Spain

Introduction: Patients who are candidates for allogeneic hematopoietic stem cell transplantation (allo-HSCT) are at high risk of nutritional deterioration due to intensive treatment regimens, gastrointestinal toxicity, and systemic inflammatory response. Conventional nutritional assessment methods may underestimate this risk, particularly in individuals with excess body weight or altered body composition. In this context, emerging tools such as bioelectrical impedance vector analysis (BIVA), nutritional ultrasound, and handgrip dynamometry enable a more accurate evaluation of body composition and muscle function, providing information with potential prognostic value.

Objectives: To assess the nutritional and functional status of patients undergoing allo-HSCT using advanced techniques such as BIVA, rectus femoris nutritional ultrasound, and dynamometry, and to analyze the relationship between these variables and clinically relevant outcomes, including hospital admissions and survival.

Materials and Methods: : A prospective observational study was conducted in adult patients undergoing allo-HSCT at the Virgen de las Nieves University Hospital. Nutritional assessment was performed at different time points before and after transplantation, including anthropometric measurements, BIVA, nutritional ultrasound, and evaluation of muscle strength by dynamometry. Associations between morphofunctional parameters and clinical outcomes were subsequently analyzed.

Results: : A total of 31 patients were included, with a mean age of 44.3 years, of whom 45% were male. Significant sex-related differences were observed in body weight, body cell mass (BCM), and fat-free mass index (FFMI) ($P < .001$). Rectus femoris nutritional ultrasound parameters, including cross-sectional area (RF-CSA) and Y-axis, as well as handgrip strength, were significantly higher in male patients. Early initiation of nutritional prehabilitation was significantly associated with improvements in body weight ($r = 0.423$) and FFMI ($r = 0.409$). RF-CSA showed strong correlations with body weight, body circumferences, BCM, and FFMI ($r > 0.5$; $P < .001$). Phase angle correlated with handgrip strength, FFMI, body circumferences, and ultrasound parameters. Survival was significantly associated ($P < .05$) with higher values of Y-axis ($r = 0.633$), BCM ($r = 0.816$), and FFMI ($r = 0.833$).

Conclusions: The incorporation of advanced nutritional assessment tools such as BIVA, nutritional ultrasound, and dynamometry allows the identification of morphofunctional alterations with prognostic relevance in patients undergoing allo-HSCT. Their integration into nutritional prehabilitation programs may improve risk stratification and contribute to better clinical outcomes.

Abstract citation ID: lvag096.1046

EP602 - ECE_3977 - Beyond waist circumference: the metabolic significance of preperitoneal circumference

Estefanía Chumbiauca[1,2], Adrián Gil Korilis[1], Lucia O. Connor[1], Javiera Concha[1], Patricia Yárnoz[1], Elena Martín[1], Camilo Silva[1], Nerea Varo[3], Gema Fruhbeck[1], Javier Escalada[1] and Carolina M. Perdomo[1]
[1]Pamplona, Spain; [2]Clinica Universidad de Navarra, Endocrinology, Pamplona, Spain; [3]Clínica Universidad de Navarra, Biochemistry Department, Pamplona, Spain

Background and Aims: Adiposopathy is characterized by metabolic dysfunction with progressive ectopic fat accumulation and lipotoxicity. Compared to subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT) is more inflammatory and metabolically active, contributing more directly to systemic inflammation, metabolic syndrome (MS), and cardiovascular risk. Traditional measurements, such as waist circumference (WC) and waist-to-height ratio (WHtR), assess metabolic risk, but their performance relative to direct ultrasound measurement of specific fat compartments remains unclear. This study aims to compare conventional and emerging adiposity parameters for predicting MS.

Method: Evaluation of a cohort of 169 patients living with obesity (PlwO) between 20 and 78 years of age without anti-obesity pharmacological or surgical treatment, who attended the outpatient clinic of the Endocrinology Unit at Clínica Universidad de Navarra. MS criteria were defined according to the modified ATP III criteria. Adiposity assessment included: a) anthropometric measurements (BMI, neck circumference, hip circumference, WC, and WHtR); b) body-fat% (assessed through bioelectrical impedance analysis [BIA], and CUN-BAE); c) Visceral adipose tissue (assessed through BIA and abdominal fat ultrasound examination [SAT, preperitoneal adiposse tissue [PAT], and preperitoneal circumference [PC]). PC was calculated as = WC – ($2\pi \times$ SAT).

Results: In PlwO, PC showed the highest correlation with the number of fulfilled MS criteria, followed by WC ($r = 0.33$ [$P < .001$] and $r = 0.26$ [$P < .01$], respectively). No correlation was found with SAT ($r = -0.06$; $P = .46$) nor PAT ($r = -0.09$; $P = .23$). PC accounted for 9.90% of the variability in the number of fulfilled MS criteria, whereas the WC, SAT, and PAT accounted for 6.88%, 0.22%, and 0.98%, respectively. After adjusting for age and sex, a higher risk of fulfilling three metabolic criteria was observed across PC tertiles (T2: OR 1.61, 95% CI 0.68-3.81 [$P = .28$]; T3: OR 2.48, 95% CI 1.02-6.05 [$P < .05$]). Patients with a PC above the median had a higher prevalence of dyslipidemia and prediabetes/diabetes, higher glucose levels, and a greater proportion of men ($P < .05$).

Conclusions: In PlwO, PC is a meaningful indicator of metabolic risk, underscoring its potential clinical value. Its positive correlation with the number of fulfilled MS criteria, stronger than that observed for conventional validated measurements (WC and WHtR), suggests that PC may more accurately reflect metabolic burden. Abdominal fat ultrasound is an accessible, cost-effective, non-invasive screening tool that may enhance the identification of metabolic risk in PlwO.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1047

EP603 - ECE_1189 - Effectiveness of a smartphone-assisted lifestyle intervention program on weight reduction: a retrospective study

Stanislav Kravchuk and Mykola Bychkov
Danylo Halytsky Lviv National Medical University, Department of Therapy No. 1, Medical Diagnostics, Hematology and Transfusion Medicine, Faculty of Postgraduate Education, Lviv, Ukraine

Background and Aims: Overweight, obesity, and metabolic dysfunction-associated steatotic liver disease (MASLD) remain major public health challenges, particularly among women of reproductive and working age. Mobile health (mHealth) programs that integrate nutritional, psychological, and behavioral components offer a scalable approach to support sustainable lifestyle change. This study aimed to evaluate the effectiveness of *The Body School*—a 3-month, smartphone-assisted lifestyle intervention combining dietary counseling, health education, guided cooking, and psychological support—in improving anthropometric outcomes among women with overweight and obesity.

Methods: A retrospective analysis was conducted using data from 101 women who completed the program between 2023 and 2024. The intervention included nutrition support delivered via a mobile app, educational modules, psychological guidance, and physical activity recommendations. Primary outcomes were changes in body weight, body mass index (BMI), and waist-to-hip ratio (WHR), self-recorded by participants within the app. The Wilcoxon signed-rank test was used for statistical analysis ($P < .001$).

Results: The program resulted in statistically significant improvements across all primary anthropometric parameters: median weight loss was 4.0 kg (–5%), BMI decreased by 1.83 kg/m^2, and WHR decreased by 0.016.

Discussion: These results are consistent with evidence supporting mHealth interventions for weight reduction, where modest (≈5%) weight loss yields meaningful metabolic benefits. Effectiveness may be driven by the program's multicomponent, personalized structure. Limitations include retrospective design and absence of a control group.

Conclusions: *The Body School* smartphone-assisted lifestyle intervention led to significant reductions in body weight, BMI, and WHR among women with overweight, with a mean participant age of 36.9 years. These findings highlight the program's potential as an effective digital tool for multidisciplinary weight management across various metabolic conditions, including MASLD.

Abstract citation ID: lvag096.1048

EP605 - ECE_1324 - Acute pancreatitis and insulin-dependent diabetes Miletus following growth hormone therapy in a patient with Kearns–Sayre syndrome: a case report

Omar Alluhayyan[1], Abdullah Alshamrani[2], Ali Alqaraishi[2], Tarek Al-Dabbagh[2], Faisal Alrashed[3] and Sultan Alotaibi[3]
[1]*King abdulaziz medical city, Riyadh, Saudi Arabia;* [2]*KAMC, Riyadh, Saudi Arabia;* [3]*KSAU-HS, Riyadh, Saudi Arabia*

Background: Kearns–Sayre syndrome (KSS) is a rare mitochondrial disorder that could present with endocrine dysfunction, including diabetes mellitus and growth hormone deficiency. Recombinant growth hormone (rGH) is frequently prescribed to address short stature; however, its potential role in precipitating severe metabolic and pancreatic complications remain underappreciated.

Case Presentation: We describe a 16-year-old female with KSS receiving long-term recombinant growth hormone therapy who presented with acute deterioration characterized by polyuria, polydipsia, severe abdominal pain, vomiting, and altered mental status. She had no prior diagnosis of diabetes mellitus. Initial evaluation revealed profound high–anion gap metabolic acidosis (pH 7.08, bicarbonate 6.7 mmol/L), marked hyperglycemia (20.2 mmol/L), positive ketones, and striking elevation of pancreatic enzymes (lipase 2963 U/L, amylase 1665 U/L). Imaging confirmed acute pancreatitis without biliary pathology or pancreatic necrosis. The patient was diagnosed with severe diabetic ketoacidosis complicated by acute pancreatitis and acute kidney injury, requiring intensive care admission, intravenous insulin infusion, aggressive fluid resuscitation, and electrolyte correction. Growth hormone therapy was suspected to be the offending cause and discontinued. Further endocrine evaluation demonstrated elevated HbA1c (10.7%), undetectable C-peptide, and persistently negative pancreatic autoantibodies, supporting the diagnosis of insulin-deficient. She improved clinically and was transitioned to basal–bolus insulin therapy. Following up after discharge, she demonstrated excellent glycemic stability with low insulin requirements and a significant improvement in HbA1c (7.1%).

Conclusions: This case illustrates a severe and uncommon metabolic disorder in a patient with KSS, where insulin-dependent diabetes and acute pancreatitis presented simultaneously while on recombinant growth hormone therapy. It highlights the vulnerability of mitochondrial patients to abrupt beta-cell failure and pancreatic injury under metabolic stress. Clinicians should maintain a high index of suspicion for pancreatitis and dysglycemia in KSS patients receiving growth hormone, particularly when gastrointestinal or osmotic symptoms emerge, and consider closer metabolic surveillance in this high-risk population.

Abstract citation ID: lvag096.1049

EP608 - ECE_3077 - Phosphocalcic profile and risk of calcium nephrolithiasis in patients with metabolic syndrome

Dhouha Ben Salah[1], Dana Jalouli[2], Mariam Mestiri[1], Khouloud Boujelben[1], Fatma Gargouri[2], Mouna Elleuch[1], Nadia Charfi[1], Faten Haj Kacem Akid[1], Mouna Mnif[1], Ayadi Fatma[2] and Nabila Rekik Majdoub[1]
[1]*Hedi Chaker University hospital, endocrinology, Sfax, Tunisia;* [2]*Habib Bourguiba University hospital, Biochemstry laboratory, sfax, Tunisia*

Background: Metabolic syndrome (MetS) is a major public health concern due to its high prevalence and associated complications. Beyond well-known metabolic and cardiovascular consequences, MetS has increasingly been linked to renal involvement, particularly urinary stone formation. Identifying early urinary risk factors in patients with MetS may help prevent future stone formation.

Methods: A descriptive cross-sectional study was conducted over a 13-month period in adult patients followed for metabolic syndrome according to the NCEP-ATP III criteria at the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Endocrinology-Diabetology Department of Hedi Chaker University Hospital, Sfax.Clinical, nutritional, biochemical, and 24-hour urinary parameters were collected. Univariate and multivariate logistic regression analyses were performed to identify factors associated with lithogenic abnormalities.

Results: A total of 85 patients were included, median age was 54.04 ± 0.88 years , a female predominance was noticed (male-to-female ratio: 0.25),median body mass index (BMI) was 37.4 kg/m^2; 82.4% of patients were obese and 64.7% had morbid obesity. Thirty-three patients (38.8%) met three MetS criteria, while 23.5% met all five criteria.

Biochemically, hypo-HDL cholesterolemia was present in 51.8%, hypertriglyceridemia in 36.5%, and dysglycemia in 77.6%. Vitamin D deficiency was observed in 88.2% of patients. The median urinary pH was 5.45 . Lithogenic urinary abnormalities included hyperuricosuria (36.5%), hypomagnesuria (34.1%), hyperphosphaturia (28.2%), hypercalciuria (16.5%), and hyperoxaluria (2.4%). Crystalluria was detected in 17.6% of cases.

Univariate analysis of predictors of lithogenic risk associated with hypercalciuria showed that, in terms of social factors, patients with hypercalciuria had significantly lower age compared with those without hypercalciuria ($P = .01$). Concerning clinical factors, hypercalciuria was significantly more frequent in patients with higher BMI, morbid obesity, and excessive salt intake ($P = .001$ for each). Biological parameters showed no significant association between hypercalciuria and serum lipids profile, or fasting glucose levels. In multivariate analysis, BMI and excessive salt intake were independently associated with hypercalciuria, with adjusted odds ratios of 1.13 (95% CI: 1.03-1.24) and 14.8 (95% CI: 2.96-74.52), respectively. No significant association was found between the number of metabolic syndrome components and lithogenic factors; however, a non-significant increase in urinary oxalate ($P = 0.07$) were observed as the number of metabolic syndrome criteria increased.

Conclusions: Metabolic syndrome is a recognized risk factor for calcium nephrolithiasis, underscoring the need for targeted preventive measures. Systematic metabolic assessment and lifestyle interventions are recommended, with intensified evaluation and annual follow-up for patients with risk factors as Obesity and high sodium intake or biochemical abnormalities

Abstract citation ID: lvag096.1050

EP609 - ECE_3125 - Hypoglycaemia awareness, nocturnal events and recurrence after severe hypoglycaemia in type 1 diabetes

Víctor Siles-Guerrero, Rosa Natalia García Pérez, Aida Elhadri-Egea and José Manuel Romero-Márquez
Hospital Universitario Virgen De Las Nieves, Granada, Spain

Introduction: Impaired hypoglycaemia awareness and nocturnal hypoglycaemia are well-recognised clinical features associated with an increased risk of severe hypoglycaemia in individuals with type 1 diabetes mellitus (T1DM). Despite advances in diabetes education and monitoring technologies, these factors continue to contribute substantially to emergency care utilisation and recurrent severe episodes. Real-world descriptive data may help to better characterise patients at particularly high risk.

Objective: To describe hypoglycaemia awareness status, nocturnal hypoglycaemia, and recurrence patterns in adults with T1DM attended for severe hypoglycaemia requiring emergency medical care.

Methods: A retrospective, descriptive study was conducted including 66 adults with T1DM who required pre-hospital emergency assistance for severe hypoglycaemia between 2018 and 2022. Clinical variables analysed included hypoglycaemia awareness status, presence of nocturnal hypoglycaemia, documented history of previous severe hypoglycaemia, and occurrence of new severe episodes after the index event during follow-up. Data were analysed using descriptive statistics.

Results: Hypoglycaemia unawareness was present in 43.9% of patients, indicating a high prevalence of impaired symptom recognition at the time of emergency attendance. Nocturnal hypoglycaemia was reported in 53.0% of cases, highlighting the frequent occurrence of events during periods of reduced supervision and delayed detection. More than half of the cohort (54.5%) had a documented history of previous severe hypoglycaemia prior to the index episode. During follow-up, 22.7% of patients experienced at least one new severe hypoglycaemic episode requiring emergency intervention. The coexistence of hypoglycaemia unawareness and nocturnal hypoglycaemia was common, defining a subgroup with particularly high vulnerability and recurrent exposure to severe events.

Conclusions: Among 66 adults with T1DM attended for severe hypoglycaemia, hypoglycaemia unawareness and nocturnal hypoglycaemia were highly prevalent, and recurrence after the index episode was frequent. These descriptive findings suggest that emergency attendance often identifies patients with persistent risk factors that may not be adequately addressed by routine diabetes care. Targeted strategies focusing on restoration of hypoglycaemia awareness and prevention of nocturnal events may be crucial following a severe episode.

Abstract citation ID: lvag096.1051

EP610 - ECE_3132 - The impact of diabetes mellitus in community-acquired pneumonia. Retrospective study

Elona Xhardo Hysenbelli[1,2], Bledar Hysenbelli[3], Sofiela Telo[4], Suada Velo[5] and Dorina Ylli[6]
[1]Tirana, Albania; [2]University Hospital Tirana, Internal Medicine, Tirana, Albania; [3]University Hospital "Mother Teresa", Tirana, Albania; [4]University Hospital :Shefqet Ndroqi", Tirana, Albania; [5]University Hospital "Shefqet Ndroqi", Pulmonology, Internal Medicine, Tirana, Albania; [6]University Hospital :Mother Teresa", Endocrinology, Internal Medicine, Tirana, Albania

Background: Diabetes mellitus (DM) increases the risk of infections such as Pneumonia due to the toxic effects of hyperglycemia and imune system dysfunction.The association with Community-Acquired Pneumonia (CAP) remains underexplored. Hyperglycaemia on admission and during hospital stay, is a major risk factor for poor outcomes in diabetics with CAP.

Objective: This study aimed to evaluate the impact of new onset or previously diagnosed DM ,on clinical severity and outcomes of hospitalised patients with CAP.

Methods: In our retrospective study we included a total of 150 patients, hospitalised in e tertiary Hospital Center in Albania

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

during 2025 with a confirmed CAP diagnosis.The study population consisted of adults patients with evidence of new pulmonary infiltrates on chest computed tomography (CT).

Diabetic patients were classified in two groups, pre-existing and new onset diabetes. The outcomes were compared with non-DM patients with CAP. Data on demography, laboratory test results, hospital stays were recorded in a specific questionnaire. One variable and mulvariable logisc regression analysis was done with 95% confidence interval and p-value < 0.05 considered significant.

Results: A total of 150 patients were enrolled. The mean age was 64 years. 92 patients(62%) were men.The risk of acute respiratory failure and need of O2 therapy is higher in the group of known diabetes 63% vs 59% in new onset diabetes. Diabetics patients with CAP had on average 1.4 days longer hospital stay as compared to patients without DM ($P = .002$) . There was a significant higher ICU admission and mortality rate in diabetes patients ($P < .001$).

Conclusions: Our results show that Diabetes is not only a relevante risk factor for Community-Acquired Pneumonia but also it is associated with a severe clinical presentation, longer hospitalization time and higher mortality rates.

Keywords diabetes mellitus, community-acquired pneumonia, outcomes

Abstract citation ID: lvag096.1052

EP611 - ECE_3247 - Diabetic foot MRSA-naries: the utility of nasal swab MRSA rule-out in moderate-to-severe diabetic foot infection

Gustavo Rodrigues, Alice Monsanto, Tânia Carvalho, Ana Margarida Sobra, Bárbara Jesus, Cristina Ribeiro and Leonor Gomes
Unidade Local de Saúde de Coimbra, Department of Endocrinology, Diabetes and Metabolism, Coimbra, Portugal

Introduction: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a relevant etiological agent in diabetic foot infections, being associated with greater therapeutic complexity and limited options for empirical antibiotic therapy. In this context, exclusion of MRSA colonization through nasal swab screening—widely used in hospital protocols—has been proposed as an indirect method to rule out infection by this microorganism. The rapid availability of results allows for narrowing of the initial antibiotic spectrum without the need to wait several days for culture results.

Goals: The aim of this study was to evaluate the clinical utility of nasal MRSA screening in excluding this microorganism as the infectious agent in patients with diabetic foot infection.

Materials and Methods: All patients hospitalized for diabetic foot infection who were assessed or admitted by the Endocrinology Department between January 2025 and January 2026 were included. Results of nasal MRSA swab screening were systematically recorded and compared with microbiological isolates obtained from wound exudate, tissue biopsy, or blood cultures.

Results: Thirty-five hospitalizations for diabetic foot infection were identified, with a median length of stay of 15.0 days (IQR 12.3-20.0). The mean age was 69.6 ± 12.7 years, and 77.1% of patients were male. Infection severity was classified as PEDIS IV in 27 cases (77.1%) and PEDIS III in 8 cases (22.9%). Microbiological isolation was obtained in 24 episodes, with the most frequently identified microorganisms being *E. faecalis* (28.5%), *M. morganii* (17.1%), and *S. agalactiae* (14.2%). Only one MRSA isolate was identified (2.9%).

Thirty-one patients (88.6%) had a negative nasal MRSA swab, and no MRSA was isolated in cultures from these patients (zero false negatives). Four patients (11.4%) had a positive nasal screening result, of whom only one had microbiological isolation of MRSA (ie, three false positives). Accordingly, nasal screening showed a sensitivity of 100% and a specificity of 91.18%; given the observed prevalence, the positive predictive value was 25.29% and the negative predictive value was 100%.

Conclusions: Despite limitations related to the small sample size and the low prevalence of MRSA, this study suggests the exclusion of MRSA colonization by nasal swab screening may represent a useful tool for optimizing empirical antibiotic therapy in patients with diabetic foot infection

Abstract citation ID: lvag096.1053

EP612 - ECE_2277 - Changes in serum leptin levels during the insulin tolerance test in children with short stature

Katarzyna Majewska[1], Joanna Budzulak[1], Maria Buczyńska-Górna[1], Monika Naskręcka[2], Dominik Majewski[3] and Andrzej Kędzia[1]
[1]*Poznan University of Medical Sciences, Department of Pediatric Diabetes, Auxology and Obesity, Poznan, Poland;* [2]*Poznan, Poland;* [3]*Poznan University of Medical Sciences, Department of Internal Medicine, Poznan, Poland*

Introduction: Insulin is an important regulator of leptin secretion. However, its effects may vary depending on the duration of exposure, energy availability, or the body's metabolic status. The insulin tolerance test (ITT) is used in children with short stature to diagnose growth hormone deficiency (GHD). During this test, the body is exposed to a unique metabolic situation, when insulin is administered without food intake. ITT induces hypoglycemia, which in turn activates a counterregulatory response, including increased secretion of growth hormone (GH), as well as catecholamines, glucagon, and cortisol. This mechanism is supposed to restore normal blood glucose levels but may also affect leptin secretion. The aim of this study was to evaluate serum leptin response during ITT in children with short stature.

Methods: The study included 21 children and adolescents with short stature, aged 5 to 17 years, who were eligible for ITT due to suspicion of GHD. The control group consisted of 21 healthy children matched for age, gender, and BMI. In children with short stature, serum leptin was measured after an overnight fast (at baseline), and 60 minutes after intravenous insulin administration, along with serum glucose and GH concentrations. In the control group, only fasting leptin was assessed.

Results: Fasting leptin levels were significantly higher in children with short stature than in the control group ($P = .010$). During the ITT in children with short stature, mean leptin levels before and after 60 minutes of the test were similar ($P = .903$). However, detailed analysis revealed significant differences in leptin responses depending on baseline levels. Patients with lower baseline leptin concentrations (below 10 ng/mL) showed further

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

decrease, while those with higher baseline leptin concentrations (above 10 ng/mL) showed further increase. Differences in these patterns were statistically significant ($P = .001$).

Conclusions: Regulation of leptin secretion during the insulin tolerance test seems to differ depending on baseline leptin concentrations. In children with short stature and suspected GHD, lower fasting leptin levels may reflect energy deficiency and lead to a further decrease in leptin in response to insulin administration and hypoglycemia. In contrast, in children with higher baseline leptin levels, usually associated with greater fat mass, a further increase in leptin following insulin administration may reflect a higher overall energy status. In children with short stature, leptin may be a useful marker of energy balance and perhaps also a modulator of the somatotropic axis.

Abstract citation ID: lvag096.1054

EP613 - ECE_2026 - Changes in β1 adrenergic receptor and tyrosin hydroxylase expression in the pancreas of male rats in a metabolic syndrome model

Abigail Hernández-Munive[1,2], Dania Pérez-Ricardo[1], Marcia Hiriart[1] and Myrian Velasco Torres[1]
[1]*Ciudad de México, Mexico;* [2]*Instituto de Fisiología Celular, Neurociencia cognitiva, 04510, Mexico*

Metabolic syndrome (MS) is a cluster of interconnected metabolic abnormalities that significantly increases the risk of developing cardiovascular diseases, type 2 diabetes (DM2), and other health problems. Characterized by insulin resistance, abdominal obesity, dyslipidemia, and hypertension, metabolic syndrome is a growing global health concern. Within this context, autonomic dysregulation, particularly sympathetic overactivity, emerges as a critical factor in the progression of islet dysfunction and impaired glucose homeostasis. Tyrosine hydroxylase (TH) is a rate-limiting enzyme in catecholamine synthesis and a key marker of sympathetic activity. Also, alterations in the expression of adrenergic receptors (AdRe), such as β1, may reflect dysfunction of pancreatic innervation under chronic metabolic stress. Therefore, we investigated these neural-endocrine markers, which are essential to understand how the sympathetic-islet axis is reorganized during the transition from insulin resistance to pancreatic failure. Aim: Analyze the abundance of β1- AdRe and TH in pancreatic islets of male rats in a MS model. Methodology: Two-month-old male Wistar rats were divided into control (tap water) and MS (20% sucrose in drinking water) for 2 (2M) and 6 (6M) months, respectively. Measurements included body weight, body length, abdominal circumference, and quantification of fat mass. An insulin resistance test was performed by measuring peripheral glucose levels after an ip insulin bolus. After 2 or 6 M treatment, the animals were anesthetized with sodium pentobarbital, the pancreas was extracted, embedded in paraffin, and sectioned (40 µm) for immunofluorescence of β1-AdRe, insulin, and TH of β in consecutive slices of the pancreas. Results: animals in the MS model showed increases in body weight, abdominal circumference, peripancreatic fat, and peripheral insulin resistance. This increase was more pronounced in those animals with 6M treatment. There was a decrease in β1- AdRe fluorescence in the islets of animals with 2M, which was not observed in the 6M treatment animals. As for insulin, there was a decrease in fluorescence in the 2M animals, which was more pronounced in the animals that spent 6 months drinking sugary water. Finally, TH abundance increased in the islets with 6 M treatment. In conclusion, our findings demonstrate that chronic sucrose consumption induces a progressive reduction in pancreatic insulin content, likely reflecting sustained hypersecretion and an early downregulation of adrenergic receptors, indicating a neural-endocrine effort to modulate pancreatic function. The significant increase in TH abundance at six months suggests a sympathetic hyperinnervation of the islets in response to sustained metabolic stress.

Abstract citation ID: lvag096.1055

EP614 - ECE_3590 - Liver receptor homolog-1 regulates aldehyde dehydrogenase 1 family member B1 in hepatic ethanol metabolism

Min-Hee Seo[1] and Seung-Soon Im[1,2]
[1]*Keimyung University School of Medicine, Physiology, Daegu, South Korea;* [2]*Keimyung University School of Medicine, Physiology, Daegu, South Korea*

Ethanol is metabolized and detoxified by multiple enzymes in the liver. Previous research has shown that ethanol consumption promotes lipid accumulation in hepatic tissue. Liver receptor homolog-1 (LRH-1) participates in controlling lipid and bile acid metabolism; however, its contribution to ethanol metabolism is not well defined. Thus, this study sought to clarify the relationship between ethanol-induced hepatic lipid accumulation and LRH-1. To investigate the role of LRH-1 in hepatic ethanol metabolism, LRH-$1^{f/f}$ and liver-specific LRH-$1^{f/cre+}$ mice were given a liquid ethanol diet for three weeks. LRH-$1^{f/cre+}$ mice displayed increased liver mass, higher neutral fat content, and elevated total cholesterol levels. Serum markers of liver injury, as well as acetaldehyde concentrations, were also higher in LRH-$1^{f/cre+}$ mice receiving ethanol. Furthermore, ethanol-fed LRH-$1^{f/cre+}$ mice showed reduced fatty acid oxidation, compromised mitochondrial function, and elevated reactive oxygen species. To identify LRH-1 targets in ethanol metabolism, RNA-sequencing was performed, revealing marked alterations in fatty acid metabolism-regulating genes between the control and ethanol-treated groups. Under LRH-1 deficiency, genes involved in ethanol metabolism showed a pronounced reduction in Aldehyde Dehydrogenase 1 Family Member B1 (ALDH1B1) expression. Conversely, LRH-1 overexpression in HepG2 cells increased ALDH1B1 levels, and ChIP-sequencing confirmed LRH-1 binding peaks within the ALDH1B1 promoter region. In summary, this study reveals that LRH-1 depletion downregulates ALDH1B1 expression, leading to acetaldehyde accumulation and enhanced intrahepatic fat deposition.

Keywords LRH-1, ALDH1B1, ethanol metabolism, liver

Abstract citation ID: lvag096.1056

EP617 - ECE_1280 - The correlation between cardiovascular autonomic neuropathy and levels of glucagon-like peptide-1 in obesity patients

Olena Stepura[1], Nadiia Zherdova[1], Ivan Todurov[2] and Svitlana Mazii[3]
[1]*State Scientific Institution "Center for Innovative Medical Technologies of the National Academy of Sciences of Ukraine", Department of diagnosis and treatment of metabolic diseases, Kyiv,*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Ukraine; [2]State Scientific Institution "Center for Innovative Medical Technologies of the National Academy of Sciences of Ukraine", Department of Surgery, Kyiv, Ukraine; [3]State Scientific Institution "Center for Innovative Medical Technologies of the National Academy of Sciences of Ukraine", Department of Laboratory diagnostic, Kyiv, Ukraine

Background: Cardiovascular autonomic neuropathy (CAN) is a serious risk factor for cardiovascular disease and mortality in patients with diabetes mellitus and obesity. Glucagon-like peptide-1 (GLP-1) is a pleiotropic incretin with numerous functions besides glucose control. However, an association between CAN and level of GLP-1 in obesity was not fully investigated.

Aims: The aim of this study was to investigate the correlation of CAN and level of GLP-1 in obesity

Materials and Methods: We examined 62 patients with obesity (aged 49.2 ± 1.77 years, BMI – 35.03 ± 0.75 kg/m^2) (data are presented everywhere as mean±SEM). All patients were performed cardiovascular autonomic reflex tests (CARTs) by Ewing and investigated level of fasting GLP-1 and GLP-1 one hour after meal. The diagnosis of CAN was confirmed in patients with two or more positive tests. The statistical analysis was performed using SPSS statistical package version 25.0 for Windows.

Results: We found positive correlation between levels of fasting GLP-1 and the total score of CARTs, B (95% CI) 1.11(0.28/1.94), $P = .01$ and levels of GLP-1 one hour after meal B (95% CI) 0.76(0.16/1.35), $P = .015$. The blood pressure response to standing up have positive correlation with levels of fasting GLP-1 B (95% CI) 0.12 (0.009/0.24), $P = .035$ and with levels of GLP-1 one hour after meal B (95% CI) 0.087 (0.006/0.168), $P = .035$.

Conclusions: We investigated correlation between the total score of CARTs by Ewing with the levels of GLP-1, GLP-1 one hour after meal, the blood pressure response to standing up which could suggest the possible effect incretin GLP-1 in the development of CAN and sympathetic autonomic dysfunction in patients with obesity.

Abstract citation ID: lvag096.1057

EP619 - ECE_3041 - Challenging diagnosis in endogenous hyperinsulinism: a case of islet cell hyperplasia mimicking insulinoma

Madalina-Bianca Stan[1,2,3], Ioana Herghea[1,2], Cristina Andreea Bordeianu[1,2], Ana-Teodora Enache[1,2], Cristian Mugur Grasu[4,5], Octav Ginghina[6,7] and Madalina Musat[1,2]
[1]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [2]C.I. Parhon Romanian National Institute of Endocrinology, Bucharest, Romania, Endocrinology, Bucharest, Romania; [3]National Institute of Endocrinology "C.I. Parhon", Endocrinology, Bucharest, Romania; [4]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [5]Fundeni Clinic Institute Romania, Department of Radiology, Bucharest, Romania; [6]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [7]Oncology Institute Bucharest Romania, Department of Surgery III, Bucharest, Romania

Introduction: Endogenous hyperinsulinism is most commonly caused by insulinoma. However, rare non-neoplastic conditions such as diffuse or focal islet cell hyperplasia (nesidioblastosis) can present with a similar clinical and biochemical picture. Differentiating between insulinoma and islet cell hyperplasia is crucial, as it impacts surgical planning and long-term outcomes. Preoperative localization is often challenging, and imaging findings may be misleading.

Case Report: We present the case of a 43-year-old woman with a 7 month history of severe hypoglycemia (30 mg/dL), accompanied by profuse sweating, dizziness, and transient dyslexia. The initial episode occurred during hospitalization, while she was diagnosed with a urinary tract infection and treated initially with ciprofloxacin, which led to acute kidney injury. Over the subsequent months hypoglycemic events reoccurred. While liver, kidney, thyroid and adrenal function tests were normal, markedly elevated insulin levels (>300 μIU/mL) and increased C-peptide (2.51 ng/mL) during a spontaneous hypoglycemic episode confirmed endogenous hyperinsulinism. As diazoxide was not available, methylprednisolone was initiated to aid glycemic control, resulting in partial improvement of hypoglycemic episodes. Imaging studies showed conflicting results: abdominal CT revealed a cephalic pancreatic lesion, while endoscopic ultrasound identified a lesion in the body-tail region, which was biopsied but without histopathological confirmation. Octreoscan was negative for somatostatin receptor-positive lesions and MRI/MRCP revealed a small nodular lesion 8/5mm, non-characteristic for insulinoma, at the border between the pancreatic body and tail. Laparoscopic surgery was performed; due to poor intraoperative localization, a corporal-caudal pancreatectomy with splenectomy was carried out. Histopathology revealed islet cell hyperplasia without evidence of a neuroendocrine tumor. Postoperatively, the patient's glycemic status normalized, and she remained asymptomatic.

Conclusions: This case highlights the diagnostic and localization challenges in endogenous hyperinsulinism. Despite biochemical and imaging findings suggestive of insulinoma, histopathology demonstrated a non-neoplastic cause.

Abstract citation ID: lvag096.1058

EP620 - ECE_1681 - Dynamics of Incidence and Prevalence of Type 2 Diabetes in the Republic of Belarus

Tatsiana Mokhort[1] and Olga Salko[2]
[1]Belarusian State medical University, Minsk, Belarus; [2]Republican Center for Medical Rehabilitation and Balneotherapy, Minsk, Belarus

Objective: To assess the dynamics of the incidence and prevalence of type 2 diabetes (T2D) in the Republic of Belarus in the period from 1993 to 2024.

Materials and Methods: Data from the official statistics of the Ministry of Health were used for the analysis.

Results: For more than 30 years in the Republic of Belarus, since 1993, there has been a steady increase in the incidence of T2D from 60.55 to 382.18 per 100,000 population, with a natural decline in the pandemic period 2020-2022. During analyzed period, the incidence increased 6.3 times. The noted increase in the incidence of diabetes mellitus 2 is the result of active detection of the disease in risk groups and popularization in the media in accordance with the state program. At the same time, there is an increase in the prevalence of T2D (from 185.3 to 4418.81 per 100,000 population), which is due to an increase in life expectancy with type 2 diabetes. The World Health Organization has set a goal of detecting T2D in 80% of patients suffering from

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

this disease. The estimated detection targets for T2D for 2025 are 5.8%, with an increase to 7.6% in 2030. Currently, the proportion of patients with DM is 4.45%, which indicates that this goal has not been achieved. When building an exponential trend based on primary morbidity data, an estimated indicator was obtained, which should reach 660.55 per 100,000 population in 2030.

Conclusions: It is necessary to step up measures to detect T2D through further screening and expansion of risk groups, as well as raising awareness about this in the media. The projected increase in primary morbidity requires management decisions to optimize the provision of care to this category of patients.

Abstract citation ID: lvag096.1059

EP621 - ECE_1794 - High prevalence of comorbid insomnia and sleep apnea in type 2 diabetes: a novel AI-wearable diagnostic approach

Ka Shing Yan[1], Pui Sze Grace Hui[2], Chak Yan Isaac Kwok[3], Hai Ka Betty Young[2], Yin San Florence Wong[2], Man Chi Wong[2], Lydia Leung[4], Cynthia Cheung[4] and Chih-Wei Tsai[4]
[1]*Tung Wah Eastern Hospital, Hong Kong, Hong Kong;* [2]*Hong Kong, China;* [3]*Tung Wah Eastern Hospital, Department of Clinical Psychology, Hong Kong, Hong Kong;* [4]*Belun Technology Company Limited, Hong Kong, Hong Kong*

Introduction: Sleep disorders, common in type 2 diabetes (T2DM), exacerbate health outcomes but are rarely screened for systematically in routine diabetes care, particularly in Asia where data remain limited. Comorbid insomnia and obstructive sleep apnea (COMISA) carries the highest cardiovascular burden, yet its prevalence and characteristics in Chinese patients with T2DM are poorly understood. This study estimated the prevalence of sleep disorders in a T2DM cohort and evaluated the utility of an artificial intelligence (AI)-powered wearable device, the Belun Ring (BR), in a novel diagnostic workflow for identifying sleep disorders.

Methods: An interim analysis included 29 adults with T2DM from a diabetes center in a community hospital. Screening used the STOP-BANG questionnaire for obstructive sleep apnea (OSA) and the Insomnia Severity Index (ISI). Those with ISI $\geq$8(indicating sub-threshold insomnia) or STOP-BANG $\geq$3 underwent $\geq$3 nights of BR assessment. The device generated objective data on sleep efficiency (SE), sleep onset latency (SOL), wake after sleep onset (WASO), apnea-hypopnea index based on 3% oxygen desaturation (AHI3%), and heart rate variability (HRV). Diagnostic thresholds were AHI3% $\geq$15 events/h for OSA and SE $\leq$85% for insomnia; COMISA was defined when both were present.

Results: Suspected sleep disorders were nearly universal (97%, 28/29). COMISA was most common (52%), followed by insomnia (24%) and OSA (21%). OSA-only patients were younger (median 51 years) versus COMISA or insomnia (63-64 years). Subjective ISI scores poorly distinguished groups ($P = .4$). In contrast, BR-derived objective metrics revealed clinically meaningful distinctions: SE was highest in OSA (86%), intermediate in COMISA (73%), and lowest in insomnia (69%) ($P < .01$). Insomnia showed prolonged SOL and WASO, while COMISA and OSA displayed elevated AHI3% (27 events/h and 31 events/h vs 11 events/h in insomnia; $P < .001$ and $P < .05$). HRV indices, including the standard deviation of NN intervals and root mean square of successive differences, were significantly higher in COMISA than in either condition alone ($P < .05$).

Conclusions: This interim analysis reveals a near-universal presence of sleep disorders, especially COMISA, among Chinese patients with T2DM. The BR provided objective insights that enhanced diagnostic precision beyond questionnaires. A stepped workflow—initial STOP-BANG and ISI screening (with ISI $\geq$8) followed by BR confirmation—offers a scalable, resource-efficient approach that reduces reliance on polysomnography while maintaining accuracy. Larger studies are needed to validate this AI-wearable-assisted pathway and support its integration into T2DM care for earlier detection and improved outcomes.

Abstract citation ID: lvag096.1060

EP627 - ECE_3175 - Pathway to treatment of pediatric patients with type 1 diabetes mellitus diagnosed in Philippine Children's Medical Center

Melissa Joyanne Tolosa[1,2,3]
[1]*Bacolod City, Philippines;* [2]*Corazon Locsin Montelibano Memorial Regional Hospital, Bacolod, Philippines;* [3]*Dr. Pablo O Torre Memorial Hospital, Bacolod City, Philippines*

Objectives: This study aims to describe the pathway to treatment of children diagnosed with type 1 diabetes mellitus (T1DM) in a pediatric tertiary government hospital, to determine the intervals between symptom onset and treatment and to compare these intervals between patients with mild and severe presentations of T1DM.

Materials and Methods: This cross-sectional study, conducted from November 2024 to January 2025, involved direct participant interviews using an interview guide. Participants included children aged 1-18 with T1DM and their caregiver. They were classified as "mild" or "severe" based on their initial presentation. Using Walter's Pathway to Treatment, intervals were analyzed and classified as prolonged if exceeding two standard deviations from the mean. Descriptive statistics summarized demographic data, while mean and standard deviation were used to analyze intervals. An independent sample t-test compared intervals between mild and severe presentations, and a chi-square test assessed differences in the proportion of "prolonged" versus "not prolonged" intervals.

Results: Among the 66 participants, most were 6-12 years old (51.52%) and female (62.12%). The pathway to treatment takes an average of 60.46 + 63.52 days, exceeding durations reported in foreign studies. Appraisal interval (41.95 $\pm$ 58.74 days) was the longest, and the help-seeking interval (4.04 $\pm$ 8.57 days) the shortest. While total duration was comparable between groups, diagnostic ($P = .035$) and treatment ($P = .002$) intervals were significantly shorter in severe cases. Despite these differences, most participants fell into the "not prolonged" category across all intervals.

Conclusions: To reduce the alarmingly long pathway to treatment, public health interventions must prioritize improving early symptom recognition among caregivers. Simultaneously, healthcare systems should be strengthened to ensure timely diagnosis and treatment for all children, regardless of symptom severity at presentation.

Keywords diabetes mellitus, type 1, pediatrics

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1061

EP630 - ECE_1981 - Ketogenic diet in adult refractory epilepsy: experience from Reina Sofía University Hospital, Córdoba

Carmen Zurera Gomez[1,2], Pilar Pérez Reyes[3], Concepción Muñoz[3], Ana María Moyano-Sánchez[3], Jose Carlos Estevez[3], Nazaret Pelaez[1], Isabel Martorell Ferrer[1], Maria Angeles Galvez Moreno[1] and Alfonso Jesús Calañas Continente[1]

[1]Hospital Universitario Reina Sofía, Endocrinology and Nutricion, Córdoba, Spain; [2]Hospital Reina Sofía, Endocrinology, Córdoba, Spain; [3]Hospital Universitario Reina Sofia-Resonancia Magnética y Tac, Córdoba, Spain

Background: The ketogenic diet (KD) is a high-fat, very low-carbohydrate dietary therapy that induces nutritional ketosis and may reduce neuronal excitability. We describe clinical/dietary characteristics and evaluate efficacy, safety and adherence in adults with drug-resistant epilepsy treated at our centre.

Methods: Observational, descriptive, prospective study of adults with drug-resistant epilepsy treated with KD between 2023 and 2025. We recorded epilepsy aetiology, KD modality, caloric prescription and ketogenic ratio, seizure response (>=50% reduction; seizure freedom), changes in anti-seizure medications, adverse events, and reasons for treatment discontinuation.

Results: Twenty-two patients were included (14 women, 8 men), median age 29 years (IQR 21-36). The most frequent aetiologies were genetic/structural epileptic encephalopathies (36%), post-infectious epilepsy (23%) and symptomatic focal epilepsies (18%). KD modalities were modified Atkins diet (41%), classical KD (3:1/4:1) (27%), medium-chain triglyceride (MCT) KD (23%) and low glycaemic index treatment (9%). Median caloric intake was 1800 kcal/day (IQR 1650-2200) with a mean KD ratio of 1.9:1; mean active follow-up was 8.6 months. Ten patients (45%) achieved >=50% seizure reduction; three (14%) became seizure-free; nine (41%) had no response. Seven patients (32%) reduced the dose and/or number of anti-seizure medications. Lennox-Gastaut syndrome and GLUT1 deficiency showed the best responses (>90% seizure reduction). Mild-to-moderate adverse events occurred in 12/22 (54%), most frequently weight loss >5% (n = 9), gastrointestinal symptoms (n = 5) and dyslipidaemia (n = 3); mild hypoglycaemia (n = 1) and hypercalciuria (n = 1) were also observed. No severe metabolic complications were reported. Seven patients discontinued the diet; reported reasons included adherence barriers (failure to achieve ketosis, difficulty maintaining dietary restrictions or unwillingness to change dietary habits), lack of efficacy, and gastrointestinal intolerance (persistent constipation or MCT-related diarrhoea).

Conclusions: In adults with drug-resistant epilepsy, ketogenic dietary therapy was effective and generally safe, with clinically relevant seizure improvement in 45% and seizure freedom in 14%, and allowed anti-seizure medication reduction in about one third of patients. Adherence remains the main challenge.

Abstract citation ID: lvag096.1062

EP632 - ECE_3944 - Acute endocrine dysfunction following Immune checkpoint inhibition

Nuno Faria, Rita Ribeiro, Patrícia Brito, Olinda Marques, Catarina MacHado and Vera Fernandes

Unidade Local de Saúde de Braga, Endocrinology department, Braga, Portugal

Immune checkpoint inhibitors (ICI) are increasingly used in the treatment of advanced-stage malignancies. Among their adverse effects, autoimmune manifestations are notable, with endocrinopathies being among the most frequently reported.

We describe the case of a 46-year-old woman with a history of autoimmune thyroiditis (not requiring replacement therapy) and triple-negative breast carcinoma, who initiated neoadjuvant chemotherapy combined with pembrolizumab. One week after the first pembrolizumab cycle, she presented to the emergency department with three days of persistent vomiting and costochondral pain. Laboratory evaluation was compatible with diabetic ketoacidosis (glucose 607 mg/dL; ketone bodies 6.8 mmol/L; pH 7.09; HCO_3^- 4.2 mEq/L; anion gap 27 mEq/L) and thyrotoxicosis (TSH 0.025 mIU/L [reference range 0.55-4.78]; free T3 2.35 pg/mL [reference range 2.3-4.2]; free T4 1.87 ng/dL [reference range 0.89-1.76]). She denied any classical symptoms of hyperglycemia or thyrotoxicosis. She required intravenous insulin, fluid resuscitation and beta-blockade, with rapid improvement of metabolic parameters.

During recovery, she developed overt hypothyroidism (TSH 32.47 mIU/L; free T4 0.54 ng/dL; free T3 1.62 pg/mL), a pattern consistent with destructive thyroiditis, prompting levothyroxine initiation. Further evaluation showed low C-peptide levels (0.09 ng/mL; glucose 249 mg/dL), HbA1c of 7.5%, and positivity for anti-GAD and anti-ZnT8 antibodies, supporting the diagnosis of pembrolizumab-induced type 1 diabetes mellitus. She was discharged with plans for continued pembrolizumab therapy and endocrinology surveillance.

Currently, the patient presents acceptable glycemic control on a basal-bolus insulin regimen (total daily dose of 42U), is euthyroid on 150 ug/day of levothyroxine, and remains in remission from breast cancer after completing immunotherapy.

This case illustrates the rare occurrence of dual autoimmune endocrinopathies induced by ICI therapy within a short time frame, presenting with minimal clinical warning signs. It reinforces the importance of close endocrine monitoring during immunotherapy, as early recognition and prompt management are essential to ensure metabolic stability and safe continuation of oncologic therapy.

Abstract citation ID: lvag096.1063

EP633 - ECE_2052 - Effects of time-restricted eating on glycemic control in type 2 diabetes: A 12-week quasi-experimental single-arm study

Kun Yang[1], Wei Fu[1], Rongsong Tang[1], Jingpin Wang[1] and Tianpei Hong[2]

[1]Peking University Third Hospital, Beijing, China; [2]Beijing, China

Background & Aims: Time-restricted eating (TRE) is a newly emerging dietary strategy that reduces body weight and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

improves glucose tolerance in individuals with overweight or obesity. However, whether TRE is effective in improving glycemic control in individuals with diabetes remains unexplored. Herein, we aimed to investigate the effects of TRE intervention on glycemic control in patients with type 2 diabetes.

Methods: In this single-center, open-label, self-controlled trial, 32 overweight or obese adults with type 2 diabetes inadequately controlled on lifestyle modification alone or in combination with metformin and/or a-glycosidase inhibitors were enrolled to receive a 10-hour TRE for 12 weeks. The effects of TRE on glucose metabolism, body weight, body composition and other metabolic parameters were evaluated in these participants following the intervention.

Results: The 12-week TRE intervention not only significantly reduced body weight (-3.37 ± 2.74 kg, $P < .001$), but also remarkably improved glycemic control, with reduced glycated hemoglobin (HbA1c; $-0.83\% \pm 0.59\%$, $P < .001$) and fasting blood glucose (-1.38 ± 1.62 mmol/L, $P < .001$) levels. In addition, TRE also significantly reduced triglyceride level (−0.24 mmol/L [−0.58 to 0.01 mmol/L], $P < .001$) after 12 weeks of intervention.

Conclusions: TRE can improve glycemic control in individuals with type 2 diabetes. Our findings indicate that TRE may represent a novel diet management option for patients with type 2 diabetes.

Abstract citation ID: lvag096.1064

EP634 - ECE_2287 - The role of Multidisciplinary team in the management of Metabolic dysfunction-associated steatotic liver disease (MASLD) in Obese individuals

Thaw Htet[1,2], Brooke Hughes[3], Julia Gordon[3], Judy Chen[1], Martina Preda[4] and Veronica Preda[1,2]
[1]*Macquarie University Hospital, Endocrine department, Sydney, Australia;* [2]*Macquarie University, Faculty of Medicine Health and Health Sciences, Sydney, Australia;* [3]*Macquarie University, Sydney, Australia;* [4]*I-MED Radiology, Sydney, Australia*

The diagnostic criteria for MASLD have evolved to incorporate the definition of hepatic steatosis with inclusion of cardiometabolic risk factors. Current management guidelines recommend lifestyle interventions, such as dietary changes and increased physical activity, supported by a multidisciplinary team (MDT). However, real-world data on the effectiveness of MDT-led care for MASLD remains limited, despite the growing prevalence of MASLD alongside rising obesity rates. This study aimed to evaluate the impact of multidisciplinary input, including dietetics and an exercise physiologist support, on MASLD and its associated biochemical markers.

A retrospective cohort study was conducted on patients presented for weight management under care of endocrinologists, with access to multidisciplinary care. Inclusion criteria required evidence of hepatic steatosis and at least one cardiometabolic risk factor (elevated BMI, HbA1c, hypertension, or dyslipidaemia) and two serial liver ultrasonograms. Outcomes were assessed before and after a minimum of six months of MDT involvement, focusing on changes in liver ultrasonograms, weight, HbA1c, fasting lipid profile, and FIB-4 scores.

In a total of 75 patients, more than 50% of the patients were managed by MDT input. Diet advice was based on principles of the Mediterranean diet and patients were encouraged to practice mindful eating, control portion servings and self-monitor their caloric intake. Exercise regimens were tailored to the individual preference including increasing incidental activity, engaging in moderate intensity aerobic exercise, and incorporating 2 resistance training sessions per week.

Participants with MDT input experienced greater weight reductions with a mean reduction of 15 kg (14%) in the MDT group compared to 6 kg (6%) in the non-MDT group. The mean reduction in BMI was also greater in the MDT group, with a 5.5 kg/m^2(13%) compared to 2 kg/m^2(6 %). Mean hepatic steatosis severity grade had improved from 1.87 to 1.23 in the MDT group, with a mean reduction of 0.65(33 %) compared with negligible improvement of 0.07(8.82%) in non-MDT group. However, the changes in FIB-4 scores was not significantly different in the two. In the type 2 diabetes patients, no significant difference in HbA1c reduction in between MDT and non-MDT groups.

Our findings support the value of structured MDT care in achieving meaningful clinical improvements in MASLD. Longitudinal patient engagement appears to be the key, highlighting the importance of integrating MASLD management into the broader obesity and metabolic health strategies.

Abstract citation ID: lvag096.1065

EP635 - ECE_2659 - Shorter smartGuard™ warm-up duration is associated with better early glycaemic control in medtronic minimed™ 780G users

Ivana Dora Vodanović[1], Antonia Precali[2], Maja Baretić[1,3], Karin Zibar Tomsic[1] and Ivana Kraljevic[1,3]
[1]*University Hospital Centre Zagreb, Department of Endocrinology, Zagreb, Croatia;* [2]*Oxivita Hyperbaric Medicine Polyclinic, Zagreb, Croatia;* [3]*School of Medicine, University of Zagreb, Zagreb, Croatia*

Background: Manufacturer guidance specifies a 48-hour warm-up period (starting at the first midnight after insulin delivery begins) before SmartGuard™ (SG) activation. In clinical practice, some centres extend manual mode beyond this period.

Aim: To assess whether the duration of SG warm-up period is associated with differences in glycaemic control.

Methods: This retrospective observational study included all nonpregnant adult patients with type 1 diabetes who initiated 780G treatment for the first time from April 2021 to November 2024 in University Hospital Centre Zagreb. Baseline patient characteristics and continuous glucose monitoring data extracted from CareLink™ Clinic software were analyzed.

Glucoregulation parameters (time in/above/below range—TIR/TAR/TBR; glucose management indicator—GMI; average glucose—AG) were analyzed at baseline (P0, prior to 780G initiation), two weeks after SG initiation (P1), and three months after SG initiation (P2).

Participants were stratified into two cohorts: SGWU1 (SmartGuard warm-up ≤ 4 days) and SGWU2 (SmartGuard warm-up > 4 days). Between-group comparisons were adjusted for baseline glycaemic control and prior use of an insulin pump.

Results: We analyzed 98 participants (age 31.4 ± 10.4 years, diabetes duration 16.7 ± 7.8 years; 62.2% female) and compared data across three periods between SGWU groups. Overall, SGWU1 showed more favorable glycaemic profiles than SGWU2: higher TIR (≈71.0% vs 66.2%; $P = .0094$), lower TAR (≈25.4% vs 30.5%, $P = .0044$), lower GMI (6.92 vs 7.08, $P =$

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

.0363), and lower AG (8.29 vs 8.74 mmol/L, $P = .0068$). No significant difference emerged for TBR.

Between-group differences were most prominent for P1 (TIR 75.7% vs 69.8%, $P = .0080$; TAR 21.8% vs 28.1%, $P = .0065$; GMI 6.79 vs 7.00, $P = .0117$; AG 8.06 vs 8.54 mmol/L, $P = .0107$), whereas findings for P2 were borderline for TIR (78.1% vs 74.9%, $P = .0606$) and TAR (19.7% vs 23.1%, $P = .0725$), with no impact on GMI, AG, or TBR.

Within-group analyses showed significant improvements from P0 to P1 and P0 to P2 in both groups, with no significant change from P1 to P2.

Conclusions: Earlier SG activation is associated with better early glycaemic profiles, while differences attenuate by 3 months. These findings do not support prolonged manual-mode warm-up beyond the manufacturer's 48-hour requirement.

Abstract citation ID: lvag096.1066

EP636 - ECE_3154 - A subgroup analysis of Phase 3 study of Semaglutide Injection in Type 2 Diabetes Mellitus patients based on BMI: <23 kg/m^2, 23 to <25 kg/m^2 and ≥25 kg/m^2

Dipesh Sonawane[1], Unnikrishnan Gopalkrishnan[2], Ameya Joshi[3], Richa Giri[4], Shalin Shah[5], Jitendra Shukla[6], Sanjiv Maheshswari[7], M.C. Rekha[8], Manish Singh[9], Aditya Bari[10], Niranjan Pathak[11], Akash Shah[12], Shweta Bhandari[13], Ambanna Gowda[14], C. Ambrish[15], Pravin Supe[16], Bharat Das[17], Prabhat Sharma[18], Mehul Virani[19], Prakash Kurmi[20], Gayatri Ghanekar[21], Mani Dasari[22], Bansidhar Sahoo[23], Sanjay Jangid[24], Manoj Srivastava[25], Prakash Shende[26], Sandesh Patil[27], Avinash Kumbhar[28], Shrikant Deshpande[29], C. Madhusudhan[30], Nitesh Patel[31], Apurva Shetty[1], Dipak Patil[1], Pravin Ghadge[1] and Suyog Mehta[1]

[1]Sun Pharma Laboratories Limited, Mumbai, India; [2]Chellaram Diabetes Institute, Pune, India; [3]Bhaktivedanta Hospital and Research, Thane, India; [4]GSVM Medical College, Kanpur, India; [5]Ratan Multi-speciality Hospital, Ahmedabad, India; [6]Motilal Nehru Medical College, Prayagraj, India; [7]Jawahar Lal Nehru Medical College, Ajmer, India; [8]Mandya Institute of Medical Science, Mandya, India; [9]Maya Hospital and Maternity Centre, Kanpur, India; [10]Pulse Multispeciality Hospital, Pune, India; [11]Ojas Multispeciality Hospital, Pune, India; [12]Health 1 Super Speciality Hospital, Ahmedabad, India; [13]Vincare Hospital, Bathinda, India; [14]Citizen Hospital, Bangalore, India; [15]Medstar Speciality Hospital, Bangalore, India; [16]Supe Heart & Diabetes Hospital & Research Centre, Nashik, India; [17]Sparsh Hospitals and Critical Care Private, Bhubaneshwar, India; [18]Maharaja Agrasen Superspeciality Hospital, Jaipur, India; [19]Global hospital, Surat, India; [20]Shivam Hospital, Ahmedabad, India; [21]Asian Institute of Medical sciences, Dombivali, India; [22]Rajalakshmi Hospital & Research Center, Bangalore, India; [23]Kanungo Institute of Diabetes Specialities, Bhubaneshwar, India; [24]Hi-Tech Medical College & Hospital, Bhubaneshwar, India; [25]Om Surgical Center and Maternity Home, Varanasi, India; [26]Lokmanya Medical Research Center, Pune, India; [27]Shree Siddhivinayak Maternity & Nursing Home, Nashik, India; [28]Aster Aadhar Hospital, Kolhapur, India; [29]Ashirwad Hospital and Research Centre, Ulhasnagar, India; [30]NRR Hospital, Bangaluru, India; [31]Samarpan Hospital, Ahmedabad, India

Objectives: To evaluate the efficacy and safety of Synthetic Semaglutide Injection manufactured by Sun Pharma (Test arm) with Ozempic® Injection (Reference arm) in Indian patients with Type 2 Diabetes Mellitus (T2DM) in three subgroups based on BMI: <23 kg/m^2 (Subgroup 1 [S1]), 23 to <25 kg/m^2 (Subgroup 2 [S2]), ≥25 kg/m^2 (Subgroup 3 [S3]).

Materials and Methods: This was a phase III, multicentre, randomized, open-label, active controlled study. Total 314 adults (18-65 years) with T2DM (HbA1c: 7.0-10.5%) on diet/exercise uncontrolled with stable metformin dose (≥1500 mg or maximum tolerated dose) for ≥12 weeks were enrolled. Eligible patients were randomized in a 1:1 ratio and received Test product or Reference product, subcutaneous injections in a weekly dose of 0.25 mg to 2 mg for 24 weeks. [CTRI Registration number: CTRI/2025/02/080592].

Results: At baseline, distribution of patients was as follows: 38 patients with BMI <23 kg/m^2 *(S1)*, 72 patients with BMI 23 to <25 kg/m^2 *(S2)* and 204 patients with BMI ≥25 kg/m^2 *(S3)*. HbA1c reduction from baseline to Week 24 in Test arm was comparable to comparator arm: *S1*: $-2.26 \pm 0.91\%$ vs $-1.89 \pm 0.87\%$ ($P = .2028$), *S2*: $-2.21 \pm 0.76\%$ vs $-2.25 \pm 0.74\%$ ($P = .9033$), *S3*: $-1.95 \pm 0.82\%$ vs $-1.85 \pm 0.95\%$ ($P = .4848$). Significant reduction from baseline HbA1c was observed across all three sub-groups at Week 24 in both the study arms. Significant reductions in post-prandial and fasting blood glucose levels at Week 24 were seen in both the study arms and the changes were comparable across all three BMI subgroups. Proportion of patients achieving HbA1c <7.0% were comparable between the Test and Comparator arms, *S1*:15 (88.2%) vs 13 (76.5%) ($P = .3697$), *S2*: 23 (74.2%) vs 27 (75.0%) ($P = .7267$), *S3*: 68 (72.3%) vs 68 (73.1%) ($P = .9184$) across all three BMI subgroups. Three patients experienced hypoglycaemia. None of the patients required rescue medication. The incidence of treatment-emergent adverse events (TEAEs) was similar in both arms. Most common TEAEs were gastrointestinal events (Diarrhoea, Nausea, Vomiting) in all three subgroups. Study medications were well tolerated.

Conclusions: Semaglutide injection (Test product) demonstrated comparable glycaemic control to Reference product in T2DM patients uncontrolled on metformin monotherapy across all three BMI subgroups of normal weight, overweight and obese patients.

Abstract citation ID: lvag096.1067

EP637 - ECE_1605 - Body mass index and waist-to-hip ratio patterns in women with and without polycystic ovary syndrome: evidence from an unselected population

Asmamaw Bizuneh[1], Chau Thien Tay[1,2], Arul Earnest[3], Ricardo Azziz[4], Larisa Suturina[5], Xiaomiao Zhao[6], Alessandra Gambineri[7], Fahimeh Tehrani[8], Bulent Yildiz[9], Jin Ju Kim[10], Liangzhi Xu[11], Christian Makwe[12], Helena Teede[1,2] and Anju Joham[1,2]

[1]Monash Centre for Health Research and Implementation, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Australia; [2]Department of Endocrinology and Diabetes, Monash Health, Clayton, Melbourne, Australia; [3]School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia; [4]Departments of Obstetrics and Gynecology, and Medicine,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

University of Alabama at Birmingham, Birmingham, Alabama, United States; [5]Department of Reproductive Health Protection, Scientific Center for Family Health and Human Reproduction Problems, Irkutsk, Russia; [6]Department of Reproductive Medicine, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China; [7]Department of Medical and Surgical Science-DIMEC, Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [8]Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [9]Division of Endocrinology and Metabolism, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Türkiye; [10]Division of Reproductive Endocrinology, Department of Obstetrics and Gynecology, Healthcare System Gangnam Center, Seoul National University Hospital, Seoul, South Korea; [11]Department of Obstetrics and Gynecology, West China Second University Hospital, Sichuan University, Chengdu, China; [12]Department of Obstetrics and Gynaecology, College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria

Background: Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder among women of reproductive age, often linked to obesity, yet how body mass index (BMI) and waist-hip ratio (WHR) vary across PCOS phenotypes in unselected populations remains unclear. Therefore, this study aimed to examine BMI and WHR patterns in a large multiethnic cohort of women with and without PCOS.

Methods: A community-based study from eight countries across four continents was included. The primary outcomes were BMI and WHR. Correlations between variables were assessed using Spearman's rank correlation coefficient, and multicollinearity was evaluated using the variance inflation factor (VIF). Clinical features were compared between non-PCOS and PCOS, and stratified across PCOS phenotypes: classic (hyperandrogenism [HA], ovulatory dysfunction [OD], and/or polycystic ovary morphology [PCOM]), phenotype C (HA and PCOM), and phenotype D (OD and PCOM). Multiple linear and logistic regression analyses were used.

Results: This study comprised 9240 women representing 11 ethnic groups, of whom 45.2% were Asian Chinese (Han), followed by 22.2% Persians. Overall, 11.4% of participants were women diagnosed with PCOS, with nearly half exhibiting the classic phenotypes (48.4%). Among women with PCOS, 58.0% had normal BMI, 18.5% were overweight, and 11.7% were obese, while 12% had WHR defined central obesity. Classic and phenotype C were statistically associated with higher BMI, whereas the odds of central obesity were higher in women with classic and phenotype D subtypes.

Conclusions: Our findings indicate that in unselected populations, the majority of women with PCOS exhibit a normal BMI, in contrast to clinic-based cohorts, where obesity is markedly overrepresented. Classic and phenotype C were characterized with increased overall adiposity, whereas classic and phenotype D were distinguished by central fat accumulation, highlighting distinct patterns of body fat distribution across PCOS phenotypes. Longitudinal, population-based studies integrating multi-omic data are essential for unraveling BMI-related heterogeneity to advance precision diagnosis and management in PCOS.

Abstract citation ID: lvag096.1068

EP638 - ECE_1879 - Nasal microbiota composition is increased in obesity and does not correlate with alterations in olfactory function

Lolita Odermatt[1,2], Vanni Benvenga[3], Anouk Hoogkamer[1], Alexander Komai[1], Lisa Hurni[1], Valerie Mettraux[1], Alexandra Gnann[2], Adrian Egli[3] and Katharina Timper[2,4,5]
[1]University Hospital Basel, Endocrinology, Diabetology and Metabolism, Basel, Switzerland; [2]University of Basel, Department of Biomedicine, Basel, Switzerland; [3]University of Zurich, Institute of Medical Microbiology, Zurich, Switzerland; [4]TUM and TUM University Hospital, Institute for Clinical Nutritional Medicine, Munich, Germany; [5]Helmholtz-Munich, Institute for Translational Metabolism Research, Munich, Switzerland

Background: While alterations of the gut microbiome and its pathophysiological role in the context of obesity have been extensively studied, the role of the nasal microbiome remains unexplored.

Methods: 50 participants with obesity and 50 age- and sex-matched lean individuals at the age 18-55 years were enrolled in the study. Each participant was assessed for olfactory function using the Burghart (ODOFIN) Sniffin' Sticks Test. Anthropometric parameters, vital signs and systemic metabolic and inflammation blood parameters were assessed. Nasal swabs were obtained from the anterior nares. Nasal swab microbiome analysis was performed using 16S rRNA gene sequencing targeting the V3–V4 region. Sequence data were processed in QIIME2 using DADA2 for denoising and taxonomic assignment against the Greengenes2 reference database. Associations were evaluated using regression and correlation analyses with adjustment for body mass index.

Aim: To assess if the nasal microbiome composition is altered in individuals with obesity compared to sex- and age-matched lean controls and to elucidate if the nasal microbiome is associated with alterations in olfactory sensory perception and systemic markers on metabolism and inflammation.

Results: In total, 50 participants with obesity with a mean age of 36.2 ± 10.73 and a BMI 37.06 ± 4.96 kg/m^2 and 50 lean participants with a mean age of 36.02 ± 10.69 and a BMI 22.68 ± 1.98 kg/m^2 were enrolled. Olfactory function and olfactory threshold was impaired in the obesity compared to the lean group. Alpha diversity analyses of the nasal microbiome revealed significantly higher microbial diversity in the obesity group compared to the lean group, as assessed by Shannon entropy ($\chi^2 = 10.562$, $P = .001$) and species richness ($\chi^2 = 12.232$, $P = .0005$). Beta diversity analysis further demonstrated a significant difference in microbial community composition between the groups (PERMANOVA: $R^2 = 0.055$, $F = 4.46$, $P = .001$). The differential abundance analysis of sequence variants between the groups revealed that the presence of *Staphylococcus hominis* was associated with an obesity phenotype and, independent of BMI, with low HDL levels ($P = .004$*), while the presence of *Dolosigranulum pigrum* was associated with a lean phenotype and low LDL levels. Alterations in olfactory function were not associated with alterations in the nasal microbiome composition.

Conclusions: The diversity and composition of the nasal microbiome are associated with BMI and differ between lean individuals and individuals with obesity. The abundance and presence of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Staphylococcus hominis are associated with an obesity phenotype and lower HDL level.

Abstract citation ID: lvag096.1069

EP639 - ECE_3171 - Efficacy and safety of semaglutide injection in weight management: a subgroup analysis in mild renal impairment patients

Unnikrishnan Gopalkrishnan[1], Ameya Joshi[2], Harish Kumar[3], Richa Giri[4], Sanjiv Maheshswari[5], Valluri Prasad[6], Jitendra Shukla[7], M.C. Rekha[8], Nutankumar Agrawal[9], Yogesh Rasal[10], Banshidhar Sahoo[11], Shweta Bhandari[12], Ambana Gowda[13], Phadke Keshav[14], Pravin Supe[15], Niranjan Pathak[16], C. Ambrish[17], Ashutosh Sonawane[18], Yash Bahulikar[19], Amit Bhaskar[20], R. Arunkumar[21], Priyanka Yadav[22], Supriya Sonowal[22], Dipak Patil[22], Sucheta Pandit[22], Pravin Ghadge[22] and Suyog Mehta[22]
[1]Chellaram Diabetes Institute, Pune, India; [2]Bhaktivedanta Hospital and Research Institute, Thane, India; [3]Amrita institute of Medical Sciences and Research Centre, Kochi, India; [4]G.S.V.M medical College, Kanpur, India; [5]Jawahar Lal Nehru Medical College, Ajmer, India; [6]King George Hospital, Visakhapatnam, India; [7]Moti Lal Nehru Medical College, Prayagraj, India; [8]Mandya Institute of Medical Science, Mandya, India; [9]M.L.B Medical college, Jhansi, India; [10]Pulse Multispecialty Hospital, Pune, India; [11]KIDS Hospital, Bhubaneswar, India; [12]Vincare Hospital, Bathinda, India; [13]Citizen Hospital, Bangalore, India; [14]Sahyadri Super Speciality Hospital, Pune, India; [15]Supe Heart and Diabetes Hospital and Research Centre, Nashik, India; [16]OJAS Multispeciality Hospital, Pune, India; [17]Medstar Speciality Hospital, Bangalore, India; [18]Panacea Hospital, Nashik, India; [19]MMFHA Joshi Hospital, Pune, India; [20]Janta Hospital and Maternity Center, Varanasi, India; [21]Chettinad Hospital & Research Institute, Chengalpattu, India; [22]Sun Pharma Laboratories Limited, Mumbai, India

Objectives: To evaluate the efficacy and safety of synthetic semaglutide injection (Test drug) compared with Wegovy® (Reference drug) dosage up to 2.4 mg subcutaneously for weight management in mild renal impairment patients (eGFR 60 to <90 mL/min/1.73 m^2).

Materials and Methods: A phase III, multicentre, randomized, open-label, active-controlled clinical study (CTRI/2025/04/085487) was conducted across 22 study sites in India after receiving regulatory and ethics committee approvals. In this study, 267 adult patients with (BMI) ≥ 30 kg/m^2 or ≥27 kg/m^2 with the presence of at least one co-morbidity of hypertension, dyslipidaemia and/or type 2 diabetes mellitus were included. Patients were randomized to receive either test drug or reference drug weekly subcutaneously for 24 weeks.

Results: Total 101 patients with eGFR 60 to <90 mL/min/1.73 m^2 at baseline were included in this study. In this group mean (±SD) percentage reduction in weight from baseline to week 24 was −14.2 (± 3.17) with test drug and −13.7 (± 2.82) with reference drug. The decrees in weight with the test and the reference drug was comparable ($P = .6248$).

The proportion of patients achieving ≥ 5% weight loss was 98.6% with test drug and 100% with reference drug ($P = .5403$) at week 24. The proportion of patients achieving ≥10% weight loss was 88.7% with test drug and 86.7% with reference drug ($P = .6028$) at week 24 At Week 24, Mean (± SD) change from baseline in BMI with test and the reference drug was − 4.76 (± 1.14) kg/m^2 and −4.67 (± 1.12) kg/m^2 respectively ($P = .5494$). Mean (± SD) change in waist circumference with test and the reference drug was −10.2 (± 4.59) cm and −9.57 (± 3.50) cm respectively ($P = .5098$) at week 24. The change in BMI and waist circumference was comparable between the test and the reference drug at week 24

In diabetic patients there was decrease in glycaemic parameters (HbA1c, FBG and PPBG) from baseline to week 24 in both S1 and S2 and was comparable between arms ($P > .05$). In non-diabetic patients decrease in glycaemic parameters (HbA1c, FBG and PPBG) from baseline to week 24 was not clinically relevant compared to diabetic patients and was comparable between arms ($P > .05$).

Study medications were well tolerated.

Conclusions: Semaglutide injection is effective in reducing weight in mild renal impairment patients and can be a treatment of choice in management of weight in patients with mild renal impairment.

Abstract citation ID: lvag096.1070

EP640 - ECE_3474 - Correlation of weight loss and SF-36 physical function score in weight management with semaglutide injection: post-hoc analysis of phase 3 Study

Unnikrishnan Gopalkrishnan[1], Ameya Joshi[2], Harish Kumar[3], Richa Giri[4], Sanjiv Maheshswari[5], Valluri Prasad[6], Jitendra Shukla[7], M.C. Rekha[8], Nutankumar Agrawal[9], Yogesh Rasal[10], Banshidhar Sahoo[11], Shweta Bhandari[12], Ambana Gowda[13], Phadke Keshav[14], Pravin Supe[15], Niranjan Pathak[16], C. Ambrish[17], Ashutosh Sonawane[18], Yash Bahulikar[19], Amit Bhaskar[20], R. Arunkumar[21], Priyanka Yadav[22], Supriya Sonowal[22], Dipak Patil[22], Sucheta Pandit[22], Pravin Ghadge[22] and Suyog Mehta[22]
[1]Chellaram Diabetes Institute, Pune, India; [2]Bhaktivedanta Hospital and Research Institute, Thane, India; [3]Amrita institute of Medical Sciences and Research Centre, Kochi, India; [4]G.S.V.M medical College, Kanpur, India; [5]Jawahar Lal Nehru Medical College, Ajmer, India; [6]King George Hospital, Visakhapatnam, India; [7]Moti Lal Nehru Medical College, Prayagraj, India; [8]Mandya Institute of Medical Science, Mandya, India; [9]M.L.B Medical college, Jhansi, India; [10]Pulse Multispecialty Hospital, Pune, India; [11]KIDS Hospital, Bhubaneswar, India; [12]Vincare Hospital, Bathinda, India; [13]Citizen Hospital, Bangalore, India; [14]Sahyadri Super Speciality Hospital, Pune, India; [15]Supe Heart and Diabetes Hospital and Research Centre, Nashik, India; [16]OJAS Multispeciality Hospital, Pune, India; [17]Medstar Speciality Hospital, Bangalore, India; [18]Panacea Hospital, Nashik, India; [19]MMFHA Joshi Hospital, Pune, India; [20]Janta Hospital and Maternity Center, Varanasi, India; [21]Chettinad Hospital & Research Institute, Chengalpattu, India; [22]Mumbai, India

Objectives: To evaluate the correlation between weight loss and quality of life as assessed by SF-36 (36 item shoer form survey) questionnaire in patients treated with Semaglutide injection for weight management

Materials and Methods: This phase III, multicentre, randomized, open-label, active-controlled clinical study (CTRI/2025/04/085487) was conducted across 22 study sites in India after receiving regulatory and ethics committee approvals. Total 267 adult patients with BMI ≥ 30 kg/m^2 or ≥ 27 kg/m^2 with the presence

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

of at least one co-morbidity of hypertension, dyslipidaemia and/or type 2 diabetes mellitus were included. Patients were randomized to either test arm to receive synthetic semaglutide injection or reference arm to receive Wegovy® every week subcutaneously for 24 weeks. The primary endpoint was change in body-weight from baseline to week 24. Secondary endpoints included change in BMI, waist circumference, SF-36, and glycaemic measures in diabetic and non-diabetic patients. Safety assessments included incidence of TEAEs and anti-drug/neutralizing antibody. This post-hoc analysis was conducted to evaluate the correlation between weight loss and improvement in quality of life as assessed by SF-36 physical function score.

Results: The Pearson's correlation coefficient between change in weight loss and SF-36 physical functioning score was −0.155 with *P* value = .0467 in test arm.

The Pearson's correlation coefficient between change in weight loss and SF-36 physical functioning score was -0.046 with *P* value = .6831 in reference arm.

There is negative correlation between weight loss and change in SF-36 physical functioning score in both test and reference arm indicating greater reduction in weight loss is associated with more increase in SF-36 score signifying improvement is SF-36 total score. The correlation between weight loss and improvement in SF-36 physical functioning score was statistically significant in test arm. The statistical significance observed in the Pearson correlation analysis in test arm supports the robustness of this association.

Conclusions: This post-hoc analysis demonstrated that there is improvement in quality of life as measured by SF-36 physical function score with reduction in weight, in patients treated with semaglutide injection for weight management.

Abstract citation ID: lvag096.1071

EP641 - ECE_2044 - Transition from autoantibody-negative to autoimmune type 1 diabetes following COVID-19 infection and vaccination: a report of four cases with delayed onset

Nurcan Ince[1], Berna Evranos Ogmen[2,3], Oya Topaloglu[2], Reyhan Ersoy[2] and Bekir Cakir[2]

[1]Trabzon Legal Training And Research Hospital, endocrinology and metabolism diseases, Yomra, Türkiye; [2]Ankara Yıldırım Beyazit Üniversitesi Tip Fakültesi, endocrinology and metabolism diseases, Ankara, Türkiye; [3]Ankara yildirim beyazit university, endocrinology and metabolism, Ankara, Türkiye

Introduction: Type 1 diabetes mellitus(T1DM) is an autoimmune disorder characterised by the destruction of pancreatic β-cells, typically identified through markers such as glutamic acid decarboxylase(GAD65) antibodies.While environmental triggers for T1DM are well-documented, the emergence of COVID-19 and its vaccines has introduced new concerns regarding their potential role in triggering autoimmune responses.This study reports four cases where patients previously diagnosed with non-autoimmune(antibody-negative) diabetes transitioned to autoimmune T1DM following COVID-19 infection and/or vaccination.

Methods: We retrospectively evaluated patients at Ankara Bilkent City Hospital whose anti-GAD levels were measured and were positive between September 2020 and August 2022. Four patients(two males, two females; age range 42-52 years) with a confirmed history of autoantibody-negative diabetes were identified.Clinical and laboratory data, including C-peptide levels, HbA1c, and vaccination/infection timelines, were extracted from electronic medical records.

Results: At the time of initial diabetes diagnosis, all four patients tested negative for GAD65 antibodies and urine ketones.Following COVID-19 infection or vaccination, all four patients developed high GAD65 antibody titres(ranging from 595 to >2000 IU/mL) and low C-peptide levels(0.16 to 0.36 ng/mL).Notably, Cases 3 and 4 also had pre-existing Hashimoto's disease. Unlike many cases in existing literature, the onset of autoimmunity in these patients was delayed; the time from infection to antibody measurement ranged from 171 to 619 days, and from vaccination to measurement ranged from 5 to 704 days(Table 1).None of the patients experienced a "honeymoon phase" or diabetic ketoacidosis at the time of antibody positivity. All four patients eventually required intensive multiple insulin therapy to maintain glycaemic control.

Discussion: These findings suggest that SARS-CoV-2 and its vaccines may act as triggers for autoimmune T1DM, even in patients with a multi-year history of non-autoimmune diabetes.The delayed presentation in these cases highlights the complexity of post-COVID autoimmunity and suggests that β-cell destruction may be progressive in some individuals.Further research and global registries are essential to clarify the long-term impact of COVID-19 on the incidence and pathogenesis of autoimmune diabetes.

Table 1

Feature	Study Cases(n = 4)	Typical Literature Cases
Initial Diabetes Status	Known autoantibody-negative (non-autoimmune)	Often, new-onset or unknown prior antibody status
Onset Timing	Delayed: 171-619 days post-infection; up to 704 days post-vaccine	Acute: Typically within 3 days to 8 weeks post-vaccination
Ketoacidosis (DKA)	None observed at the diagnosis of autoimmunity	Common:~41.7% in some vaccine-related reviews
Clinical Symptoms	Absence of overt/acute hyperglycemic symptoms	Often present with acute clinical symptoms
Honeymoon Phase	None observed; required immediate intensive insulin	Possible; some cases managed with diet or OADs temporarily

Abstract citation ID: lvag096.1072

EP642 - ECE_3992 - The first case of insulin autoimmune syndrome (Hirata's Disease) in A Qatari female: a case report

Shafik Mansour[1,2] and Shaimaa Arroub[1]

[1]Doha, Qatar; [2]Hamad Medical Corporation, Qatar Metabolic Institute, Doha, Qatar

Background: Insulin Autoimmune Syndrome (IAS), also known as Hirata's disease, is a rare cause of insulin-mediated hypoglycemia, mostly reported in East Asian populations. This condition is characterized by circulating autoantibodies that bind to endogenous insulin, creating large complexes that act as a reservoir, releasing high amounts of "free" insulin unexpectedly, causing hypoglycemia. Fewer than 10 cases have been reported

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

in Arab nationals, and to date, no cases have been documented in Qatari national. Herein, we report the first case of IAS in a Qatari woman.

Case Presentation: A 39-year-old Qatari woman presenting with a three- week history of recurrent symptomatic hypoglycemia occurring approximately two weeks after discontinuing a short course of prednisolone therapy prescribed for recurrent pregnancy loss. The hypoglycemic episodes are mainly 2-4 hours after meals. Continuous glucose monitoring revealed a characteristic pattern of postprandial hyperglycemia (200-220 mg/dL) followed by severe hypoglycemia (40-50 mg/dL). She has normal liver, renal, and adrenal functions. Laboratory evaluation during a documented hypoglycemic episode (plasma glucose 59 mg/dL) revealed markedly elevated insulin levels (760 μU/mL; reference 2.6-24.9 μU/mL) and C-peptide levels (21 ng/mL; reference 1.1-4.4 ng/mL) with an insulin-to-C-peptide molar ratio of 1.1. Cross-sectional imaging excluded pancreatic lesions. Insulin autoantibody testing confirmed the diagnosis with markedly elevated titers at 84 nmol/L (reference <0.4 nmol/L). Treatment with prednisolone 20 mg daily resulted in complete symptom resolution and progressive normalization of antibody titers to 0.62 nmol/L after eight weeks of therapy. At three months post-steroids discontinuation, the patient remained free of hypoglycemia evident by normal continuous glucose monitoring.

Conclusions: This represents the first documented case of IAS in a Qatari national, highlighting the importance of recognizing this condition outside the traditionally affected East Asian populations to avoid unnecessary invasive diagnostic procedures or pancreatic surgery.

Abstract citation ID: lvag096.1073

EP645 - ECE_3285 - A comprehensive analysis of significant muscle loss associated with weight loss after sleeve gastrectomy

Ie Byung Park[1], Seung Joon Choi[2,3] and Dae Ho Lee[4]
[1]*Gachon University Gil Medical Center, Department of Endocrinology and Metabolism, Incheon, South Korea;* [2]*Incheon, South Korea;* [3]*Gachon University Gil Medical Center, Department of Radiology, Incheon, South Korea;* [4]*Shihwa Medical center, Department of Endocrinology and Metabolism, Siheung-si, South Korea*

Background and Purpose: Changes in body composition after bariatric surgery, particularly skeletal muscle alterations, are important determinants of metabolic health during weight loss. This study evaluated post-sleeve gastrectomy (SG) changes in body composition, focusing on skeletal muscle parameters and their metabolic associations.

Materials and Methods: This prospective cohort study included 83 morbidly obese patients undergoing SG. Clinical and metabolic variables, including 101 plasma metabolites, were measured preoperatively and at six months postoperatively. Body composition was assessed using dual-energy X-ray absorptiometry (DXA) for appendicular skeletal muscle mass (ASM), lean body mass, and total body fat, and magnetic resonance imaging (MRI) for abdominal adipose tissue, intramuscular fat, skeletal muscle index (SMI), contractile mass index (CMI) at the L3 level, and proton density fat fractions of skeletal muscle, liver, and pancreas. Statistical analyses were performed to identify factors associated with skeletal muscle loss after SG.

Results: After SG, significant reductions were observed in total body fat (−37.0%) and muscle fat (−21.1%) with a dramatic reduction in liver fat (−70.5%), which was accompanied by muscle loss (ASM −12.4%, SMI −23.9%, CMI −21.0%).Changes in SMI were positively correlated with changes in body weight and total body fat. Of note, SMI changes were negatively correlated with 3-hydroxybutyric acid ($r = -0.465$) and 3-hydroxyoctanoic acid ($r = -0.400$).

Conclusions: Weight loss after SG causes significant skeletal muscle loss, potentially impairing metabolic health, underscoring the need for muscle preservation strategies postoperatively.

Abstract citation ID: lvag096.1074

EP646 - ECE_3942 - A comparative study of the well-being of patients with varicose disease of the subcutaneous veins of the lower extremities and type 2 diabetes during treatment with various thermal ablation methods

Khrystyna Moskva, Taras Kikhtiak and Olesya Kikhtyak
STATE NON-PROFIT ENTERPRISE "DANULO HALYTSKY NATIONAL MEDICAL UNIVERSITY IN LVIV", Lviv, Ukraine

Objective: To evaluate the efficacy of endovenous laser ablation (EVLA, 1470 nm wavelength) and radiofrequency ablation (RFA) in the management of patients with varicose vein disease (VVD) and type 2 diabetes mellitus (T2DM), utilizing both individualized and standardized questionnaires.

Materials and Methods: The study involved 82 patients with VVD and T2DM from Lviv between 2022 and 2024, with no prior treatment history. Patients were divided into two groups: Group I with VVD and Group II with VVD plus T2DM. Each group was further split into two subgroups: EVLA-I, RFA-I, and EVLA-II, RFA-II. Follow-up assessments were conducted before treatment (Visit 1), on day 3 (Visit 2), and 1 month post-treatment (Visit 3). At each visit, patients were assessed using the VCSS (Varicose Clinical Severity Score), VAS (Visual Analogue Scale), and a self-administered questionnaire (SAQ).

Results: VCSS scores dropped significantly ($P < .05$) after 1 month in all subgroups of VVD and VVD + T2DM, showing both thermal ablation techniques are effective. Comparing the pain intensity on the VAS scale between EVLA-I and RFA-I, and EVLA-II and RFA-II, a significant difference ($P < .05$) was found during control examination Visit 1 (4.3 ± 0.43 and 2.7 ± 0.36 for EVLA-I; 4.5 ± 0.41 and 2.4 ± 0.33 for RFA-I) and Visit 2 (3.6 ± 0.25 and 2.4 ± 0.17 for EVLA-II; 3.1 ± 0.27 and 2.1 ± 0.2 for RFA-II), indicating a higher pain intensity under the influence of ELA regardless of the study group (VCH or VCH+CD-2). At Visit 1, 46% of patients in EVLA-I and 67% in RFA-I reported no complaints. After one month (Visit 3), these numbers rose to 92% and 97%, respectively. The choice of thermal technique didn't significantly affect the "no complaints" rate between Visits 1 and 3. The VVD + T2DM group showed a smaller increase, indicating that carbohydrate metabolism disorders impact recovery, seen in more frequent and longer neurological symptoms (numbness, tingling).

Conclusions: Total VCSS scores dropped after one month in both groups, regardless of the ablation method. RFA caused less pain than EVLA during and three days post-treatment. According to a

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

self-questionnaire, RFA led to fewer complications like numbness and tingling after a month, although paresthetic symptoms were worse in VVD + T2DM patients, no matter the method.

Abstract citation ID: lvag096.1075

EP647 - ECE_3971 - Impact of anthropometric measures and obesity on left ventricular remodeling

Cvetanka Volkanovska Ilijevska, Irfan Ahmeti, Valentina Velkoska Nakova, Natasha Nedeska Minova, Ljubica Georgievska Ismail, Valnetina Andova and Marija Zivkovic
Medical Faculty, Ss. Cyril and Methodius, University Clinic for Endocrinology, Diabetes and Metabolic Disorders, Endocrinology, Skopje, North Macedonia

Obesity is a major risk factor for heart failure, causing structural and functional myocardial changes. This study evaluated whether obesity independently predicts alterations in myocardial structure and function in overweight and obese individuals and assessed correlations of obesity severity and duration with myocardial remodeling and deformation.

In this cross-sectional study, 126 participants (mean age 45 ± 9.6 years; 58.7% female) with BMI > 25 kg/m² were classified into four BMI groups. Mean BMI was 35 kg/m², waist circumference was 111.9 cm, and hip circumference was 118.4 cm; 74% had obesity for >10 years. Cardiac structure and function were assessed by 2D transthoracic echocardiography, and myocardial deformation by speckle tracking echocardiography (GLS%, GRS%, GCS% for LV; PALS%, PACS% for LA). Correlations were analyzed using Pearson and/or Spearman coefficients, and stepwise linear regression identified independent predictors of remodeling.

LV and LA structural and functional changes significantly correlated with obesity degree and duration. Increased interventricular septal and posterior wall thickness correlated with waist circumference ($r = 0.216$, $P = .015$; $r = 0.385$, $P = .0001$) and waist-to-hip ratio ($r = 0.208$, $P = .02$; $r = 0.293$, $P = .001$), particularly in females. Reduced LVEF correlated with obesity duration ($r = -0.201$, $P = .040$). GLS% correlated with BMI ($r = -0.410$, $P = .000$), waist circumference ($r = -0.430$, $P = .0001$), waist-to-hip ratio ($r = -0.241$, $P = .007$), and duration ($r = -0.290$, $P = .001$). GCS% showed similar correlations (BMI: $r = -0.322$, $P = .0001$; waist: $r = -.284$, $P = .002$; waist-to-hip: $r = -0.203$, $P = .031$; duration: $r = -0.309$, $P = .001$).Indexed LV mass (LVMh, LVMh²) correlated with BMI and waist circumference, stronger in females (BMI: $r = 0.489$, $P = .0001$ vs $r = 0.352$, $P = .010$; waist: $r = 0.396$, $P = .0001$ vs $r = 0.380$, $P = .006$). LV end-diastolic volume correlated with BMI ($r = 0.182$, $P = .041$); MAPSE changes with waist circumference ($r = 0.202$, $P = 0.024$); lower LA PALS% with waist circumference ($r = -0.232$, $P = .009$).Regression analysis showed obesity duration and BMI independently predicted increased LV mass, LA volume, and reduced GCS %; waist circumference independently predicted higher relative wall thickness, lower GLS%, and decreased PALS% (all $P < .05$).

Obesity promotes structural and functional myocardial remodeling, with anthropometric parameters serving as key independent predictors of left heart changes.

Abstract citation ID: lvag096.1076

EP649 - ECE_2874 - Setmelanotide treatment in severe hypothalamic obesity: report of two cases

Dimitra Sinni, Panagiotis Karageorgiou, Maria Zotou, Marinella Tzanela and Dimitra Argyro Vassiliadi
Department of Endocrinology "D. Ikkos"- Diabetes Center-EndoERN-Evangelismos General Hospital, Athens, Greece

Background: Hypothalamic obesity is a rare, severe, and treatment-resistant condition caused by genetic or acquired hypothalamic damage. It is characterized by hyperphagia, impaired satiety, rapid weight gain, and high cardiometabolic risk. Conventional lifestyle and pharmacological treatments are largely ineffective, and bariatric surgery shows limited benefit due to impaired central satiety signaling. Setmelanotide, a selective melanocortin-4 receptor (MC4R) agonist, may bypass disrupted hypothalamic pathways and represent a targeted therapeutic option.

Patients and Methods: We report two patients with severe hypothalamic obesity treated with setmelanotide. The first patient is a 22-year-old male who developed hypothalamic dysfunction after surgical resection of a craniopharyngioma, with complete loss of satiety and rapid weight gain of approximately 50 kg within four months. At baseline, body mass index (BMI) was 42.1 kg/m². Weight gain persisted despite optimized pituitary hormone replacement, dietary intervention, and off-label semaglutide. Setmelanotide was initiated and titrated to the maximum recommended dose. The second patient is a 19-year-old female with hypothalamic obesity associated with a possible hypothalamic amartoma. She gained 30 kg within a year, reaching a BMI of 50.2 kg/m². She was recently initiated on setmelanotide.

Results: In the first patient, treatment resulted in a weight loss of 16.5 kg over seven months, with BMI decreasing from 42.1 to 37.5 kg/m². In the second patient, body weight decreased by 10.5 kg after 1.5 months of therapy, with BMI reducing from 50.2 to 46.7 kg/m².

Safety: Setmelanotide was generally well tolerated. The first patient experienced skin hyperpigmentation, transient nausea, and episodes of prolonged erections, none requiring discontinuation. Despite reduced thirst perception in the context of central diabetes insipidus, serum sodium remained stable under desmopressin therapy. No significant adverse effects were observed in the second patient.

Conclusions: These cases support the potential efficacy and acceptable safety of setmelanotide in severe hypothalamic obesity of acquired or idiopathic origin. Early targeted therapy may help limit progressive weight gain when conventional treatments fail. Further prospective studies are warranted.

Abstract citation ID: lvag096.1077

EP651 - ECE_3960 - Circulating Meteorin-like protein and irisin in PCOS and their association with metabolic parameters

Katarzyna Paczkowska[1], Joachim Sobczuk[2], Katarzyna Zawadzka[3], Diana Jędrzejuk[3], Agnieszka Zembska[3], Jacek Konieczny[4], Dorota Kaszubkiewicz-Wardęga[5], Marek Bolanowski[3] and Jacek Daroszewski[6]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Endocrinological Ambulatory Care, Turek, Poland; [2]Department of Endocrinology, Diabetes and Isotope Therapy, University Clinical Hospital, Wroclaw, Poland; [3]Department of Endocrinology, Diabetes and Isotope Therapy, Wroclaw Medical University, Wroclaw, Poland; [4]CodeAI, Poznan, Poland; [5]2nd Department of Gynecology and Obstetrics, University Clinical Hospital, Wroclaw, Poland; [6]Wroclaw University of Science and Technology, Faculty of Medicine, Wroclaw, Poland

Introduction: Muscle tissue is being investigated as an endocrine active organ that secretes signaling molecules known as myokines. Numerous studies have evaluated myokines concentrations in a range of disorders, including polycystic ovary syndrome (PCOS) and metabolic syndrome. Among these myokines, irisin and meteorin-like protein (Metrnl) have been suggested to play important roles in promoting adipose tissue browning and enhancing insulin sensitivity.

Material and Methods: The study population included a total of 49 women, 31 diagnosed with PCOS and 18 healthy controls; all patients were between 18 and 40 years old. PCOS was diagnosed based on revised 2003 Rotterdam criteria.

Multiple anthropometrical, hormonal and biochemical parameters were assessed, including body composition with dual energy X-ray absorptiometry. Metrnl and irisin levels were measured with commercially available immunoassays.

Results: PCOS individuals and healthy controls do not differ in terms of age, BMI, WHR, fasting glucose, HOMA-IR, or body mass composition.

Assessment of Meteorin-like protein and irisin concentrations revealed no significant differences between PCOS and healthy women. Simultaneously, comparison of patients with BMI equal or greater than 25 to normal weight women showed significantly higher concentrations of irisin in the second group and no differences in Metrnl levels (11.53 ± 4.95 vs 15.96 ± 5.01, $P < .05$ and 16.73 ± 15.41 vs 18.0 ± 20.43, $P = .77$, respectively). Additionally, irisin level was negatively correlated with BMI, body fat mass, fasting glucose and insulin concentrations. No association between myokines levels was found.

Conclusions: Although irisin seems to be a promising biomarker, inconsistent research limits its value in clinical use in the assessment or treatment of obesity. Taking into consideration the similarity in physiological functions of irisin and Metrnl, no relationship between circulating levels of those particles suggests individual roles rather than synergetic actions in physiological adaptation to metabolic disease.

Abstract citation ID: lvag096.1078

EP653 - ECE_1285 - Global patterns and determinants of diabetic ketoacidosis at diagnosis of type 1 diabetes in children and adolescents: a 10-year global perspective

Ashraf Soliman[1], Noor Hamed[1], Manal Musallam[1], Fawziya Alyafei[1], Shayma Ahmed[1], Nada Alaaraj[1] and Nada Soliman[2]

[1]Hamad Medical Center, Pediatric Endocrinology, DOHA, Qatar; [2]Alexandria Health Directorate, MOH, Public Health, Alexandria, Egypt

Background: Diabetic ketoacidosis (DKA) remains a significant and potentially life-threatening complication at the onset of type 1 diabetes (T1D) in children and adolescents. Despite global improvements in diabetes awareness and care, DKA incidence at diagnosis continues to vary widely across regions. Understanding these disparities is essential for developing targeted prevention strategies.

Objective: To evaluate the global incidence of DKA at T1D diagnosis in children and adolescents over the past 10 years, and to explore the sociodemographic and health system factors contributing to this variability.

Methods: A review of epidemiological studies published between 2013 and 2023 was conducted using PubMed, Scopus, and global diabetes registries. Included studies reported DKA incidence at diagnosis in youth populations. Data were extracted on incidence rates, healthcare access, public health campaigns, and population-level characteristics across countries in Africa, Asia, the Americas, Europe, and Oceania.

Results: The DKA incidence at T1D diagnosis showed wide international variation:

- Middle East: UAE (80%), Saudi Arabia (59%)—Cultural and healthcare system barriers play significant roles.
- Asia: Malaysia (54-75%), China (50%), India (39%), Thailand (6.2%)—Wide range due to variable healthcare infrastructure and public education efforts.
- Europe: Romania (67%), Luxembourg (67%), Italy (58%), Germany (30%), Sweden and Denmark (15%)—Low rates in Northern Europe attributed to universal healthcare and early detection initiatives.
- Americas: United States (35%)—Increasing trend; disparities exist by ethnicity and insurance status.
- Oceania: Australia (26%)—Moderate incidence, reflecting robust healthcare systems but room for improvement.

Key Determinants:

- Age <5 years is consistently associated with higher DKA risk due to diagnostic delays.
- Lower socioeconomic status correlates with higher DKA prevalence.
- Public health infrastructure, national screening policies, and education campaigns significantly influence early recognition.
- Countries with widespread pediatric care and diabetes awareness campaigns (eg, Sweden, Denmark, Australia) report lower DKA rates.

Conclusions: The global burden of DKA at T1D diagnosis remains substantial, especially in low- and middle-income countries. Efforts to reduce DKA incidence must prioritize early detection through improved public awareness, training of primary care providers, and expansion of pediatric diabetes services. Tailored strategies are essential for addressing the socioeconomic and systemic gaps contributing to DKA disparities worldwide.

Abstract citation ID: lvag096.1079

EP654 - ECE_1870 - Ethnic differences in pregnancies complicated by gestational diabetes mellitus: a multiethnic cohort study

Kleoniki I. Athanasiadou[1], Georgios Markozannes[2], Fotini Kanouta[3], Marina Mitropoulou[3], Panagiotis Antsaklis[4], Kalliopi Pappa[4], Theodora Psaltopoulou[1], George Daskalakis[4], Dimitrios Goulis[5], Vasiliki Vasileiou[3] and Stavroula A. Paschou[1]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Endocrine Unit and Diabetes Centre, Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [2]Department of Hygiene and Epidemiology, School of Medicine, University of Ioannina, University Campus, Ioannina, Greece; [3]Department of Endocrinology and Diabetes Centre, Alexandra Hospital, Athens, Greece; [4]1st Department of Obstetrics and Gynecology, Alexandra Hospital, National and Kapodistrian University of Athens, Athens, Greece; [5]Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynaecology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece

Aim: To identify ethnic differences among women with gestational diabetes mellitus (GDM) in a multiethnic cohort.

Methods: This observational study included pregnant women with GDM (IADPSG criteria) attending a tertiary centre between January 2020-December 2023, classified according to their ethnic group as White, Black, Asian, or Other. Multivariable logistic and linear regression analyses were performed.

Results: A total of 633 women (513 White, 64 Black, 32 Asian, and 24 Other/Middle Eastern) were considered eligible for inclusion. Asian women had higher HbA1c than White, Black, and Other (5.5% (37 mmol/mol) vs 5.1% (32 mmol/mol), 5.2% (33 mmol/mol), and 5.1% (32 mmol/mol), respectively, $P < .001$). At the same time, Asian women had the lowest body mass index (BMI) compared to the other groups both pre-pregnancy (25.7 ± 3.6 kg/m^2 vs 27.1 ± 6.7 kg/m^2, 28 ± 5.9 kg/m^2, and 28.1 ± 5.6 kg/m^2, respectively, $P = 0.574$) and at OGTT (28.3 ± 4.2 kg/m^2 vs 30.2 ± 6.3 kg/m^2, 30.6 ± 5 kg/m^2, and 30.4 ± 4.9 kg/m^2, respectively, $P = .525$). Insulin therapy during pregnancy was more common in Asian and Other/Middle Eastern than White and Black women (71% and 79.2% vs 54.5% and 52.4%, respectively, $P = .03$). The percentage of women who were ex-smokers was significantly higher in White compared to Asian, Black, and Other groups (9.4% vs 3.1%, 1.6%, and 0%, $P = .04$), and the difference was even higher for White women who were actively smoking during pregnancy (15.7% vs 3.1%, 3.1%, and 0% $P = .002$). Pre-existing hypothyroidism was more common in White women compared to Black, Asian, and Other (17.4% vs 6.3%, 9.4%, and 0%, $P = .01$). A proportion of total cohort delivered in the Obstetric unit of our hospital (n = 271). Neonatal birth weight was higher in the Asian group compared to White, Black, and Other groups [(3429 ± 368 g) vs (3102 ± 488 g), (3279 ± 526 g), and (3159 ± 352 g), $P = .05$]. In the multivariable analysis, Middle Eastern ethnicity (aOR 6.73, 95% CI 1.31-34.46, $P = .02$), history of GDM in previous pregnancy (aOR 2.09, 95% CI 1.35-3.24, $P < .01$) and history of macrosomia (aOR 2.53, 95% CI 1.11-5.75, $P = .03$) were independently associated with an increased risk of insulin therapy requirement during pregnancy.

Conclusions: The study confirmed the presence of ethnic differences in pregnancies complicated by GDM. The results indicate a higher metabolic burden in Asian and Middle Eastern populations. Future research should focus on implementing ethnic-specific strategies for GDM prevention and early GDM screening.

Abstract citation ID: lvag096.1080

EP656 - ECE_2458 - Uric acid/albumin ratio as a marker of prediabetes and OGTT-derived glycemic abnormalities

Irem Sonmezoglu Kutuk, Sabri Engin Altıntop, Ethem Turgay Cerit, Altinova Alev, Mehmet Muhittin Yalcin, Mujde Akturk, Fusun Toruner and Ayhan Karakoc
Gazi University Faculty of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, Ankara, Türkiye

Background: Prediabetes and early glucose dysregulation during oral glucose tolerance testing (OGTT) represent early stages of metabolic impairment that may not be fully captured by conventional glycemic thresholds. The uric acid–to–albumin (UA/Alb) ratio reflects the balance between metabolic burden and antioxidant capacity and may serve as a practical biomarker for early metabolic risk. This study evaluated the association of the UA/Alb ratio with prediabetes, OGTT-derived dynamic abnormalities, and intermediate OGTT glycemic load.

Methods: Individuals undergoing OGTT were analyzed in this cross-sectional study. Glycemic status was defined according to ADA/WHO criteria. The UA/albumin ratio was compared between normoglycemic and prediabetic individuals. In participants classified as OGTT-normal (fasting <100 mg/dL and 120-minute <140 mg/dL), mid-OGTT glucose values at 30, 60, and 90 minutes were evaluated. A glucose threshold of ≥155 mg/dL was used to define mid-OGTT glycemic burden, and individuals were further categorized according to the timing of glucose elevation. Non-parametric tests, age-adjusted logistic regression, and ROC analyses were performed.

Results: The UA/albumin ratio was associated with metabolic risk independently of conventional OGTT criteria. The UA/albumin ratio was significantly higher in individuals with prediabetes compared with normoglycemic participants ($P < .001$). After adjustment for age, the UA/albumin ratio remained independently associated with prediabetes, conferring approximately a 2.5-fold increased odds ($P < .01$). ROC analysis demonstrated a modest but significant discriminative ability for identifying prediabetes (AUC ≈ 0.62).

Importantly, among individuals considered OGTT-normal by conventional criteria, those exhibiting mid-OGTT glucose elevations ≥155 mg/dL had significantly higher UA/albumin ratios than those without such excursions ($P = .002$). Furthermore, a stepwise increase in UA/albumin ratio was observed according to the timing of glucose elevation, with the highest values seen in individuals whose glucose peaked at later OGTT time points (Kruskal–Wallis $P = 0.002$).

Conclusions: The UA/Alb ratio is associated with metabolic dysregulation across the glycemic spectrum, including prediabetes and early OGTT-derived abnormalities not captured by conventional thresholds. These findings underscore the clinical value of dynamic OGTT assessment and suggest that the UA/Alb ratio may serve as a simple adjunctive biomarker for identifying individuals at early cardiometabolic risk.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1081

EP657 - ECE_2738 - On the road to type 2 diabetes: metabolomic profiling for early detection, risk stratification, and complementary assessment of metabolic trajectories

Diana Drettwan[1,2], Franziska Beitz[1], Tobias Ameismeier[1], Ali Tinazli[1] and Ronny Baber[3]
[1]*lifespin GmbH, Regensburg, Germany;* [2]*lifespin GmbH, Customer Management, Regensburg, Germany;* [3]*Leipzig Medical Biobank, Leipzig, Germany*

Prediabetes represents a major and growing global health burden, affecting hundreds of millions of individuals worldwide and substantially increasing the risk of progression to type 2 diabetes mellitus (T2D). As metabolic dysfunction precedes overt hyperglycemia by several years, improved characterization of early systemic metabolic alterations is critical for timely risk stratification and prevention.

In this study, we analyzed large-scale quantitative metabolomic profiles from more than 8,000 participants of the LIFE Adult Study using high-resolution H-NMR–based metabolomics. Over 250 metabolites and metabolic features per sample were quantified to characterize metabolic states associated with normoglycemia, prediabetes, and manifest T2D. Emphasis was placed on metabolite patterns reflecting insulin resistance, altered lipid and amino acid metabolism, and early disturbances in glucose and energy homeostasis.

Integration of metabolomic data with clinical phenotypes enabled the identification of distinct metabolic signatures associated with increased future T2D risk. These signatures extend beyond single biomarkers and capture system-level metabolic dysregulation, supporting metabolomics-based risk stratification as a complementary approach to conventional glycemic markers. The findings underline the potential of metabolomic profiling to improve early detection of prediabetes and to support targeted preventive interventions before irreversible disease progression occurs.

Beyond risk assessment, metabolomics-based measures of insulin resistance may also provide a complementary framework for assessing longitudinal metabolic response trajectories in the context of emerging antidiabetic therapies, including incretin-based treatments such as GLP-1 receptor agonists. While GLP-1 therapies exert pleiotropic effects extending beyond insulin resistance—such as glucose-dependent insulin secretion, appetite regulation, gastric emptying, and weight reduction—metabolomic insulin resistance markers may offer additional system-level insight into metabolic adaptation over time. Such approaches are intended to complement, rather than replace, established clinical endpoints including glycemic control, body weight, and treatment tolerability.

In summary, large-scale quantitative metabolomics combined with digital analytics provides valuable insights into early metabolic trajectories from health to prediabetes and type 2 diabetes, with implications for prevention, risk stratification, and complementary assessment of metabolic responses.

Abstract citation ID: lvag096.1082

EP658 - ECE_2900 - Pre-conception care in women with pre-gestational diabetes in a multi-ethnic population

Zi Jin[1], Naeemah Khalisadar[1], Isata Barrie[1], Gideon Mlawa[2] and Godwin Simon[2]
[1]*London, United Kingdom;* [2]*Barking, Havering and Redbridge University Hospitals NHS Trust, Internal Medicine and Diabetes and Endocrinology, London, United Kingdom*

Background: An increasing number of pregnancies are complicated by pre-gestational diabetes mellitus, especially Type 2 diabetes. Data from some studies and the UK National Pregnancy in Diabetes Audit reported poorer pregnancy preparation and higher adverse outcome rates in women with Type 2 diabetes compared with Type 1 diabetes. Potential barriers to pre-conception care include limited patient awareness, language and cultural factors, and restricted access to specialist services. The UK NICE guidelines recommend optimisation of HbA1c to <48 mmol/mol (6.5%) prior to conception, renal assessment, and retinal assessment. This audit aimed to assess glycaemic control and the completion of pre-conception assessments in a multi-ethnic population.

Methods: We retrospectively reviewed women with pre-gestational diabetes attending the antenatal services at Queen's Hospital and King George Hospital between August and October 2025. We retrieved data on patient demographics including age, ethnicity, primary language, and deprivation index, as well as BMI, pre-conception HbA1c (defined as the most recent value within 6 months prior to conception), early pregnancy HbA1c, pre-conception urine albumin-and-creatinine ratio (uACR), and diabetic retinopathy status.

Results: Of the 32 females included, 29 (90.6%) had Type 2 diabetes and 3 (9.4%) had Type 1 diabetes. The mean age was 33.9 years (range 20-47) and mean BMI was 31.4 kg/m^2. The cohort was predominantly of Asian (65.6%), followed by White British (21.9%), and Black African or Caribbean (15.6%) ethnicity, with a high proportion residing in areas of socioeconomic deprivation. Preconception HbA1c was recorded in 24/32 (75%) women. Only 6/32 (22.2%) achieved the recommended target of <48 mmol/mol (6.5%) prior to pregnancy. While HbA1c improved between pre-conception and early pregnancy in 18/32 (56.3%) women, less than half achieved target glycaemic control by the first trimester (46.9%). Recent uACR was recorded in 4/32 (12.5%) individuals.

Conclusions: In this multi-ethnic, socioeconomically deprived population, a large proportion of women with pre-gestational diabetes have inadequate metabolic optimisation and a low rate of pre-conception assessments. There is a need for a structured pre-conception diabetes service to improve pregnancy preparedness and to reduce avoidable maternal and fetal complications.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1083

EP664 - ECE_3183 - Clinical significance of DM phenotype differentiation via digital algorithm in predicting retinopathy onset

Kateryna Ukrainets[1,2,3], Natalija Pashkovska[1] and Oleh Ukrainets[4]
[1]Chernivtsi, Ukraine; [2]Central City Clinical Hospital of Chernivtsi City Council, Chernivtsi, Ukraine; [3]Bukovinian State Medical University, Chernivtsi, Ukraine; [4]Yuriy Fedkovych Chernivtsi National University, Chernivtsi, Ukraine

Relevance: Clinical experience suggests that the phenotypic diversity of diabetes often leads to diagnostic errors in daily practice. Many cases of LADA or pancreatogenic diabetes are misclassified as Type 2 (T2DM), while MODY can be confused with Type 1 (T1DM). This directly impacts ophthalmological care, as screening schedules are often based on the initial diagnosis. Since diabetic retinopathy (DR) is a major cause of vision loss, precise classification is vital. We aimed to see if a Telegram-based diagnostic algorithm could help identify these atypical cases and better predict the risk of eye complications.

Materials and Methods: We re-evaluated the clinical data of 151 patients using a custom-developed Telegram bot. The algorithm analyzed parameters such as age of onset, BMI, C-peptide levels, GAD antibodies etc. Based on the digital verification, we grouped the patients into: T1DM (n = 40), LADA (n = 32), T2DM (n = 52), MODY (n = 12), and pancreatogenic DM (n = 15). Ophthalmological evaluation included fundoscopy for all participants, with Optical Coherence Tomography (OCT) utilized as an additional diagnostic tool where clinically indicated. Statistical analysis was performed using standard descriptive and comparative methods.

Results: The digital check led to a diagnostic shift in 21.8% of the total cohort. Some patients previously labeled as T2DM were found to have LADA or markers of pancreatic insufficiency. Additionally, n = 5 patients previously treated for T1DM were identified as MODY cases.

The most significant finding for ophthalmological practice was in the LADA group. These patients showed signs of DR on average 3.0 ± 0.3 years earlier than those with classic T2DM ($p < 0.01$). On the other hand, patients reclassified as MODY had a very low risk of microangiopathy, with 91.7% of them showing no signs of DR. For pancreatogenic DM, we observed that while proliferative DR was less common than in T1DM, early changes in the pigment epithelium occurred more frequently.

Conclusions: Our study indicates that a simple digital algorithm can be an effective tool for differential diagnosis in a clinical setting. Identifying the specific phenotype–especially LADA–is crucial because it predicts a much earlier onset of retinopathy (3 years earlier than T2DM). This supports the need for personalized ophthalmological monitoring instead of a "one-size-fits-all" approach, allowing for earlier intervention in high-risk patients.

Abstract citation ID: lvag096.1084

EP667 - ECE_1254 - Comparative Impacts of Maternal Obesity with Normoglycemia, Impaired Glucose Tolerance, and Gestational Diabetes on Offspring Growth and Metabolic Outcomes: A Systematic Review

Ashraf Soliman, Fawziya Alyafei, Manal Musallam, Noora Alhemaidi, Noor Hamed, Shayma Ahmed, Nada Alaaraj and Ahmed Elawwa
Hamad Medical Center, Pediatric Endocrinology, DOHA, Qatar

Background: Maternal obesity is an established risk factor for adverse fetal programming. When combined with abnormal glucose metabolisms such as impaired glucose tolerance (IGT) or gestational diabetes mellitus (GDM)offspring are at elevated risk for early and lifelong growth and metabolic disorders. Differentiating these risks is vital for precision-targeted antenatal and postnatal care.

Objectives: To compare the short- and long-term impacts of maternal obesity with normal glycemia, IGT, and GDM on offspring growth (weight, BMI) and metabolic parameters (insulin resistance, lipid profile, blood pressure), and to estimate the magnitude of these effects from published data (2000-2025).

Methods: A systematic search of PubMed, Embase, and Web of Science identified 20 studies (n > 18,000 total offspring). Data were stratified into three exposure groups:

1. Obese mothers with normal glucose tolerance (NGT)
2. Obese mothers with IGT
3. Obese mothers with GDM

Outcomes were categorized as:

- Short-term: birth weight, neonatal adiposity, early weight gain
- Long-term: childhood obesity, BMI z-score, insulin resistance (HOMA-IR), systolic BP, lipid abnormalities

Effect sizes were extracted or calculated where possible.

Results:

- Obese-NGT:
  - 18-22% increased risk of childhood overweight compared to non-obese controls
  - Birth weight +150-250 g on average
  - Mild rise in insulin levels and HOMA-IR by adolescence (12-15%)
- Obese-IGT:
  - 38-45% increased risk of obesity in school-age children
  - 1.4-1.7× increase in HOMA-IR and fasting insulin
  - Increased triglycerides (+18%) and LDL cholesterol (+11%) at 8-12 years
- Obese-GDM:
  - 55-70% prevalence of overweight/obesity by adolescence
  - Macrosomia (>4 kg) in up to 30-35% of neonates
  - 2.5× increase in childhood metabolic syndrome risk

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

- Insulin resistance and impaired fasting glucose in 40-55% by mid-adolescence
- Hypertension (≥90th percentile) in 22-28% by 14-18 years

Dose-response trends were consistent across cohorts, showing the greatest burden among GDM-exposed offspring.

Conclusions: The severity of maternal glucose dysregulation modulates the magnitude of offspring metabolic risk. Children of obese GDM mothers experience the most pronounced growth acceleration and metabolic dysfunction. Those obese-IGT mothers are an intermediate-risk group, highlighting the need for early detection and targeted interventions.

Public Health Implications: This evidence reinforces the need for aggressive glycemic monitoring in obese pregnancies, not only for maternal outcomes but for offspring health. Public health policy should integrate tailored prenatal counseling, early postnatal screening, and long-term growth/metabolic follow-up for at-risk children to break the intergenerational cycle of metabolic disease.

Abstract citation ID: lvag096.1085

EP668 - ECE_1495 - Galectin-3 and obesity in patients with type 2 diabetes mellitus: a prospective case–control study

Danijela Radojković[1,2], Milica Pesic[1,2], Saša Radenković[1,2], Vojislav Ćirić[1,2], Milena Velojić Golubović[1,2], Milan Radojkovic[1,2], Valentina Nikolic[2], Aleksandra Ignjatovic[2], Petra Popovic[1] and Jovana Zlatkovic[1]

[1]University Clinical Center, Nis, Serbia; [2]Medical Faculty, University of Nis, Nis, Serbia

Introduction: Obesity plays a central role in the development of metabolic disturbances in type 2 diabetes mellitus (T2DM). Galectin-3, a β-galactoside-binding lectin involved in inflammation and fibrosis, has been implicated in obesity-related metabolic disorders; however, its role in T2DM patients with different nutritional status remains insufficiently defined.

Objective: To investigate the role of galectin-3 in obese and normal-weight patients with type 2 diabetes mellitus and to evaluate its association with glycemic control, insulin resistance, and anthropometric parameters.

Patients and Methods: A prospective case–control observational study was conducted at the Clinic of Endocrinology, Diabetes and Metabolic Disorders, University Clinical Centre Niš, Serbia. The study included 42 patients with type 2 diabetes mellitus (T2DM), classified according to body mass index (BMI) into two groups: obese patients (group O, BMI ≥30 kg/m^2; n = 21) and normal-weight patients (group N, BMI 18.5-24.9 kg/m^2; n = 21). All participants underwent detailed medical history assessment and clinical examination, including anthropometric measurements (waist and hip circumference). Laboratory investigations included fasting blood glucose (FBG), glycated hemoglobin (HbA1c), insulin, C-peptide, calculation of HOMA-IR, renal function tests (urea, creatinine), estimated glomerular filtration rate (eGFR), albumin-to-creatinine ratio (ACR), lipid profile (total cholesterol (Hol) triglycerides (Tg), high density lipoproteins (HDL) and low density lipoproteins (LDL)), and serum galectin-3 levels. Diabetes duration was recorded. Multivariate regression analysis was performed to identify independent predictors of waist circumference.

Results: Patients in group O had significantly higher HbA1c ($P = .012$), HOMA-IR ($P < .001$), insulin ($P < .001$), and C-peptide levels ($P < .001$) compared with group N. Waist and hip circumferences were also significantly greater in obese patients ($P < .001$ for both). Diabetes duration was significantly shorter in group O compared with group N ($P = .042$). In the multivariate model, galectin-3 levels ($P = .021$) and HbA1c emerged as independent predictors of waist circumference.

Conclusions: Galectin-3 is independently associated with central adiposity in patients with T2DM, suggesting a potential role as a biomarker linking obesity, glycemic control, and metabolic dysfunction in type 2 diabetes.

Abstract citation ID: lvag096.1086

EP669 - ECE_2029 - Impact of pre-pregnancy obesity on metabolic control and perinatal outcomes in gestational diabetes

Franco Nicolas Lopez Lopez, Rocio Villar Taibo, Eva Gomez Vazquez, Ana Canton Blanco and Miguel Angel Martinez Olmos

Hospital Clínico Universitario de Santiago de Compostela, Santiago de compostela, Spain

Objectives: To compare maternal–fetal variables in women with gestational diabetes (GD) according to the presence of pre-pregnancy obesity (PPO); to analyze HbA1c levels and their relationship with macrosomia (M); and to evaluate the association between PPO and insulin requirement (IR).

Materials and Methods: A retrospective observational study including pregnant women diagnosed with GD between 2022 and 2023. Participants were classified according to the presence of PPO (BMI ≥30 kg/m^2). Clinical and biochemical variables at the time of GD diagnosis were recorded.

Results: A total of 300 women were included. Table 1 summariezes the clinical, biochemil charecteistics and complications. Women with PPO were diagnosed with GD at an earlier gestational age and showed significantly higher HbA1c levels compared with non-obese women. Receiver operating characteristic (ROC) curve analysis identified HbA1c as a predictor of macrosomia, with an area under the curve (AUC) of 0.845. The optimal cut-off value was HbA1c >5.4%, yielding a sensitivity of 90% and a specificity of 61%. PPO was associated with higher HbA1c levels OR 1.095, 95% CI 1.047-1.145; $P < .001$). Insulin therapy was required in 54.5% of women with PPO compared with 21.5% of non-obese women (OR 4.38; $P < .001$). In multivariate analysis, PPO was independently associated with macrosomia (OR 3.36, 95% CI 1.34-8.98; $P = .01$), whereas insulin requirement was not independently associated (OR 0.65; $P = .38$).

Conclusions: Pre-pregnancy obesity was associated with higher insulin requirements, poorer glycemic control, and an increased

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

risk of macrosomia in women with gestational diabetes. An HbA1c value >5.4% demonstrated good discriminative capacity for predicting macrosomia. PPO remained an independent risk factor, highlighting the importance of strict metabolic control and individualized follow-up in this population.

	Sin OBP (177) 59%	Con OBP (123) 41%	
Age	36 (19-46) RIC 8	36 (25-45) RIC 9	$P=0.741$
Pre-pregnancy BMI	24.70 (15.90-29.80) RIC 4.8	33.6 (30-66.2) RIC 5	$P<.001$
BMI at diagnosis	27.1 (17.30-36.10) RIC 4.5	34 (28.60-64.50) RIC 4.25	$P<.001$
History of prediabetes	5.6% (10)	22% (27)	$P<.001$
Gestational age at GMD diagnosis (weeks)	25 (6-37.40) RIC 5.6	22 (5-35.4) RIC 16.35	$P<.001$
Insulin requirement	21.5% (38)	54.5% (67)	$P<.001$
HbA1c (%)	5.1 (4.2-6.2) RIC 0.4	5.3 (3.4-6.3) RIC 0.5	$P<.001$
Preeclapsia	2.3% (4)	6.5% (8)	$P=.077$
Macrosomia	4.5% (8)	12.2% (15)	$P=.025$
Preterm birth	6,2% (11)	9.7% (12)	$P=.361$
Low birth weight	7.3% (13)	5.7% (7)	$P=0.741$

Abstract citation ID: lvag096.1087

EP670 - ECE_2372 - Liraglutide versus tirzepatide: real-world effects on lipid and carbohydrate metabolism in adults with class III obesity

Maria Evangelia Koloutsou[1], Maria Yavropoulou[1], Maria Mateniadou[1], Evanthia Kassi[1], Georgia Argyrakopoulou[2], Kyriaki Cholidou[3], Polyzois Makras[4], Nikolaos Tentolouris and Alexander Kokkinos

[1]Laiko University Hospital, Medical School, National and Kapodistrian University of Athens, First Department of Propaedeutic Internal Medicine, Joint Academic Rheumatology Program, Endocrinology Unit, Athens, Greece; [2]Athens Medical Center, Diabetes and Obesity Unit, Athens, Greece; [3]Sotiria Chest Disease Hospital, 1st Respiratory Medicine Department, Athens, Greece; [4]251 Hellenic Air Force & VA General Hospital Athens, LCH Adult Clinic, Department of Endocrinology and Diabetes and Department of Medical Research, Athens 11525, Greece; 5Laikon General Hospital, First Department of Propaedeutic Internal Medicine, Athens, Greece

Introduction: Obesity is a global health challenge associated with cardiometabolic morbidity and mortality. GLP-1 receptor agonists, such as liraglutide, and the dual GIP/GLP-1 receptor agonist tirzepatide are used in obesity and glycaemic control. Although randomized clinical trials have demonstrated efficacy, real-world head-to-head comparative data remain limited. This study aimed to compare the short-term effects of liraglutide versus tirzepatide on lipid and glycaemic parameters in adults with class III obesity, without changes in concomitant pharmacological treatment.

Methods: This prospective observational study included adults with BMI >40 kg/m^2 without diabetes who received liraglutide (n = 14; once daily, up-titrated to 3 mg) or tirzepatide (n = 15; once weekly, up-titrated to 7.5 mg) over a 3-month follow-up period. Demographic and anthropometric data were collected, body composition was assessed using bioelectrical impedance analysis, and laboratory measurements (HbA1c, glucose, insulin, total cholesterol, LDL-C, HDL-C, triglycerides) were obtained at baseline and at 3 months. Insulin resistance and sensitivity were estimated using HOMA-IR and HOMA-S. Statistical analyses were performed using SPSS version 26.

Results: A total of 29 adults with class III obesity were included (mean age 47 years, mean body weight 129 kg, mean BMI 44 kg/m^2). After 3 months of treatment, weight loss was comparable between the liraglutide and tirzepatide groups (11.5 vs 11.9 kg, $P=.83$), as was percentage weight loss (10% vs 9%, $P=.75$). Reductions in fat percentage (−2.3% vs −2.6%, $P=.76$), fat mass (−7.3 vs −7.6 kg, $P=0.86$), and fat-free mass (−4.2 vs −3.9 kg, $P=0.79$) were also similar comparable.

In the liraglutide group, total cholesterol decreased significantly (194.0 ± 33.7 to 173.3 ± 32.6 mg/dL, $P=.022$), whereas changes in LDL-C, HDL-C and triglycerides were not significant. HbA1c decreased significantly ($P=.003$), while glucose, insulin, HOMA-IR and HOMA-S showed no significant changes.

In the tirzepatide group, total cholesterol also decreased significantly (219.2 ± 55.3 to 191.7 ± 38.9 mg/dL, $P=.034$), without statistically significant changes in LDL-C, HDL-C or triglycerides. Tirzepatide induced significant decreases in fasting glucose ($P<0.001$), insulin ($P=.030$) and HbA1c ($P<.001$). HOMA-IR declined and HOMA-S increased, indicating enhanced insulin sensitivity.

Conclusions: Both incretin-based therapies improved lipid and carbohydrate metabolism over three months. Tirzepatide (up to 7.5 mg weekly) demonstrated greater short-term glycaemic control compared with liraglutide (3 mg daily), while weight loss was comparable. These findings support the real-world cardiometabolic effectiveness of incretin-based therapies beyond obesity management.

The study protocol was prospectively registered at ClinicalTrials.gov (NCT07094568).

Abstract citation ID: lvag096.1088

EP673 - ECE_1193 - Sleep disorders in polycystic ovary syndrome a comparative study In Pakistani women

Shahina Ishtiaq

Ziauddin university hospital, South city hospital, Obstetrics and gynecology, Karachi, Pakistan

Background: Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine disorder associated with metabolic and psychological co morbidities. While reproductive and metabolic features are well studied, sleep disturbances remain underappreciated.

Objective: To compare sleep quality and emotional distress in women with and without PCOS, and contextualize findings using metabolic data from a MASLD (Metabolic Dysfunction-Associated Steatotic Liver Disease) cohort.

Methods: In a case-control design, 200 women (100 PCOS, 100 age-matched controls) were evaluated using structured questionnaires and the CES-D 10 depression scale. Latent Class Analysis was used to cluster sleep symptom patterns. A secondary MASLD dataset (n=172) was analyzed for BMI, liver enzyme levels, and lipid profiles.

Results: Women with PCOS reported significantly more restless sleep ($P=.015$, d = 0.35), fatigue ($P=.041$, d = 0.29), and higher depression and anxiety symptoms ($P<.05$). MASLD participants showed elevated BMI (29.5 ± 5.0), ALT (31.3 IU/L), GGT (74.7 IU/

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

L), and borderline-high LDL and triglycerides.

Conclusions: Sleep issues in PCOS are closely associated with emotional distress and metabolic stress. Findings from the MASLD cohort support a systemic mechanism involving liver-related oxidative stress. Interventions must address metabolic and psychological domains to improve sleep in PCOS.

Keywords PCOS, sleep disturbances, depression, MASLD, metabolic stress, liver enzymes

Abstract citation ID: lvag096.1089

EP674 - ECE_2456 - Clinical characteristics and prognostic factors of malnutrition in patients with diabetes: diades project

Víctor Simón-Frapolli[1,2,3] and Raquel De la Iglesia Arnaez[4]
[1]*Hospital Universitario Virgen De La Victoria, Endocrinology and Nutrition, Málaga, Spain;* [2]*Ibima Plataforma Bionand, Málaga, Spain;* [3]*Facultad de Medicina-UMA, Málaga, Spain;* [4]*Laboratorios Ordesa, Barcelona, Spain*

Diabetes mellitus (DM) is associated with a high prevalence of disease-related malnutrition (DRM), which worsens patients' health status. Clinical guidelines recommend medical nutrition therapy as an essential complement to the treatment of the disease.**Objective:** To understand the attitude of healthcare professionals toward DRM in patients with DM, their diagnostic methods, and their clinical practices.

Method: An online questionnaire on the general profile of diabetic patients was sent to healthcare specialists on the clinical management of patients with DM in the Spanish healthcare context. In addition, a retrospective online questionnaire for patients with DRE who were treated with oral nutritional supplementation (ONS) was sent to these specialists.

Results: A total of 235 specialists from the public and private sectors participated in the study, representing various specialties and regions and providing information on the treatment of 927 hospitalized patients at nutritional risk. 90.6% of specialists reported performing nutritional screening, with the Mini Nutritional Assessment (MNA) being the most widely used tool (65.3%).

Among patients with DM, most were type 2 (96.0%), with a mean age of 70.6 years. Most physicians (81%) reported that the diagnosis of DM had been made more than 12 months prior to the nutritional assessment. For 64.8% of specialists, the nutritional status of patients with DM at the time of diagnosis was classified as "malnourished."

Regarding the retrospective study of patients with DRM, ONS was recommended for more than 2 months in 80.9% of cases, and to improve adherence, frequent follow-up with the patient (92.8%) and better communication (92.5%) were highlighted. Unintentional weight loss was the main reason for recommending ONS (43.0%). 66.6% of patients with DRM had a previous diagnosis of DM. In terms of communication with patients, aspects such as understanding when and how to take ONS and highlighting their importance were highlighted. Almost unanimously, face-to-face consultations are the preferred channel of communication for patients, followed by telephone consultations.

In those patients who were prescribed complete oral nutrition, an average of 2 daily doses was recommended, and nutritional improvement was observed after an average of 31.0 days, with a high degree of satisfaction with the treatment.

Conclusions: The results indicate the high incidence of DRM in patients with DM and the delay in its diagnosis. Oral nutritional supplementation can improve the DRE condition of these patients at an early stage.

Abstract citation ID: lvag096.1090

EP676 - ECE_1786 - Ketamine induced Hyponatremia

Huma Humayun Khan[1] and Jeremy Tomlinson[2]
[1]*Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford University Hospital, Oxford, United Kingdom;* [2]*NIHR Oxford Biomedical Research Centre, Radcliffe Department of Medicine, University of Oxford, Oxford, United Kingdom*

Ketamine is a dissociative anaesthesia which also has analgesic properties and is also used in pain management and depression[1]. As it produces an out-of-body and rewarding experience, there is a potential danger for abuse of this medication[2].Cystitis and cholangiopathy are recognized side effects of ketamine use[3],however, published data on ketamine-induced hyponatremia is scarce.The exact pathophysiology is not clear though it has been postulated that ketamine stimulates the release of antidiuretic hormone from the hypothalamus.

Here, we describe an unusual case of acute hyponatremia likely induced by ketamine recreational use.

A 25-year-old malnourished gentleman presented with 1-week history of progressive lethargy and global weakness, having used ketamine recreationally for several years. He did not have recent GI losses (vomiting or diarrhoea) and did not ingest excessive amount of water or alcohol. The initial biochemistry revealed profound hyponatremia (Na 100 mmol/l). The paired serum (205 mosm/kg) and urine osmolality (313 mosm/kg) and urine sodium 93, suggested SIADH, however clinically patient appeared dehydrated and malnourished. The cortisol level was sufficient (561 nmol/l). It was unclear if hyponatremia was acute or subacute-on-chronic with last normal sodium level noted five years earlier.

Given the neurological symptoms of acute confusion and unsteadiness, the patient was treated with half the usual volume hypertonic saline (75 ml of 2.7% NaCl) over 20 minutes. A cautious approach was implemented due to the potential risk of overcorrection given his apparent malnourishment.

He was admitted to ICU and treated with slow intravenous fluid (0.9% NaCL 80 ml/hr). His Na level overcorrected by 11 mmol/l in 24-hours with polyruia, and was halted by stat 1 mcg dose of desmopressin. The patient went on to develop acute kidney injury with polyuria needing repeat administration of desmopressin which had minimal effect, suggesting ADH resistance and possible tubular injury.

It was deemed that hyponatremia was multifactorial, secondary to ketamine-induced renal salt-wasting (likely tubular damage) and an element of inappropriate ADH secretion in the context of critical illness. The sodium level steadily improved with slow IVF and by day-8 of admission, the patient had full recovery.

This case uniquely highlights ketamine as a rare cause of hyponatremia which was severe enough to warrant use of hypertonic saline and ITU admission.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1091

EP677 - ECE_3643 - Reactive hypoglycaemia: challenges in clinical practice

Zaynah Islam[1], Naychi Kyaw Kyaw[2], Carmela Therese Chan[2], Raj Tanday[2], Anna Hawkins[2] and Khash Nikookam[2]
[1]Queen Mary University of London, Main Medical School Campus, London, United Kingdom; [2]Barking, Havering and Redbridge Hospitals NHS Foundation Trust, Diabetes and Endocrinology, Ilford, London, United Kingdom

Background: Reactive hypoglycaemia is an under-recognised condition that can significantly compromise patients' quality of life. The diagnostic process is often intricate, necessitating comprehensive evaluations to rule out alternative differential diagnosis. This not only demands considerable time and resources from clinicians and the multidisciplinary care team but also imposes psychological and physical burdens on patients in search of diagnostic clarity which may be delayed for years. Nevertheless, with appropriate therapeutic strategies, symptom control is achievable.

This is the case of a 38-year-old lady presented with a long-standing history of postprandial episodes of intermittent tremors, excessive sweating, profound fatigue, and occasional tachycardia lasting at least 15 minutes. These episodes occurred one to three times per week, primarily 2 to 3 hours post meal. During one severe episode, her blood glucose level fell to 2.1 mmol/L, resulting in transient aphasia and necessitating external assistance for oral intake.

Extensive investigations were undertaken to exclude other endocrinological and metabolic disorders. These included assessments of serum basal cortisol, a 72-hour inpatient fasting, IGF-1, 24-hour urinary metanephrines, 5-HIAA, and a short Synacthen test with normal results. 5 hours oral glucose tolerance test (OGTT) confirmed the diagnosis of reactive hypoglycaemia.

Subsequent lifestyle modifications including proportionate balanced protein, carbohydrate and fat, weight reduction advice and adherence to a high-protein, low-carbohydrate diet and fat resulted in marked symptomatic relief and stabilisation of glycaemic control. Repeat OGTT demonstrated a return to normoglycaemia.

Conclusions: Reactive hypoglycaemia is a rare and diagnostically challenging condition that may present with non-specific or atypical symptoms. A high index of clinical suspicion is essential. This case underscores the diagnostic value of OGTT and MMTT and highlights the critical role of early dietary intervention in mitigating symptom progression and reducing the risk of long-term metabolic sequelae.

Abstract citation ID: lvag096.1092

EP682 - ECE_1914 - Increased collagen IV protein in renal proximal tubular epithelial cells under high-glucose condition was enhanced by dickkopf-1 but attenuated by brain-derived neurotrophic factor

I-Te Lee and Junyi Wu
Taichung Veterans General Hospital, Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung, Taiwan

Background: In addition to glomerular injury, tubulointerstitial fibrosis is one of the pathophysiological mechanisms in the diabetic kidney disease. Brain-derived neurotrophic factor (BDNF), a member of neurotrophin family, promotes cell growth and survival mainly through tropomyosin receptor kinase B (TrkB). Previously we have reported that serum BDNF level was positively correlated with renal function. Moreover, Wnt/β-catenin signaling is involved in the repair and regeneration after kidney injury. The circulating dickkopf-1 (DKK-1), a Wnt signaling inhibitor, is inversely correlated with renal function. In the present study, we aimed to examine the effects of BDNF and DKK-1 on the expression of collagen IV protein, an indicator of fibrosis.

Methods: This study included three parts: [1] We pretreated human renal proximal tubular epithelial cells with different doses of BDNF (0, 1, 10, 50 and 100 ng/mL) for 24 hours and cultured in high-glucose (HG, 33 mM) medium for another 24 hours. [2] We blocked BDNF signaling using Trk inhibitors, followed by treating the cells with BDNF (50 ng/mL) for 24 hours and cultured in HG medium for another 24 hours. [3] We pretreated the cells with BDNF (50 ng/mL) and/or DKK-1 (50 or 500 ng/mL) for 24 hours and cultured in HG medium for another 24 hours. Total protein from each experimental group was extracted and subjected to western blot analysis. Collagen IV protein intensity was normalized to total protein and compared to normal-glucose (NG, 5.6 mM) condition.

Results: First, HG condition resulted in a 1.63-fold increase in collagen IV level compared to the NG condition, and a dose-depend suppression was observed by BDNF (1.55-, 1.45-, 1.23-, 1.08-fold with 1, 10, 50, and 100 ng/mL of BDNF; respectively). Second, the HG-increased collagen IV (2.05-fold) was suppressed by BDNF (1.78-fold), but the BDNF effect was abolished (2.68-fold) after adding pan-Trk inhibitor (K252a, 200 nM). Finally, the HG-increased collagen IV (1.87-fold) was augmented (2.74-fold) by high-dose (500 ng/mL) of DKK-1, and the augmentation was attenuated (1.98-fold) by BDNF (50 ng/mL).

Conclusions: We showed a dose-depend effect of BDNF on the suppression of collagen IV protein expression, and the BNDF effect was abolished by pan-Trk inhibitor. In addition, BDNF attenuated the overexpression of collagen IV protein induced by DKK-1. Our results shed light on the roles of BDNF and Wnt/β-catenin signaling in the regulation of tubulointerstitial fibrosis. Further in vivo investigations for the synergistic effects between BDNF and Wnt/β-catenin signaling on renal tubular protection are warranted.

Abstract citation ID: lvag096.1093

EP683 - ECE_3959 - The importance of integrating FIB-4 and transient elastography in detecting advanced liver fibrosis among patients with type 2 diabetes

Marin Pecani[1] and Paola Andreozzi[2]
[1]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy; [2]Policlinico Umberto I University Hospital, Sapienza University of Rome, Rome, Italy

Background: Metabolic dysfunction–associated steatotic liver disease (MASLD) with advanced liver fibrosis is highly prevalent among patients with cardiometabolic risk factors, particularly in those with type 2 diabetes, but is often asymptomatic. With normal or mildly elevated liver enzymes, it is frequently underdiagnosed in primary care and endocrinology settings. Although liver biopsy remains the gold standard for diagnosis,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

it is not feasible for population-level screening. Current clinical guidelines recommend a stepwise approach: initial non-invasive fibrosis assessment with a simple serum-based score, such as FIB-4, followed by imaging with vibration-controlled transient elastography (VCTE). This case report underscores the value of this approach in routine clinical practice.

Case Presentation: During a routine endocrinology visit, a 58-year-old man (body mass index [BMI] 31.1 kg/m^2) with a two-year history of type 2 diabetes treated with metformin and a history of hypertension was noted to have a FIB-4 score of 1.56, corresponding to an indeterminate risk for advanced hepatic fibrosis. He reported no significant alcohol consumption and had no known history of liver disease. Physical exam showed no signs of chronic liver disease. Laboratory results were within normal limits for GGT, ALP, bilirubin, albumin, PT, and INR, and the patient's hemoglobin A1c was 7.8%. Serologic testing was negative for viral hepatitis. Given the elevated FIB-4 score, VCTE was performed, revealing a liver stiffness of 9.6 kPa, indicating significant fibrosis, and a controlled attenuation parameter of 324 dB/m, confirming hepatic steatosis. Lifestyle counseling was provided, focusing on dietary modification, alcohol avoidance, and increased physical activity. Consequently, semaglutide was initiated to improve glycemic control, promote weight loss, and address MASLD. The patient was referred to a hepatologist for further evaluation and follow-up.

Conclusions: Even in seemingly low-risk patients, combining FIB-4 with VCTE can uncover moderate to advanced fibrosis, supporting its use in routine MASLD evaluation. This case highlights the value of a stepwise, non-invasive assessment strategy in enabling earlier identification of advanced fibrosis and timely referral and surveillance in patients with metabolic risk factors. Without this approach, recognition of advanced fibrosis would likely have been delayed.

Abstract citation ID: lvag096.1094

EP684 - ECE_1028 - Characteristics of cases of body weight rebound after metabolic /bariatric surgery

Bunzo Matsuura[1], Norio Horiike[2], Kojiro Michitaka[2], Hironobu Nakaguchi[1], Teruki Miyake[1] and Shinya Furukawa[1]
[1]*Ehime University Graduate School of Medicine, Toon, Japan;* [2]*Saiseikai Imabari daini Hospital, Imabari, Japan*

Background & Aim: Since 2006 at our hospital, lifestyle modification for obese patients has been provided through a team approach with a physician, dietician, nurse, physical therapist and psychologist. From 2016, a surgeon and anesthesiologist were added to the team for metabolic/bariatric surgery (laparoscopic sleeve gastrectomy: LSG). The aim of this study is to clarify the characteristics of cases of body weight rebound after LSG.

Subjects and Methods: Of 51 patients who were received LSG between January 2017 and May 2024, 40 patients (19 males and 21 females, mean age 44 years) who had been followed for more than 2 years were included. Rebound cases were defined as those in whom postoperative weight loss had increased to 90% or more of the preoperative weight. Comorbidities and the rate of change in preoperative weight loss rate, postoperative weight loss rate, and postoperative body composition were compared. We examined their body composition using InBody 720 or 770.

Results: There were 13 rebound cases and 27 non-rebound cases. There were significantly more rebound cases among women and cases with diabetes mellitus, low preoperative weight, low 6-month postoperative weight loss, weight gain from 6 months to 1 year after surgery, and postoperative muscle mass loss. There were no differences in age or preoperative weight loss rate.

In summary: Women with diabetes mellitus and those with little postoperative weight loss should be visited frequently for diet and exercise modification to detect rebound early.

Abstract citation ID: lvag096.1095

EP685 - ECE_1281 - Public concern about GLP-1 analogues: a google trends analysis of global search patterns

Vasiliki Tsiama[1], Stella Proikaki[1], Konstantinos Belis[1], Efthymia Kallistrou[1], Dimitra Ragia[1], Dimitra Motsiou[1], Ioannis Ilias[1], Lina Zabuliene[2] and Christos Savvidis[1]
[1]*Hippocration General Hospital of Athens, Department of Endocrinology, Athens, Greece;* [2]*Vilnius University, Faculty of Medicine, Vilnius LT-03101, Lithuania*

Introduction: GLP-1 receptor agonists, notably semaglutide (Ozempic) and tirzepatide (Mounjaro), are increasingly used for type 2 diabetes and weight loss. Despite a favorable safety profile, rare adverse effects such as pancreatitis and vision loss have raised concern. Internet search data offer insights into public health anxieties and can inform clinical and regulatory communication.

Aim: To assess global public interest in GLP-1 analogues using Google Trends data, focusing on pancreatitis, vision loss, diet, and exercise.

Methods: Weekly Relative Search Volumes (RSVs) were obtained from Google Trends for "Mounjaro," "Ozempic," "Diet," "Exercise," "Pancreatitis," and "Blindness," from Dec 26, 2021, to Jun 22, 2025 (183 weeks). Trends were analyzed using the Mann-Kendall test, Loess smoothing, and autocorrelation functions. Synchrony was assessed via cross-approximate entropy (Cross-ApEn), with normalized RSVs. Temporal relationships were evaluated with cross-correlation analysis using differenced series to ensure stationarity.

Results: Search interest rose significantly for Mounjaro ($\tau = 0.30$, $P < .001$) and Ozempic ($\tau = 0.38$, $P < .001$), peaking at RSVs of 31 and 41. Diet showed a mild downward trend ($\tau = -0.05$, $P = .001$), with seasonal peaks; Exercise was stable but also seasonal. Searches for Pancreatitis and Blindness remained low and stable, with occasional spikes (eg, Pancreatitis RSV = 21). Cross-ApEn indicated high synchrony between Mounjaro and Ozempic (0.85), moderate with Diet and Exercise (1.22-1.32), and low with Blindness and Pancreatitis (1.35-1.45). Cross-correlation analysis showed strong contemporaneous correlation between Mounjaro and Ozempic ($r = 0.68$), weak inverse correlations with Diet and Exercise (r: −0.3), and non-significant positive correlations with Blindness and Pancreatitis (r: 0.15-0.20).

Discussion: Public interest in GLP-1 agonists is rising, likely reflecting expanding use and media coverage. Stable interest in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

traditional methods (Diet, Exercise) with weaker associations suggests a shift toward pharmacological weight loss. Limited correlation with side-effect terms implies that public concern about adverse events is event-triggered rather than sustained. Limitations include the relative nature of RSVs and possible influence of unmeasured events. Future work should focus on media-driven search spikes to enhance real-time pharmacovigilance.

Abstract citation ID: lvag096.1096

EP686 - ECE_3423 - Multidisciplinary approaches in weight management clinic: weight and psychological outcomes

Conor Bentley, Gavita Kaur, Anna Hawkins and Khash Nikookam

Barking, Havering and Redbridge University Hospitals NHS Trust, King George Hospital, Department of Endocrinology, London, United Kingdom

Obesity is a complex chronic disease frequently associated with depression and anxiety, which may adversely affect quality of life, treatment engagement and long-term outcomes. NICE guidance recommends specialist multidisciplinary weight management services incorporating dietetic, psychological, lifestyle and medical input. However, early psychological outcomes are infrequently reported alongside weight change, despite their importance to patient-centred care and service evaluation.

This service included adults attending a specialist NHS weight management clinic (November 2024 and March 2025). Participants met NICE criteria for specialist weight management and received a multidisciplinary intervention comprising lifestyle modification, at least six individual dietetic and psychological support sessions, including medical assessment. A pilot programme which combined dietetic and psychological group intervention was offered to all participants. Weight, depression (Patient Health Questionnaire-9; PHQ-9) and anxiety (Generalised Anxiety Disorder-7; GAD-7) were assessed at baseline and at interim follow-up of up to four months. Analyses were conducted on a pairwise basis using paired non-parametric tests for within-participant comparisons. Weight outcomes are reported using both median and interquartile range (IQR) and mean ± SD to aid interpretability. Clinically meaningful change was defined as a ≥5-point reduction in PHQ-9 or GAD-7 scores and ≥5% weight loss. Ethical approval was not required as this was registered as a service evaluation.

Of the twenty-four participants enrolled, thirteen had paired weight data. Median weight change at interim follow-up was −0.8 kg (IQR 3.5), with a mean reduction of −1.2 ± 2.6 kg. Weight change ranged from −7.5 kg to +1.3 kg. This change was not statistically significant ($P = .24$), and one participant (7.7%) achieved ≥5% weight loss.

In contrast, significant improvements were observed in psychological outcomes. Median PHQ-9 scores improved by −9 points (IQR −15 to −4; $P = .002$), with 69% of participants achieving clinically meaningful improvement. Median GAD-7 scores improved by −7 points (IQR −11 to −3; $P = .009$), with 62% achieving clinically meaningful improvement. Participants with severe baseline psychological symptoms demonstrated greater benefit, with those scoring ≥15 on PHQ-9 or GAD-7 showing substantially larger median reductions compared with those with lower baseline scores. No significant correlation was observed between changes in weight and changes in PHQ-9 or GAD-7 scores.

Early engagement with a multidisciplinary team in NHS weight management service was associated with clinically meaningful improvements in depression and anxiety at interim follow-up, while changes in weight were modest and variable.

Abstract citation ID: lvag096.1097

EP689 - ECE_2790 - Efficacy and Safety of Semaglutide Injection in Weight management: A subgroup analysis of patients based on BMI

Unnikrishnan Gopalkrishnanl, Ameya Joshi[2], Harish Kumar[3], Richa Giri[4], Sanjiv Maheshswari[5], Valluri Prasad[6], Jitendra Shukla[7], M.C. Rekha[8], Nutankumar Agrawal[9], Yogesh Rasal[10], Banshidhar Sahoo[11], Shweta Bhandari[12], Ambana Gowda[13], Phadke Keshav[14], Pravin Supe[15], Niranjan Pathak[16], C. Ambrish[17], Ashutosh Sonawane[18], Yash Bahulikar[19], Amit Bhaskar[20], R. Arunkumar[21], Supriya Sonowal[22], Priyanka Yadav[22], Dipak Patil[22], Sucheta Pandit[22], Pravin Ghadge[22] and Suyog Mehta[22]

[1]Chellaram Diabetes Institute, Pune, India; [2]Bhaktivedanta Hospital and Research Institute, Thane, India; [3]Amrita institute of Medical Sciences and Research Centre, Kochi, India; [4]G.S.V.M medical College, Kanpur, India; [5]Jawahar Lal Nehru Medical College, Ajmer, India; [6]King George Hospital, Visakhapatnam, India; [7]Moti Lal Nehru Medical College, Prayagraj, India; [8]Mandya Institute of Medical Science, Mandya, India; [9]M.L.B Medical college, Jhansi, India; [10]Pulse Multispecialty Hospital, Pune, India; [11]KIDS Hospital, Bhubaneswar, India; [12]Vincare Hospital, Bathinda, India; [13]Citizen Hospital, Bangalore, India; [14]Sahyadri Super Speciality Hospital, Pune, India; [15]Supe Heart and Diabetes Hospital and Research Centre, Nashik, India; [16]OJAS Multispeciality Hospital, Pune, India; [17]Medstar Speciality Hospital, Bangalore, India; [18]Panacea Hospital, Nashik, India; [19]MMFHA Joshi Hospital, Pune, India; [20]Janta Hospital and Maternity Center, Varanasi, India; [21]Chettinad Hospital & Research Institute, Chengalpattu, India; [22]Sun Pharma Laboratories Limited, Mumbai, India

Objectives: To evaluate the efficacy and safety of synthetic semaglutide injection (Test drug) with Wegovy® (Reference drug) 2.4 mg in weight management in two subgroups of patients based on BMI <35 kg/m^2 (Subgroup 1 [S1]) and BMI ≥ 35 kg/m^2 (subgroup 2 [S2])

Materials and Methods: This phase III, multicentre, randomized, open-label, active-controlled clinical study (CTRI/2025/04/085487) was conducted across 22 study sites in India after receiving regulatory and ethics committee approvals. Total 267 adult patients with BMI ≥ 30 kg/m^2 or ≥ 27 kg/m^2 with the presence of at least one co-morbidity of hypertension, dyslipidaemia and/or type 2 diabetes mellitus were included. Patients were randomized to receive either test drug or reference drug every week subcutaneously for 24 weeks. The primary endpoint was change in body-weight from baseline to week 24. Secondary endpoints included change in BMI, waist circumference, SF-36, and glycaemic measures. Safety assessments included incidence of TEAEs and anti-drug/neutralizing antibody.

Results: At baseline, 159 patients in S1 and 108 patients in S2 were included. Mean (±SD) percentage reduction in weight from baseline to week 24 was -14.6 (±4.10) with test drug and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

-14.1 (±3.87) with reference drug in S1 ($P = .5173$) and -12.6 (±4.32) with test drug and -14.0 (± 4.50) with reference drug in S2 ($P = .1232$) respectively.

Proportion of patients achieving ≥ 5% and ≥10% body weight reduction was comparable between test and the reference drug in both S1 and S2 ($P = .3741$ and .5587 for S1 and $P = .4795$ and $P = .7910$ for S2 respectively).

Mean (± SD) change in BMI with test and the reference drug was -4.66 (±1.32) kg/m^2 and -4.53 (±1.24) kg/m^2 respectively in S1 ($P = .5808$) and -4.83 (±1.64) kg/m^2 and -5.57 (±1.72) kg/m^2 in S2 ($P = .0982$) respectively at week 24.

Mean (±SD) decrease in waist circumference with test and the reference drug was -10.3 (±3.06) cm and -10.9 (±11.27) cm respectively in S1 ($P = .5098$) and -11.4 (± 8.28) cm and -12.7 (±5.12) cm respectively in S2 (0.6749) at week 24.

In both subgroups decrease in glycaemic parameters (HbA1c, FBG and PPBG) from baseline to week 24 was comparable ($P > .05$) between test and reference drug in both diabetic and non-diabetic patients. In non-diabetic patients decrease was not clinically relevant.

Study medications were well tolerated.

Conclusions: Semaglutide injection is effective in weight management irrespective of baseline BMI and can be a treatment of choice in weight management with or without co-morbidities

Abstract citation ID: lvag096.1098

EP692 - ECE_1510 - Blood glucose–lowering and skeletal muscle enhancing effects of YU-25-NC01 via dipeptidyl peptidase-4 inhibition

Eun Ju Lee[1,2], Sibhghatulla Shaikh[1,2], Jin Hee Lee[1,2] and Inho Choi[1,3]
[1]*Yeungnam University, Department of Medical Biotechnology, Research Institute of Cell Culture, Gyeongsan, South Korea;* [2]*Yeungnam University, Research Institute of Cell Culture, Gyeongsan, South Korea;* [3]*Gyeongsan, South Korea*

Dipeptidyl peptidase-4 (DPP4) disrupts glucose homeostasis by degrading glucagon-like peptide-1 (GLP-1), thereby reducing insulin secretion and contributing to the development of type 2 diabetes mellitus; **YU-25-NC01** was identified through an in silico screening approach as a natural compound targeting this enzyme. The compound potently inhibited DPP4 enzymatic activity, and its direct interaction with the target protein was confirmed by a cellular thermal shift assay. In DPP4-expressing Caco cells, both mRNA and protein levels of DPP4 were significantly reduced, indicating regulation at transcriptional and translational levels. In a high-fat diet–induced hyperglycemic mouse model, treatment restored circulating GLP-1 levels and improved glycemic control, accompanied by increased expression of GLUT4 in skeletal muscle and GLUT2 in the liver. In addition, skeletal muscle development was enhanced, as evidenced by elevated myosin heavy chain expression and increased muscle fiber diameter. Collectively, these findings demonstrate that **YU-25-NC01** improves glucose metabolism while simultaneously promoting skeletal muscle growth, highlighting its therapeutic potential for both type 2 diabetes mellitus and diabetes-associated muscle atrophy.

Abstract citation ID: lvag096.1099

EP693 - ECE_1396 - Double Diabetes in a Newly Diagnosed 18-yearl-old female with Obesity: Diagnosis, Treatment Strategies, and Lifestyle Interventions

Ivana Mickovski[1,2], Radmila Milosheska[3] and Daniela Buklioska Ilievska[1,3]
[1]*Faculty of Medical Sciences, Goce Delcev University, Stip, North Macedonia;* [2]*PZU Vasileva Kardio, Skopje, North Macedonia;* [3]*General City Hospital 8th September, Skopje, North Macedonia*

Background: Double diabetes, a hybrid form of diabetes combining autoimmune β-cell destruction with insulin resistance, is increasingly recognized among adolescents and young adults due to rising obesity rates. It presents diagnostic ambiguity and therapeutic complexity requiring both insulin replacement and insulin sensitization strategies.

Case Presentation: A 18-year-old female presented with fatigue, polyuria, polydipsia, and a 10-kg weight loss over three months. Despite weight loss, she remained obese (BMI 35.8 kg/m^2). Laboratory results revealed fasting glucose 240 mg/dL, HbA1c 10.3%, fasting insulin 22 µU/mL, and C-peptide 3.0 ng/mL. Both GAD-65 and islet cell antibodies were positive, confirming autoimmunity, while an elevated HOMA-IR (6.1) indicated marked insulin resistance. Lipid profile showed dyslipidemia, and acanthosis nigricans was present.

Diagnosis and Management: Double diabetes was diagnosed based on concurrent autoimmune and insulin-resistant features. Treatment included a basal-bolus insulin regimen (glargine and lispro) combined with metformin (up-titrated to 1000 mg twice daily). Intensive lifestyle modification focused on calorie restriction, low glycemic index nutrition, and structured exercise (150 minutes of aerobic activity weekly plus resistance training). At six months, HbA1c improved to 7.1%, weight reduced by 10 kg, and insulin requirements declined by 30%, reflecting enhanced insulin sensitivity.

Discussion: This case underscores the growing prevalence of double diabetes in young obese individuals and highlights the importance of early recognition and multidisciplinary management. The integration of insulin therapy with metformin and lifestyle interventions can significantly improve metabolic outcomes and reduce cardiometabolic risk.

Conclusions: Double diabetes requires a tailored approach addressing both autoimmune and metabolic components. Early combination therapy with insulin, metformin, and structured lifestyle modification is effective in achieving glycemic and weight control in young adults with this emerging phenotype.

Keywords diabetes type 1, diabetes type 2, double diabetes, obesity, weight loss

Abstract citation ID: lvag096.1100

EP695 - ECE_1041 - Components of a collaborative hybrid primary–specialty integrated diabetes care model leveraging CGM technology platforms to optimize outcomes: a pilot community-based quality improvement initiative

Pendar Farahani
NFMPC - Endocrinology Clinic, Milton, Canada

Background: The rising prevalence of diabetes and its associated complications demands innovative care models that bridge

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

gaps between primary and specialty care. Continuous Glucose Monitoring (CGM) technologies have transformed diabetes management, offering real-time insights that can enhance clinical decision-making and patient engagement.

Objective: This community-based quality improvement initiative aims to pilot a Hybrid Primary–Specialty Integrated Diabetes Care Model in Milton, Ontario, Canada, leveraging CGM platforms to optimize glycemic outcomes, streamline care coordination, and improve access to multidisciplinary support.

Methods: Eligible patients are enrolled through family medicine clinics based on clinical discretion. Upon enrollment, patients receive structured education on CGM use, data sharing, and self-monitoring. Lab results and medication reconciliation are integrated via provincial health data systems by care coordinators. Within two weeks, patients are evaluated by a multidisciplinary team—including endocrinologists, diabetes educators, and if it is indicated by mental health professionals—either virtually or in person. Longitudinal follow-up is conducted using CGM data and digital platforms, modeled after the "Get With The Guidelines" framework.

Results: So far, we conducted outreach to assess interest and feasibility among primary care stakeholders. Early engagement efforts have yielded promising results: Ongoing outreach is underway with family medicine clinics and health teams across the Milton region, Ontario, Canada. Multi-physician family health team clinics and solo-practice family physicians have expressed interest in joining the network. Clinics are proactively establishing shared CGM accounts, enabling collaborative data review and care coordination. This reflects a growing appetite for integrated, technology-enabled diabetes care among community-based providers. In next steps, we will proceed to formalize the onboarding process, including the development of shared protocols, training resources, and clearly defined roles within the pilot cohort. This will ensure consistency, accountability, and scalability as the program evolves.

Conclusions: This pilot will demonstrate the feasibility and potential impact of a hybrid care model that integrates CGM technology into community-based diabetes management. It will lay the groundwork for broader implementation and future research into technology-enabled chronic disease care.

Abstract citation ID: lvag096.1101

EP696 - ECE_1437 - Efficacy and safety of finerenone in adults with diabetic kidney disease: insights from a retrospective cohort study

Ana Luísa Barbosa, Ana Rita Leite, Mafalda Canudas Costa, Juliana Gonçalves, Diana Alexandra Festas Silva, Sílvia Monteiro, João Neves and Joana Queirós
São João Local Health Unit, Department of Endocrinology, Diabetes and Metabolism, Porto, Portugal

Introduction: Finerenone, a non-steroidal selective mineralocorticoid receptor antagonist, has been shown to reduce albuminuria and the risk of chronic kidney disease (CKD) progression in patients with type 2 diabetes (T2D). Evaluating its safety and efficacy in real-world clinical practice, including in patients with other types of diabetes, remains essential.

Methods: We conducted a retrospective cohort study at a tertiary center including adults with diabetic kidney disease (DKD) who initiated finerenone. Participants who started/modified renoprotective therapies other than finerenone were excluded. We collected clinical and laboratory parameters, including blood pressure (BP), serum potassium levels (mEq/L), estimated glomerular filtration rate (eGFR; mL/min/1.73 m^2) and urinary albumin-to-creatinine ratio (UACR; mg/g), before finerenone initiation and after 1, 3-6 and 10-15 months. Changes in these parameters over the follow-up period were evaluated using paired t-tests or Wilcoxon signed-rank tests. Correlations between the variations in these parameters at 3-6 months were assessed using Spearman´s rank correlation.

Results: We included 38 patients (aged 64.6 ± 10.0 years; 73.6% male; 22 with T2D, 6 with type 1 diabetes (T1D) and 10 with other or unknown type; median follow-up duration of 6 months). Serum potassium levels showed a statistically significant increase after 1 month of finerenone initiation (4.51 ± 0.33 at baseline vs 4.68 ± 0.33 at 1 month, $P = .004$, $n = 37$), with no significant differences at 3-6 and 10-15 months. eGFR showed a significant decrease after 1 month (73.3 ± 23.2 at baseline vs 70.9 ± 24.8 at 1 month, $P = .040$, $n = 33$) and 3-6 months (69.9 ± 22.8, $P = .040$, $n = 27$), with no significant differences at 10-15 months. UACR decreased significantly from 146.7 (83.3-399.3) at baseline to 47.1 (30.2-92.9) at 3-6 months ($n = 25$, $P < .001$) and 72.9 (28.7-185.5) at 10-15 months ($n = 16$, $P = .003$), with no statistically significant differences between the latter two time points. No significant differences were observed in BP between baseline and 3-6 months. Hyperkalemia and finerenone discontinuation did not occur in any patient. Greater K+ increases between baseline and 3-6 months were associated with greater UACR reductions in the same period ($\rho = -0.597$, $P = .003$).

Conclusions: Finerenone was safe and effective in reducing UACR in adults with DKD. Greater serum potassium increases were associated with a stronger effect of finerenone on albuminuria.

Abstract citation ID: lvag096.1102

EP697 - ECE_2662 - Effect of Glucagon like Peptide-1 Receptor Agonist therapies on metabolic dysfunction-associated steatotic liver disease in overweight and obese adults

Thaw Htet[1,2], Julia Gordon[3], Brooke Hughes[3], Judy Chen[1], Juliana Chen[4] and Veronica Preda[1,2]
[1]Macquarie University Hospital, Endocrine department, Sydney, Australia; [2]Macquarie University, Faculty of Medicine Health and Health Sciences, Sydney, Australia; [3]Macquarie University, Sydney, Australia; [4]University of Sydney, Department of Nutrition and Dietetics, Sydney, Australia

Metabolic dysfunction-associated steatotic liver disease (MASLD) affects one in three adults globally and is currently considered the leading cause of chronic liver disease. However, it still remains substantially underdignosed. Its burden lies in the risk of progression to decompensated cirrhosis and hepatocellular carcinoma. While GLP-1 receptor agonists (GLP-1 RAs) show promising metabolic and hepatoprotective effects in trials, real-world data in overweight and obese populations remain limited. The aim of this study is to evaluate the effect of incretin analogues (semaglutide, liraglutide, tirzepatide) on hepatic steatosis in overweight or obese adults (BMI $\geq$ 25 kg/m^2) with a diagnosis of MASLD established by ultrasonography or elastography at baseline and after $\geq$ 12 months of pharmacotherapy.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

We reviewed the records and serial imaging data from 45 patients with MASLD and BMI ≥ 25 kg/m^2 who attended a multidisciplinary obesity clinic at Macquarie University Hospital, Sydney, Australia. The degree of hepatic steatosis was reported using a semi-quantitative ordinal scale (mild = 1, moderate = 2, severe = 3) to facilitate statistical analysis. The mean follow up duration was 18 months. The results of a paired t-test demonstrated a statistically significant reduction in hepatic steatosis, with a mean difference of 0.55 (95% CI [0.19, 0.93], $P = .001$). The mean pre-treatment steatosis grade was 2.04 which decreased to 1.48 post-treatment, suggesting hepatic steatosis improved in severity by approximately two-thirds of one steatosis grade, on average, following drug therapy. Greater improvements in hepatic steatosis severity were seen with larger reduction in body weight following incretin analogue therapy. A mean reduction in total body weight by 12% ± 6.7% was associated with a 2-grade improvement in steatosis, while reductions of 5% ± 0.1% and 4% ± 2.1% corresponded to a 1.5-grade and 1-grade improvements, respectively.

Our findings showed that the use of GLP-1 RAs and dual GLP-1/GIP receptor agonists was associated with an improvement in hepatic steatosis in over-weight and obese adults with MASLD. The findings of this study support the use of GLP-1 RAs and dual GLP-1/GIP receptor agonists as a part of the future clinical practice guidelines for MASLD management in over-weight and obese individuals.

Abstract citation ID: lvag096.1103

EP698 - ECE_2130 - Systemic effects of patient-derived serum from a multidisciplinary prehabilitation and postoperative program on colon cancer tumor biology: the ONCOFIT study

Juan Luis López-Cánovas[1,2], Manuel Fernandez-Escabias[1,2], Sofia Carrilho-Candeias[1,2], Andrea Orellana-Jaen[1,2], Maria Tomas-Garcia[2], Rodrigo Fernandez-Escabias[2], Cristian Garcia-Sanchez[1,2], Alberto Millan-Martin[2], María Martínez-Carrillo[3], Benito Mirón[3], Teresa Nestares[4,5], Manuel D. Gahete[7,8] and Francisco J. Amaro-Gahete[29]

[1]Department of Physiology, Faculty of Medicine, University of Granada, 18016, Granada, Spain; [2]Sport and Health University Research Institute (iMUDS), Granada, Spain; [3]Service of Surgery, Hospital Universitario Clínico San Cecilio, 18016, Granada, Spain; [4]Department of Physiology, Faculty of Pharmacy, University of Granada, 18071, Granada, Spain; [5]Biomedical Research Centre (CIBM), Institute of Nutrition and Food Technology "José Mataix", University of Granada, Granada, Spain; 6CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Institute of Salud Carlos III, 28029, Madrid, Spain; [7]Cordoba, Spain; [8]Department of Cell Biology, Physiology and Immunology, University of Córdoba, 14004, Córdoba, Spain; [9]Department of Physiology, Faculty of Medicine, University of Granada & Biosanitary Research Institute, Ibs.Granada, 18006, Granada, Spain

Multidisciplinary prehabilitation and postoperative programs (PPP), combining physical activity, nutritional optimization and psychological support, are increasingly implemented to improve outcomes in oncology. In colon cancer, one of the most prevalent tumors in Europe, unhealthy lifestyle behaviors markedly increase the risk of postoperative complications following surgery, the first-line treatment. Within the ONCOFIT study (4-week prehabilitation plus 12-week postoperative program), perioperative participation resulted in reduced postoperative complications and improved clinical and functional outcomes in patients with colon cancer ($n = 90$). However, the systemic biological mechanisms underlying these benefits remain insufficiently characterized.

This translational study aimed to determine whether patient-derived serum obtained during ONCOFIT modulates tumor-related functional properties in vitro and to characterize associated systemic metabolic signatures. A mechanistic sub-cohort of patients receiving usual care ($n = 12$) or the PPP ($n = 12$) provided serum at three time points: baseline (T0, at diagnosis), after the prehabilitation phase (T1, 1-3 days before surgery), and after the postoperative program (T2, 3 months after surgery). Serum was applied to three human colon cancer cell lines (DLD1, HCT-116, and SW620) to assess key tumor functional properties (cell proliferation, colony formation, and cell invasion). In parallel, serum metabolic profiling was performed using nuclear magnetic resonance (NMR).

Across cell lines and functional assays, exposure to serum from PPP patients resulted in lower proliferative capacity, reduced clonogenicity, and decreased invasiveness compared with serum from usual care patients. Metabolomic profiling revealed a distinct signature in the PPP, characterized by lower LDL cholesterol and circulating fatty acids, alongside higher levels of glucose, several amino acids (Leu, Ile, Val, Lys, Thr, Phe, His, Gln, Cit, Gly, and Tyr), nitrogen-related metabolites (urea and creatinine), relative to usual care. Collectively, these findings are consistent with an intervention-associated shift toward a less pro-tumorigenic circulating milieu, potentially linking lifestyle-driven systemic remodeling to tumor cell behavior.

In conclusion, our PPP appears to modify serum-mediated regulation of colon-cancer cell proliferation, colony formation, and invasion compared with the usual care. Further research should determine the specific circulating mediators driving these effects and their clinical relevance.

Funding: MICINN (PID2023-147665OA-I00; JDC2022-049274-I); CIBERobn.

Abstract citation ID: lvag096.1104

EP699 - ECE_2343 - Mature onset of diabetes of young in paediatric patients - case series presentation

Milica Jakovljevic, Sandra Stankovic, Vesna Cvetkovic, Milica Ignjatović and Tatjana Stankovic

University Clinical Centre Nis, Pediatric Clinic, Endocrinology, Nis, Serbia

Introduction: Maturity-Onset Diabetes of the Young (MODY) is a group of rare, inherited types of diabetes caused by a single gene mutation, typically appearing before age of 25, characterized by positive family history and lack of autoantibodies.

Case series: The genetic testing for MODY was requested for patients with hyperglycaemia, positive family history and lack of antibodies. Out of 6 suspected patients, 4 were diagnosed with MODY, 3 boys and 1 girl. First patient, a boy aged 12 years in his annual checkup had fasting glucose levels 8 mmol/L. During oral glucose test (OGTT), glycaemia in 120. minute was 8.3mmol/L, HbA1c was 7.5%, C peptide 1.57 ng/mL. He was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

started with Metformin. After 2 years, current HbA1c is 5.4% and C peptide is 2.53 ng/mL. A heterozygous pathogenic variant in the HNF4A gene (c.734G>A; (p.Arg245His)) associated with MODY type 1 was detected. Second patient, a 4 year old boy was diagnosed with systemic juvenile idiopathic diabetes (JIA) and received systemic corticosteroid and immunosuppressive therapy. During therapy, fasting glucose levels were above 7mmol/L, C peptide 1.2 ng/mL and HbA1c 5.9%. Dietary changes were advised. The therapy for JIA lasted for 2 years. At the age of 11 years, fasting glycaemia was 7.3 mmol/L, glycaemia after 2 hours in OGTT was 8.4 mmol/L, HbA1c was 6.5%, C peptide 1.3 ng/mL. Metformin was started. Current laboratory findings at the age of 13 years are HbA1c 6.3%, C peptid 1.41 ng/mL. A heterozygous pathogenic variant in the GCK gene (missense type c.763A>G) associated with MODY type 2 was detected. A 7 year old twins, a boy and girl were referred because of fasting hyperglycaemia, 7.3 and 6.3 mmol/L respectively. OGTTs were in reference range, with HbA1c 5.7% and 5.3% and C peptides 1.37 and 1.4 ng/mL. Dietary changes were advised. A heterozygous pathogenic variant in the GCK gene (nonsense type c.1261G>T) associated with MODY type 2 was detected in both twins. At the age of 13 years the boy had HbA1c 7.0%, while the girl had HbA1c 6.6%. Dietary change was advised.

Conclusions: Glucose intolerance in MODY starts in early childhood, so annual checkups for fasting blood glucose and urine samples should be advised in patients with positive family history. Although MODY has relatively slow progression and mild complications, early diagnosis with dietary and life style modifications and treatment can slow down progression of disease. Genetic counseling and testing should also be advised.

Abstract citation ID: lvag096.1105

EP701 - ECE_3570 - Synergistic effect of vitamin D deficiency and cold season on mortality in hospitalized adults

Juraj Smaha, Martin Kužma, Peter Jackuliak and Juraj Payer
Comenius University Faculty of Medicine, 5th Department of Internal medicine, Comenius University Bratislava, Bratislava, Slovakia

Background: Vitamin D deficiency is highly prevalent and shows strong seasonal variability. In hospitalized patients, low serum 25-hydroxyvitamin D (25(OH)D) concentrations may be linked to increased mortality. These relationships may be modified by season and by pandemic-related changes in supplementation during the COVID-19 period.

Objective: To quantify seasonality of serum 25(OH)D and evaluate the joint effect of vitamin D deficiency and cold months on in-hospital mortality in a large Central European inpatient cohort, including analyses across the COVID-19 period in Slovakia.

Methods: We conducted a retrospective cohort study of adult hospitalizations at a tertiary university hospital in Bratislava, Slovakia, between 2018 and 2023. Patients with serum 25(OH)D measured at admission were included (n = 6,914; women 50.3%). Vitamin D deficiency was defined as 25(OH)D <20 ng/mL. Seasonality was assessed by month/season and by warm versus cold months (warm: April–September; cold: October–March). To reflect the potential impact of COVID-19 on vitamin D status and seasonal patterns, analyses were stratified by calendar periods 2018-2019, 2020-2021 (COVID-19 period), and 2022-2023. Logistic regression models were used to identify independent predictors of in-hospital mortality and to test interaction between vitamin D deficiency and cold months.

Results: Mean serum 25(OH)D concentration at admission was 18.0 ± 11.2 ng/mL; vitamin D deficiency (<20 ng/mL) was present in 62% of admissions. 25(OH)D concentrations demonstrated significant seasonal variability with lower values in cold months. Seasonal patterns differed between 2018 and 2021, indicating attenuation of seasonal variability during the COVID-19 period. Overall in-hospital mortality was 16.8% and differed significantly by season ($P < .001$), with lower mortality in warm compared with cold months ($P < .001$). In multivariable models, admission 25(OH)D remained independently associated with mortality ($P = .02$), alongside age ≥65 years ($P < .001$) and malignancy ($P < .001$). In the combined season–deficiency model (reference: warm months without deficiency), mortality odds increased in warm months with deficiency (OR 1.40) and cold months without deficiency (OR 1.28), and were highest in cold months with deficiency (OR 2.38). A significant synergistic interaction between vitamin D deficiency and cold months was confirmed (OR ~1.33; 95% CI 1.12-1.58; $P < .001$).

Conclusions: In a large real-world inpatient cohort, vitamin D deficiency was frequent and strongly seasonal. The combination of vitamin D deficiency and cold months conferred the greatest mortality risk (OR 2.38), supporting season-aware risk stratification using admission 25(OH)D in hospitalized adults.

Abstract citation ID: lvag096.1106

EP702 - ECE_1038 - Health inequalities in diabetes care over the last five decades (1975-2025): a global perspective

Pendar Farahani
NFMPC - Endocrinology Clinic, Milton, Canada

Background: Diabetes is growing epidemic, globally. Diabetes care is complex. Many factors can impact optimal diabetes care and access.

Objectives: 1—To explore determinant factors contributing to health inequalities in diabetes care, globally; 2—To explore the trends of changes in these factors in the last five decades.

Methods: systematic review of medical databases between 1975 and 2025.

Results: Sources of inequalities include geographical, social and personal factors. Geographical factors contributing to access to diabetes care have been studied by continents, countries, regions, and rurality. Social factors include household income, education level, food security, housing stability, and employment status, while personal factors include gender/sex, ethnicity/race, and culture. There are significant interactions between these risk factors in all levels (*P*-value .01-.0001).

Trends and Changes: conducted research studies between 2010 and 2025 demonstrated more than two-fold increase in publications compared to previous four decades (1975-2010) [*P*-value .0001]. Although the number of females, minorities and lower socioeconomic status participants in studies significantly and continuously increased in the last five decades [*P*-value .001, .001, .01], still significant inequality gaps exist in clinical studies related to diabetes care. Utilization of technologies such as

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

telemedicine and establishing local and integrated networks for diabetes care were increased significantly (*P*-value .0001). Trends of change in all continents are positive with different magnitude and velocity (*P*-value .0001). Although, technological and pharmacological advancements for diabetes care significantly improved over the last five decades, the rising prices of medication and equipment led to additional inequality in diabetes care.

Conclusions: Over the last five decades there have been tremendous efforts to address inequalities in diabetes care; there has been more awareness, more inclusion of minorities and women in studies, more publication, more evidence-based care, more patient-centered and tailored models of care. Although all trends are positive globally, the rising prices of medications and care impacted this trend negatively.

Abstract citation ID: lvag096.1107

EP704 - ECE_1135 - Identification of risk factors for cardiovascular autonomic neuropathy in patients with type 2 diabetes mellitus and cardiovascular diseases based on insulin production

Olha Monashnenko[1] and Borys Mankovsky[2]
[1]*Kyiv, Ukraine;* [2]*D.F.Chebotarev State Institute of Gerontology NAMS of Ukraine, Kyiv, Ukraine*

Background and Aims: Cardiovascular autonomic neuropathy (CAN) is a serious complication of type 2 diabetes mellitus (T2DM) that significantly worsens patient prognosis. The aim of this study was to evaluate the relationship between clinical and laboratory parameters, particularly insulin secretion, and the development of CAN in patients with T2DM and concomitant cardiovascular diseases (CVD).

Materials and Methods: We included 82 patients diagnosed with T2DM and CVD. Based on the presence of cardiovascular autonomic neuropathy, patients were divided into two groups: a main group with existing CAN (n = 66) and a control group without CAN (n = 16). All participants underwent a detailed examination, including medical history, anthropometry, and laboratory tests. C-peptide levels were used as a key marker of endogenous insulin production. For statistical analysis, the Student's t-test and χ^2 test were used, and the significance level was set at $P < .05$.

Results: A comparative analysis showed that patients with CAN were significantly older (67.1 ± 8.4 vs 62.3 ± 9.1 years, $P < .05$) and had a longer duration of T2DM (12.8 ± 6.1 vs 8.5 ± 5.2 years, $P < .01$) compared to the control group. The CAN group also had a significantly lower glomerular filtration rate (72.5 ± 18.0 vs 84.2 ± 15.1, $P < .05$) and a markedly lower C-peptide level (2.1 ± 0.9 vs 2.9 ± 1.1 ng/mL, $P < .01$). A strong negative correlation was found between C-peptide levels and the duration of diabetes ($r = -0.65$, $P < .01$), indicating the depletion of insulin secretion over time.

Conclusions: The key risk factors for the development of CAN in patients with T2DM and CVD are older age, a longer duration of diabetes, reduced kidney function, and decreased endogenous insulin secretion. Impaired insulin production, confirmed by low C-peptide levels, is an independent and statistically significant risk factor for the development of CAN in this patient population. C-peptide assessment may serve as a useful tool for risk stratification and identifying patients who require more careful monitoring and preventive measures.

Abstract citation ID: lvag096.1108

EP710 - ECE_2689 - Budget impact analyses for the management of obesity: a literature review

Timothy Quek[1,2,3] and Leela Barham[3]
[1]*Tan Tock Seng Hospital, Singapore, Singapore;* [2]*Singapore, Singapore;* [3]*University of South Wales, Pontypridd, United Kingdom*

Background: Obesity is a common chronic disease with many major medical complications, resulting in a significant rising global economic burden. While lifestyle modifications, anti-obesity medications (AOMs), and bariatric surgery are three established modalities of treatment for obesity, the high cost of newer therapies such as GLP-1 agonists has intensified the need for budget impact analyses (BIAs) to aid in decision making on resource allocation. A literature review was performed to synthesize the findings of recent published BIAs.

Methods: A literature review was conducted following PRISMA 2020 guidance. PubMed and EMBASE databases were searched for English-language studies published between January 2015 and November 2025 reporting standalone BIAs or economic evaluations with a distinct BIA component. Data extraction was guided by the CHEERS 2022 framework, and results were synthesized narratively.

Results: Nine studies met the inclusion criteria: two on lifestyle interventions (both from the United States), three on AOMs (all from the United States), and four on bariatric surgery (two from the United States, one from Thailand, and one from Canada). All the included studies demonstrated a negative short-term budget impact, primarily driven by up-front treatment costs. Lifestyle programs typically showed lower program costs with healthcare utilization offsets from a reduction in obesity related complications and their treatment. For AOMs and bariatric surgery, cost savings were primarily observed in studies with longer time horizons exceeding five years. Two BIAs on anti-obesity medications and one BIA on bariatric surgery showed long-term savings driven by a reduction in metabolic complications and costs related to their treatment (eg, remission of Type 2 diabetes mellitus). Notably, four of the nine studies were industry-funded, all of which reported favourable budget impacts. Comparability and transferability of the study findings were limited by significant heterogeneity in study methodology and reporting.

Conclusions: Obesity treatments present a clear tension between shorter-term affordability and longer-term economic benefits. Although BIAs are often performed with shorter time horizons, such BIAs may fail to capture the full cost-offset potential of preventing chronic complications for chronic conditions like obesity. For sustainable implementation, policymakers could consider phased or targeted strategies focusing on high-risk populations, and/or the use of cheaper generic biosimilars as these become available. At the same time, it is important to remain mindful of the sensitivity of BIA estimates to underlying assumptions and industry influence.

This work was completed in partial fulfillment of an MSc in Applied Health Economics at the University of South Wales.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1109

EP711 - ECE_3662 - Interactions between obstructive sleep apnea and endocrine and metabolic functions

Zachary Friedman and Hassan Heshmati
Endocrinology Metabolism Consulting, LLC, Hassan Heshmati and Valerie Shaw Endocrine Research, Anthem, AZ, United States

Introduction: Sleep is important for health. There are bidirectional interactions between sleep and the endocrine and metabolic systems. Obstructive sleep apnea (OSA) is a common sleep disorder that is caused by or does promote multiple endocrine and metabolic conditions. This review presents an update on the interactions between OSA and endocrine and metabolic functions.

Methods: A systematic search of literature was conducted for the period 2003 to 2025 using the search terms sleep, OSA, interactions, hormones, endocrine function, and metabolic function.

Results: Sleep is essential for health and well-being. There are complex interactions between normal sleep and multiple endocrine and metabolic functions. OSA, the most common sleep disorder, is characterized by disturbances in sleep patterns (arousals), snoring, and recurrent episodes of apnea or hypopnea, with a frequency of at least 5 episodes/hour. It is caused by partial or total obstruction of the pharynx. OSA affects approximately 1 billion people worldwide and is more prevalent in men than women for multiple reasons including differences in upper airway anatomy and sex hormones. Obesity is the leading cause of OSA. Indeed, more than 40% of patients with OSA have obesity. Type 2 diabetes is another risk factor to develop OSA. Gonadal hormones in women (eg, estrogen and progesterone) play an important role in the pathogenesis of OSA. They impact the upper airway patency, contractility of the genioglossus muscle, airway collapsibility, and fluid shifts. Estrogen and progesterone have a protective effect against OSA before menopause and their deficiency during menopause is responsible for an increased prevalence of OSA in postmenopausal women (prevalence may exceed 50%). Polycystic ovary syndrome (PCOS) is significantly associated with OSA in women. In return, OSA can promote or aggravate several endocrine and metabolic diseases such as hyperprolactinemia, hypercortisolism, hyperaldosteronism, type 2 diabetes, hypogonadism with infertility, and obesity. Regular exercise, continuous positive airway pressure (CPAP) therapy, and management of hormonal dysfunctions and obesity (diet, exercise, and behavioral change) have beneficial effects.

Conclusions: Obesity, type 2 diabetes, and gonadal deficiency (eg, menopause) are important risk factors for the development of OSA. People with OSA are also at increased risk of several endocrine and metabolic diseases including hyperprolactinemia, hypercortisolism, hyperaldosteronism, type 2 diabetes, hypogonadism, and obesity. Regular exercise, CPAP therapy, correction of hormonal abnormalities, and weight management (when indicated), are among the most recommended interventions.

Abstract citation ID: lvag096.1110

EP712 - ECE_2513 - Hidden burden of iron deficiency without anemia in women with type 2 diabetes and heart failure with preserved ejection fraction

Lileia Petrovska[1,2], Iryna Kostitska[1], Taras Petrovskyy[1] and Roman Petrovskyy[1]
[1]*Ivano-Frankivsk National Medical University, Endocrinology, Ivano-Frankivsk, Ukraine;* [2]*Ivano-Frankivsk National Medical University, Endocrinology, Ivano-Frankivsk, Ukraine*

Background and Aims: Iron deficiency, particularly common in women, often remains underdiagnosed without anemia (IDWA) and can worsen quality of life and exacerbate cardiovascular and metabolic symptoms in those with type 2 diabetes (T2D) and heart failure with preserved ejection fraction (HfpEF). The aim of the study was to investigate the prevalence of IDWA and its relationship with clinical characteristics in women with T2D and HFpEF.

Materials and Methods: 30 women with T2D and HFpEF (mean age 59.1 ± 1.5 years; body mass index (BMI)- 34.2 ± 2.3 kg/m^2, waist circumference (WC) – 104.1 ± 2.1 cm, glycated hemoglobin (HbA_1C)- 7,.2 ± 0.2% and duration of T2D −7.4 ± 0.9 years) were comprehensively phenotyped including physical examination (blood pressure, heart rate, BMI, WC); laboratory tests: ferritin, transferrin saturation (TSAT), hemoglobin, and N-terminal pro–brain natriuretic peptide (NT-pro-BNP); instrumental evaluation: echocardiography to confirm LVEF >50%; functional assessment: NYHA class. All patients received standard therapy including SGLT2 inhibitors. IDWA was defined as ferritin <100 ng/mL or TSAT <20% with normal hemoglobin levels. Prevalence, functional status, and metabolic parameters were analyzed using descriptive statistics and compared between women with IDWA and women without confirmed iron deficiency.

Results: IDWA was present in 23 out of 30 women (76.7%), defined as ferritin <100 ng/mL or transferrin saturation (TSAT) <20% with normal hemoglobin levels. Women with IDWA had higher NYHA class (2.6 ± 0.5) compared to women without confirmed iron deficiency (1.9 ± 0.4), indicating worse functional capacity and more pronounced fatigue. Women with IDWA tended to have poorer glycemic control, with slightly higher HbA1c (7.3 ± 0.2%) versus women without confirmed iron deficiency (6.9 ± 0.1%). At the same time, BMI (34.5 ± 2.2 kg/m^2) and WC (104.7 ± 1.8 cm) were slightly higher in IDWA women compared to women without confirmed iron deficiency (BMI 33.4 ± 2.4 kg/m^2, WC 102.8 ± 1.9 cm), although these differences were not statistically significant. In summary, IDWA was common in women with T2D and HFpEF and was associated with worse functional status and trends toward adverse metabolic parameters.

Conclusions: IDWA is common in women with T2D and HFpEF, often underdiagnosed due to nonspecific symptoms, and is associated with worse functional status and metabolic trends, highlighting the clinical importance of routine iron assessment.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1111

EP713 - ECE_1311 - Treatment of latent tuberculosis infection attenuating serum aryl hydrocarbon receptor in patients with type 2 diabetes

I-Te Lee
Taichung Veterans General Hospital, Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung, Taiwan

Backgrounds: Latent tuberculosis (TB) infection is a state of TB immunoreactive response without an active TB manifestation. The prevalence of latent TB infection is increased in the population with diabetes mellitus (DM). Latent TB infection has been reported to induce inflammatory reactions, including an elevated level of circulating aryl hydrocarbon receptor (AhR) in patients with type 2 DM. We hypothesized that tuberculosis preventive therapy (TPT) could reduce the circulating AhR.

Methods: In this prospective observational study, patients with type 2 DM and age $\geq$ 45 years received QuantiFERON-TB (QFT) test for screening latent TB infection. The patients with a positive result of the QFT test were enrolled for TPT. The enrolled patient received either 9 months of daily isoniazid (9H) or 3 months of weekly rifapentine plus isoniazid (3HP) according to their decision after evaluation by the pulmonologist and excluding active TB. Serum AhR concentrations were determined at baseline and after TPT.

Results: Among the 88 enrolled patients, serum AhR levels significantly decreased (median: −26.3 pg/mL; interquartile range [IQR]: −43.2, −6.0 pg/mL; $P < .001$). Based on the TPT regiments, 47 (53.4%) patients received the 3HP regimen and 41 (46.6%) received the 9H regimen, respectively. Subgroup analysis revealed that serum AhR levels significantly decreased in both groups of patients treated with 3HP (median: −28.3 pg/mL; IQR: −42.3, −5.9 pg/mL; $P < .001$) and patients treated with 9H (median: −23.9 pg/mL; IQR: −49.0, −6.9 pg/mL; $P < .001$). There was no significant difference in the magnitude of change in the AhR level ($P = .983$) between the 3HP and 9H groups. Linear regression analysis showed that the magnitude of change in AhR levels after TPT was not significantly associated with different TPT regimens ($P = .286$).

Conclusions: The serum AhR level significantly decreased after the TPT program in patients with type 2 DM and latent TB infection, and the magnitude of the decrease in the serum AhR level did not significantly differ between the 3HP regimen and the 9H regimen.

Abstract citation ID: lvag096.1112

EP714 - ECE_2588 - Role of vitamin D-binding protein in the correction of vitamin D deficiency in patients with diabetic kidney disease

Viktoriia Yerokhovych[1], Yeva Ilkiv[1], Olena Karpenko[1], Maryna Bobryk[1], Veronika Zinych[1], Nazarii Kobyliak[1,2] and Iuliia Komisarenko[1]
[1]*Bogomolets National Medical University, Kyiv, Ukraine;* [2]*Kyiv, Ukraine*

Background: The increasing prevalence of kidney injury in patients with type 2 diabetes mellitus (T2D) is a significant clinical concern. Bone-mineral disorders are common in this population and require timely diagnosis and intervention. Vitamin D metabolism is regulated by various factors, including vitamin D-binding protein (VDBP), which has recently attracted attention due to its potential role in the pathogenesis of diabetic kidney disease (DKD).

Objective: To evaluate phosphorus-calcium metabolism in patients with DKD and investigate the association between serum VDBP levels and the effectiveness of vitamin D deficiency correction.

Methods: A total of 84 patients with T2D and chronic kidney disease (CKD) stages I–III were examined. Participants were divided into three groups based on estimated glomerular filtration rate (eGFR), and baseline calcium-phosphorus metabolism indicators were assessed. In the second phase, 32 patients received cholecalciferol supplementation and were followed for three months to evaluate changes in 25(OH)D levels.

Results: Median 25(OH)D levels indicated vitamin D deficiency across all groups. The third group had the lowest values - 13 (8.48-16.4) ng/mL - significantly lower than in the first and second groups ($P < .05$). Serum VDBP levels increased with declining eGFR: 93.6 (68.17-109.67) ng/mL in group I; 101.07 (75.34-132.84) ng/mL in group II; and 132.82 (97.3-168.8) ng/mL in group III. A statistically significant difference was observed between groups I and II ($P < .01$). Vitamin D correction was more effective in patients with lower baseline VDBP levels. Among those who failed to reach optimal 25(OH)D levels ($\geq$30 ng/mL), 31% had significantly higher serum VDBP concentrations.

Conclusions: VDBP is an important factor in vitamin D metabolism and should be considered when correcting bone-mineral imbalances in patients with DKD. The study showed that there is an increase in the level of VDBP with the progression of CKD against the background of T2D. Probably, elevated VDBP levels may impair treatment efficacy by reducing the bioavailability of free vitamin D, due to enhanced binding of its active form, $1,25(OH)_2D$.

Abstract citation ID: lvag096.1113

EP722 - ECE_1774 - Nivolumab-induced pancreatitis and diabetes mellitus in a patient with metastatic melanoma

Ourania Psoma, Christos Zessides and Stelios Tigas
University of Ioannina, Department of Endocrinology, Ioannina, Greece

Introduction: The introduction of immune checkpoint inhibitors (ICIS) inaugurated a new era in the management of metastatic malignancies. However, their molecular action is inextricably linked to a plethora of immune-related adverse events (irAEs).We report a rare case of diabetes mellitus (DM) and chronic pancreatitis co-emerging in a patient on nivolumab (a PD-1 checkpoint inhibitor antibody) treatment for metastatic melanoma.

Case Description: A 27-year-old woman presented with right parotid enlargement and ipsilateral cervical lymphadenopathy. She reported that a blue nevus in the head area had been surgically excised 6 years prior to presentation. She underwent right parotidectomy and lymph node dissection; the histopathology report was consistent with metastatic melanoma stage IIIB (TxN2bM0). Systemic therapy with nivolumab (at a dose of 480

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

mg intravenously every 28 days) was initiated, and 2 months later she developed abdominal pain accompanied by elevated serum amylase levels. Magnetic resonance imaging revealed a suspicious lesion in the pancreatic tail, with increased metabolic activity on 18F-FDG PET-CT scan. Two months later she underwent endoscopic ultrasonography showing a diffusely edematous pancreas and mild parenchymal heterogeneity. Fine-needle biopsy was consistent with pancreatitis. Lymphocytic infiltration was noted with no evidence of malignancy or IgG4-related disease. Six months following nivolumab onset, the patient developed xerostomia and osmotic symptoms. Laboratory investigations demonstrated a fasting plasma glucose of 239 mg/dL, reduced C-peptide levels (0.16 ng/mL) and HbA1c 5.3%. The serum titers of islet-associated antibodies were negative. The patient was initially managed with multiple daily insulin injections and was subsequently started on continuous subcutaneous insulin infusion.

Discussion: ICI-induced DM is a rare irAE (incidence of less than 1%). Its pathophysiology, appears to be multifaced and remains incompletely elucidated. Type 1 diabetes related autoantibodies are commonly, though not always present. Although pancreatitis and DM have each been individually described in patients receiving ICIs, their coexistence has only sparsely been reported in the literature. Notably, a subset of affected patients exhibits radiological or biochemical features consistent with pancreatitis either preceding or coinciding with the diagnosis of DM, suggesting immune-mediated destruction of both the exocrine and endocrine pancreatic compartments.

We describe the case of a patient treated with nivolumab who presumably developed autoimmune pancreatitis followed by fulminant DM. Given the expanding use of ICIs, prompt recognition through careful monitoring of plasma glucose levels—prior to therapy initiation, throughout each treatment cycle, and following treatment discontinuation—is crucial.

Abstract citation ID: lvag096.1114

EP724 - ECE_2170 - Clinical characteristics and outcomes in patients with T2DM admitted to an interventional stent placement procedure

Oyshabonu Sobirjonova[1], Mohammed Abdul Haseeb[2], Askar Sabirov[3] and Zulaykho Shamansurova[1]
[1]Tashkent, Uzbekistan; [2]Kimyo International University in Tashkent (KIUT), Tashkent, Uzbekistan; [3]AKFA Medline University Hospital, Tashkent, Uzbekistan

Background: Diabetes mellitus (DM) is a major risk factor for cardiovascular disease and is commonly associated with obesity, impaired cardiac function, and coronary artery disease. Nowadays, acute myocardial infarction is easily prevented and treated by interventional cardiac surgery, such as a stent. The aim of our study was a comparative analysis of clinical characteristics and outcomes in patients with and without DM admitted to a stent placement procedure.

Methods: A retrospective observational study was conducted at Akfa Medline University Hospital in Tashkent, Uzbekistan, by gathering data from medical records in a total of 12,026 patients treated in 2024 and 2025. Patients were divided into two groups: with and without DM. Demographic data, body mass index (BMI), echocardiographic ejection fraction (EF), coronary angiography reports, and mortality rate were analyzed. EF and angiography analyses were performed in patients with available data. Results were presented as absolute numbers and percentages.

Results: Of the total cohort, 196 patients (1.6%) had diabetes mellitus, and 11,830 patients (98.4%) did not have DM. The mean BMI in the overall 2025 cohort was 27.5 kg/m^2. Patients with diabetes had a higher mean BMI compared with non-diabetic patients (31.1 vs 26.8 kg/m^2). Echocardiographic data showed the mean EF was consistently lower (37% vs 42%) in patients with diabetes compared with non-diabetic patients. Coronary angiography, available in a limited subgroup, demonstrated more impaired coronary circulation among diabetic patients. Overall mortality was comparable across the cohort.

Conclusions: In this large hospital-based cohort, patients with diabetes mellitus had higher BMI and reduced cardiac function compared with non-diabetic patients. And suggested to underscore the cardiovascular vulnerability associated with DM and highlight the importance of comprehensive cardiovascular assessment in this population.

Abstract citation ID: lvag096.1115

EP725 - ECE_1845 - Exploring the metabolic risks of weight loss therapy in Type 1 Diabetes: A case of DKA following Retatrutide injections

Hasan Jamjoom
LONDON, United Kingdom

Introduction: Retatrutide is a novel experimental weight loss agent which, in comparison to more commonly known weight modulators, is a triple agonist of the GIP, GLP-1, and glucagon receptors, and is currently undergoing phase 3 clinical trials to establish long term safety and efficacy. Its use remains predominantly research based and it is not licensed for clinical use within the United Kingdom or elsewhere. Although it has shown some promising results in relation to obesity and type 2 diabetes, its safety profile in patients with type 1 diabetes is yet to be established.

Case Report: A 20-year-old, 60-kg female patient with a background history of type 1 diabetes, on basal-bolus insulin (Levemir and Fiasp), presented to the emergency department following a period of intractable vomiting and reduced oral intake. On questioning, the patient reported being dissatisfied with her current weight and therefore had started a new weight loss injection which later transpired to be Retatrutide. She purchased it off a friend who had bought it from the United States. She reported only having had x3 doses, with the last dose being the day prior to admission. On presentation to the emergency department, she was mildly tachycardic but otherwise haemodynamically stable with no oxygen requirement. She appeared unwell with persistent nausea and retching. Her biochemistry showed her to be in severe diabetic ketoacidosis with blood sugars of 20mmol/l, ketones of 6.4mmol/l, pH of 6.8, and a Bicarbonate level of 4 mmol/l. She was commenced on a fixed rate insulin infusion at 0.1 units/kg/hour, in addition to fluid resuscitation and administering her basal insulin. She made steady progress as her labs improved, allowing her to be switched to variable rate insulin initially and then back to her usual subcutaneous insulin. She was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

discharged from hospital with the recommendation of definitively discontinuing Retatrutide.

Discussion: While traditional GLP-1 receptor agonists have shown some efficacy in type 1 diabetes, particularly in cases of co-existent metabolic syndrome, this case illustrates the need for more comprehensive data when it comes to the safety of Retatrutide, especially in patients with type 1 diabetes. It also emphasises the importance of patient education and promoting vigilance when it comes to weight loss medication, particularly for those who purchase them from the black market or from non-reputable sources, which clearly poses a higher risk of potential drug contamination and hence adverse outcomes.

Abstract citation ID: lvag096.1116

EP726 - ECE_3628 - Anaphylaxis after initiation of insulin glargine/lixisenatide in a patient with long-term tolerance to insulin glargine: a case report

Gökhan Rıza Baykal[1], Aslı Altınbezer[1], Şadan Soyyiğit[2], Oya Topaloglu[3], Reyhan Ersoy[3] and Bekir Cakir[3]
[1]*Ankara Bilkent City Hospital, Department of Endocrinology and Metabolism, Ankara, Türkiye;* [2]*Ankara Yıldırım Beyazıt University Faculty of Medicine, Ankara Bilkent City Hospital, Department of Pulmonary Diseases, Immunology and Allergy, Ankara, Türkiye;* [3]*Ankara Yıldırım Beyazıt University Faculty of Medicine, Ankara Bilkent City Hospital, Department of Endocrinology and Metabolism, Endocrinology and Metabolism, Ankara, Türkiye*

Background: Fixed-ratio combinations of basal insulin and GLP-1 receptor agonists, such as insulin glargine/lixisenatide, are increasingly used in type 2 diabetes mellitus (T2DM). Although hypersensitivity reactions have been reported, anaphylaxis remains rare. We describe an immediate-type systemic reaction fulfilling clinical criteria for anaphylaxis shortly after initiation of insulin glargine/lixisenatide in a patient who had tolerated insulin glargine for years.

Case: A 42-year-old woman with a long-standing history of T2DM and hypothyroidism had been treated for several years with a basal–bolus regimen consisting of daytime insulin aspart and evening insulin glargine, without any previous local or systemic allergic reactions. Her regimen was simplified by switching to once-daily insulin glargine 100 U/mL plus lixisenatide. On the third day of therapy, shortly after the evening injection, she developed generalised erythema and pruritic urticaria, lip and tongue swelling, dyspnea, palpitations and presyncope. She was admitted to the emergency department with a diagnosis of anaphylaxis and treated with intramuscular adrenaline, intravenous antihistamines, corticosteroids, and fluids. She required three days of intensive care unit monitoring followed by four days in a medical ward, with full clinical recovery. Thereafter, she was evaluated in an allergy and clinical immunology clinic. Based on the temporal relationship, clinical severity and her documented long-term tolerance to insulin glargine, the reaction was classified as an immediate-type, drug-induced anaphylaxis most likely related to lixisenatide. Permanent avoidance of lixisenatide-containing medications was recommended. Her previous regimen with insulin aspart and insulin glargine was restarted and has been continued without recurrence of allergic symptoms during follow-up.

Conclusions: This case illustrates that life-threatening anaphylaxis may occur early after starting insulin glargine/lixisenatide in a patient who has previously tolerated insulin glargine alone. Clinicians should be aware that the GLP-1 receptor agonist component of fixed-ratio combinations can unmask severe hypersensitivity reactions. Immediate discontinuation of insulin glargine/lixisenatide, referral for specialist allergy assessment and resumption of a previously tolerated insulin regimen represent a pragmatic management strategy, and reporting such events is essential to better characterise the safety profile of lixisenatide-containing therapies.

Abstract citation ID: lvag096.1117

EP729 - ECE_2411 - Effect of short term subcutaneous liraglutide treatment on respiratory function in individuals with clinical obesity and obstructive sleep apnea

Maria Christou[1], Charikleia Tselepi[2], Panagiota Christou[1], Nikolaos Kavrakis[1], Paschalis Karagkiozakis[1], Eleni Christou[1], Katerina Papathanassiou[1], Athanasios Siolos[1], Christos Zessides[1], Christos Kyriakopoulos[2], Konstantinos Kostikas[2], Athanasios Konstantinidis[2] and Stelios Tigas[1]
[1]*University of Ioannina, Department of Endocrinology, Ioannina, Greece;* [2]*University of Ioannina, Department of Respiratory Medicine, Ioannina, Greece*

Introduction: Tirzepatide has demonstrated benefit in reducing the apnea-hypopnea index (AHI) in individuals with obstructive sleep apnea (OSA), while liraglutide and phentermine/topiramate have shown potential benefit. This study aimed to assess the effect of liraglutide on anthropometric characteristics and respiratory function in individuals with clinical obesity and OSA followed-up at a Greek tertiary center.

Methods: Individuals with class III obesity [body mass index (BMI) ≥40 kg/m^2] and OSA, already receiving continuous or bi-level positive airway pressure (CPAP or BiPAP) therapy, participated in the study and were treated with liraglutide 3 mg sc once daily. Anthropometric, spirometric and device-derived sleep apnea parameters were recorded at baseline and at 4 months. Results are presented as number (percentage), mean (standard deviation) or median (range).

Results: Forty-one individuals were recruited, of whom 29 completed the 4-month follow-up (mean age 58 ± 10 years, 48% males). Prediabetes, type 2 diabetes, dyslipidemia, hypertension, coronary heart disease and heart failure were present in 66%, 24%, 69%, 62%, 14% and 21%, respectively. Twenty-two (76%) received CPAP and 7 (24%) BiPAP therapy. Most individuals had severe OSA (87%) with a sleep study-derived AHI of 72 ± 29. Body weight decreased with liraglutide from 136.4 ± 26.8 to 126.4 ± 26.5 kg ($P < .01$) and BMI from 45.6 (40.1-66.3) to 43.0 (34.6-62.3) kg/m^2 ($P < .01$). Absolute and relative weight change were −9.9 (−28.2 + 0.6) kg and −7.4% ± 4.8, respectively with 76%, 24%, and 7% of individuals achieving ≥5%, ≥10%, and ≥15% weight loss, respectively. Waist circumference in men and women, neck circumference in men, waist-to-hip ratio in men and waist-to-height ratio were also significantly improved at 4 months. HbA1c decreased significantly [6.2% (5.1-9.1) to 5.7% (4.7-8.0), $P < 0.01$]. Spirometric indices did not show

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

statistically significant changes. Mean and 95th percentile positive airway pressure improved significantly (9.7 ± 2.5 to 8.5 ± 2.3 cmH2O, $P < .01$ and 11.3 ± 2.2 to 10.7 ± 2.2 cmH_2O, $P < .01$, respectively). Device use during sleep was also significantly decreased (402 ± 136 to 357 ± 90 minutes, $P = .04$). Adverse events were reported in 45% of individuals, mostly gastrointestinal (86%).

Conclusions: Among individuals with clinical obesity and OSA, liraglutide treatment was associated with clinically significant weight loss, along with reductions in positive airway pressure requirements and sleep device usage time.

Abstract citation ID: lvag096.1118

EP730 - ECE_2742 - Relationship between inflammation and micronutrients status in a cohort of obese Romanian paediatric patients

Ioana-Maria Crasan[1], Corina Delia[1,2], Anisoara Cimpean[1], Bogdan Pascu[2] and Elena Ionica[1]
[1]*University of Bucharest, Departament of Biochemestry and Molecular Biology, Bucharest, Romania;* [2]*National Institute for Mother and Child Health "Alessandrescu-Rusescu", Laboratory of Biochemistry, Bucharest, Romania*

Paediatric obesity is increasingly recognized as a state of low-grade, chronic inflammation that may coexist with micronutrient disturbances, yet integrated data in Romanian children and adolescents remain scarce.

This study aimed to (i) evaluate the relationship between inflammatory biomarkers and micronutrient status, focusing on vitamin D [25(OH)D] and iron, and (ii) assess whether BMI-for-age percentiles are useful for obesity classification in patients <18 years, complemented by Tanita bioimpedance measurements of body composition. We conducted a cross-sectional analysis of 60 paediatric patients (0.9-17 years; 31 females/29 males), stratified into two age groups (0-12 years, n = 31; 13-18 years, n = 29). We measured 25-hydroxyvitamin D, total calcium, phosphorus, serum iron and ferritin, inflammatory markers (high-sensitivity C-reactive protein, CRP; interleukin-6, IL-6), lipid profile (total cholesterol, LDL-C, HDL-C, triglycerides, VLDL-C) and glucose-insulin indices (fasting glucose, insulin, HOMA-IR). Weight status was classified using BMI-for-age percentiles (underweight, normal weight, overweight, obesity); in a subset (n = 21), Tanita bioimpedance provided fat percentage (FATP), fat mass (FATM), fat-free mass, total body water (TBW/WATERM), water percentage (WATERP) and predicted muscle mass (PMM). Vitamin D insufficiency/deficiency was frequent, with most participants presenting 25(OH)D below commonly used adequacy thresholds and adolescents showing lower values than younger children. BMI showed an inverse association with 25(OH)D, supporting an adiposity-linked reduction in vitamin D status. Inflammatory biomarkers were consistent with predominantly low-grade inflammation, with CRP distributions shifted upward in adolescents and the widest variability observed in obesity; IL-6 also displayed marked heterogeneity, including high outliers in participants with obesity. Metabolic markers suggested a more adverse cardiometabolic profile in higher adiposity categories, characterized by higher insulin and HOMA-IR and a lipid pattern compatible with obesity-associated dyslipidemia (higher TG/VLDL and less favourable HDL-C). In the Tanita subset, adiposity quantified by bioimpedance (FATM/FATP) correlated strongly with triglyceride-rich lipoproteins, while WATERP correlated inversely with TG/VLDL, indicating that body composition metrics may capture clinically relevant metabolic variation beyond BMI percentiles alone. Iron and ferritin suggested that reduced iron stores may coexist with obesity, while associations with CRP/IL-6 were not robust, implying that nutritional factors and growth-related demands may contribute in addition to inflammation.

Overall, BMI-for-age percentiles are useful for paediatric obesity screening in this Romanian cohort, and integrating Tanita body composition with biochemical profiling may improve phenotyping and support more targeted cardiometabolic and micronutrient risk stratification, particularly in adolescents.

Abstract citation ID: lvag096.1119

EP731 - ECE_2992 - Clinic and metabolic profile in bariatric surgery candidates

Beatriz Gonçalves, Marta Lopes, Mariana Severino, Jose Rocha, Carolina Peixe, João Vieira, José Camolas, Raquel Lalanda, Filipa Nogueira, Olavo Gomes, André Paulino and Ana Paula Barbosa
Faculty of Medicine Lisboa, Endocrinology Department, Hospital Santa Maria, Lisboa, Endocrinology Department, Hospital Santa Maria, Lisboa, Lisboa, Portugal

Introduction: Obesity is a multifactorial chronic and systemic disease, characterized by multiple biochemical and hormonal changes which impact negatively both morbidity and mortality of obese individuals. In a hospital setting, it becomes crucial to characterize their clinical, metabolic and inflammatory profile in order to optimize risk stratification, plan appropriate therapeutic interventions, and reduce the burden of disease on the healthcare system.

Aims: This study aimed to evaluate the clinic and metabolic profile of the obesity surgery candidates.

Methods: The study included individuals with BMI ≥ 35 kg/m^2 candidates to obesity surgery, followed in both Endocrinology and Surgery Departments. Sociodemographic and anthropometric data were collected and laboratory tests were analyzed, including hemoglobin, ferritin, folic acid, vitamin B12, calcium, 25-OH-vitamin D, fasting blood glucose, HbA1c, total cholesterol, LDL, HDL, triglycerides, TSH, fT4, cortisol, AST, ALT, uric acid, urea, and creatinine. The statiscal analysis was done with software SPSS®, version 29.

Results: 29 individuals, 16(55.2%) females, mean age 51±9 years, mean weight 114.8 ± 17.4 Kg, mean height 1.68 ± 0.10 m and mean BMI 41.1 ± 1.4 Kg/m^2. Family history of obesity was present in 34.5%. There was a high prevalence of hypertension (82.8%) and dyslipidemia (82.8%) while type 2 diabetes was present in 34.5%. Hypovitaminosis D in 92.6%, mean elevated ferritin (162.1 ± 138.3 ng/ml), mean HbA1c 6.6 ± 1.2%, and reduced HDL (46 ± 9 mg/dl) were found. Men showed a higher prevalence of type 2 diabetes and sleep apnea, while women presented more primary hypothyroidism and anxiety-depressive symptoms. Furthermore, the comparison between the different BMI classes showed a trend towards higher values of glycemia, HbA1c and triglycerides in individuals with higher BMI, reflecting

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

a worsening of the metabolic profile with the degree of obesity.

Discussion and Conclusions: The results of this study reinforce the multifactorial and complex nature of obesity, highlighting that this condition goes far beyond simple excess weight, involving multiple domains such as metabolic, inflammatory, hormonal, and psychological changes. These findings underscore the importance of implementing individualized clinical strategies that integrate not only weight control but also an approach directed at the metabolic and inflammatory profile of each patient, as well as the identification and management of frequently associated psychological comorbidities.

Abstract citation ID: lvag096.1120

EP732 - ECE_3081 - Insulin secretion assessment during oral glucose tolerance test

Tzvetelina Totomirova[1], Mila Arnaudova[2] and Nikolay Kostadinov[3]
[1]*Military Medical Academy, Clinic of Endocrinology and metabolic diseases, Sofia, Bulgaria;* [2]*MBAL Vita, Sofia, Bulgaria;* [3]*Burgaski Universitet Pfor. D-R Asen Zlatarov, Burgas, Bulgaria*

Background: Oral glucose tolerance test (OGTT) defines carbohydrate metabolism disorders. Glucose measurement should be performed on 0 minute and minute 120. There are different modifications of OGTT with measurement of glucose and insulin level on additional minutes and thus more detailed information is available.

The **aim** of our study is to evaluate the value of measurement of insulin secretion during oral glucose tolerance test

Materials and Methods: Our survey includes 107 patients (55 women, 52 men, mean age 44.01 ± 12.87 years). Mean weight was 99.07 ± 18.73 kg and mean BMI was 34.86 ± 6.0 kg/sq.m. All patients underwent OGGT. Measurement of insulin and glucose was performed on minute 0, 60, 120 and 180. HOMA-IR was calculated for assessment of hyperinsulinaemia. Correlation between glucose and insulin level on different minutes was assessed.

Results: On 60th minute there was significant moderate positive correlation between 60th minute glucose (7.81 ± 1.89 mmol/l) and 180th minute insulin (58.05 ± 32.01 mU/l) level ($r = -0.502$, $P < .001$). Difference between glucose level on minute 60 and minute 0 correlates negatively with minute 180 insulin level ($r = 0.402$), presenting the delay in first insulin response. No difference was found depending on age, gender and weight of patients.

Conclusion: Measurement of insulin level during OGTT presents additional information about insulin secretion curve and could be used for assessment of pathologically elevated insulin level as result of glucose stimulation and reveals early insulin secretion disorder.

Abstract citation ID: lvag096.1121

EP733 - ECE_1804 - Diabetic ketoalkalosis with QT prolongation following diabetic ketoacidosis treatment

Merve Akkaş[1,2,3], Zeynep Karkın[1,2], Gürkan Bozan[1,4], Pelin Köşger[1,5], Aslı Kavaz[1,6] and Birgul Kirel[1,2,7,8,9]
[1]*Eskişehir Osmangazi University Faculty of Medicine, Internal Medicine, Endocrinology, Eskişehir, Türkiye;* [2]*Eskişehir Osmangazi University Faculty of Medicine, Pediatric Endocrinology, Eskişehir, Türkiye;* [3]*Eskişehir Osmangazi University Faculty of Medicine, Pediatric Endocrinology, Eskisehir, Türkiye;* [4]*Eskişehir Osmangazi University Faculty of Medicine, Pediatric İntensive Care, Eskişehir, Türkiye;* [5]*Eskişehir Osmangazi University Faculty of Medicine, Pediatric Cardiology, Eskişehir, Türkiye;* [6]*Eskişehir Osmangazi University Faculty of Medicine, Pediatric Nephrology, Eskişehir, Türkiye;* [7]*Eskisehir Osmangazi University Hospital, Pediatric Endocrinology, Eskisehir, Türkiye;* [8]*Eskişehir Osmangazi University, Pediatri Endocrinology, Eskisehir, Türkiye;* [9]*Eskişehir, Pediatric Endocrinology, Eskişehir, Türkiye*

Objective: Diabetic ketoalkalosis (DKALK) is a rare but potentially life-threatening condition characterized by metabolic alkalosis accompanied by persistent ketosis, which may develop during or after treatment of diabetic ketoacidosis (DKA). It may be associated with severe electrolyte disturbances and cardiac rhythm abnormalities. We report a pediatric case of DKALK complicated by significant QT prolongation following DKA treatment.

Case: A 12-year-old girl with newly diagnosed type 1 diabetes mellitus was referred to our center after receiving treatment for severe DKA at another hospital (glucose: 355 mg/dL, pH: 6.9, HCO_3: 6.5 mEq/L), including intravenous fluids, bicarbonate, and insulin infusion. On admission, she was conscious, hemodynamically stable, and showed no signs of dehydration.

Laboratory evaluation revealed partial resolution of metabolic acidosis with persistent ketonemia. Standard DKA management without bicarbonate therapy was continued in the pediatric intensive care unit. At 36. hour of treatment, the patient developed DKALK characterized by metabolic alkalosis, hypokalemia, hypomagnesemia, hypocalcemia, and ongoing ketosis. Concurrent electrocardiography demonstrated marked QTc prolongation (500-510 ms). Electrolyte replacement therapy and temporary discontinuation of insulin until correction of hypokalemia resulted in normalization of metabolic parameters and QTc interval. No ventricular arrhythmias occurred during follow-up.

Conclusions: DKALK developing after DKA treatment may be accompanied by persistent ketosis, significant electrolyte abnormalities, and marked QT prolongation, creating a substrate for potentially life-threatening ventricular arrhythmias. Therefore, careful and continuous monitoring of acid-base status, electrolyte balance, and cardiac rhythm is essential in patients with DKA, not only during acute management but also after transition to subcutaneous insulin therapy.

Keywords diabetic ketoalkalosis, diabetic ketoacidosis, QT prolongation, electrolyte disturbances, children

Abstract citation ID: lvag096.1122

EP735 - ECE_2086 - Effect of obesity in progression of diabetic kidney disease in Korean patients with type 2 diabetes

Dong Hyeok Cho, Jin Ook Chung and Dong Jin Chung
Chonnam National University Hospital, Gwangju, South Korea

Background: The impact of obesity on progression of diabetic kidney disease is debated. We evaluated whether baseline obesity predicts renal deterioration in Korean patients with type 2 diabetes (T2D) and established CKD.

Methods: In this longitudinal cohort, 319 Korean T2D patients with CKD stage ≥2 (mean age 61.0 ± 11.4 years) were followed for 2.9 ± 1.1 years. Renal function was assessed by serum

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

creatinine, eGFR (Cockcroft-Gault), and urinary albumin-to-creatinine ratio (ACR). BMI categories (WHO Asia-Pacific): normal <23 kg/m^2, overweight 23-24.9 kg/m^2, obese ≥25 kg/m^2. Primary outcome was renal function decline, defined as sustained ≥30% eGFR reduction or progression to a higher albuminuria category. Multivariate logistic regression adjusted for age, sex, diabetes duration, HbA1c, total cholesterol, triglycerides, and hypertension.

Results: At baseline, mean diabetes duration was 12.6 ± 9.8 years, HbA1c 8.1%, and mean eGFR 52.2 mL/min/1.73 m^2. 41.5% (n = 132) of patients were obese. Obese patients had higher HbA1c (mean 8.5% vs 7.9%, $P = .01$), higher ALT (mean 36 vs 28 U/L, $P < .01$), and adverse lipid profiles. Baseline eGFR and median ACR did not differ significantly across BMI groups. Over follow-up, mean annual eGFR decline was greater in the obese group (−3.8 vs −2.4 mL/min/1.73 m^2/year; between-group difference −1.4; $P = .01$). Worsening albuminuria occurred in 28.0% of obese versus 17.2% of normal-BMI patients ($P = .02$). The composite renal decline endpoint occurred in 62 patients (19.4%): 38 (28.8%) obese and 24 (11.4%) non-obese (log-rank $P < .001$). In multivariate analysis, baseline obesity was independently associated with increased odds of renal function decline (adjusted OR 1.31; 95% CI 1.05-1.63; $P = .02$). Results were robust after additional adjustment for baseline ACR and use of renin-angiotensin blockers.

Conclusions: In this cohort of Korean T2D patients with CKD stage ≥2, baseline obesity was independently associated with faster eGFR decline and higher risk of clinically meaningful renal deterioration. These findings support incorporating weight-management strategies to potentially slow progression of diabetic kidney disease in this population.

Abstract citation ID: lvag096.1123

EP739 - ECE_3957 - A novel secreted protein, JUV-161, reverses structural and functional muscle decline in Sarcopenia

Ashil Koranne, Hee Ju Kim, Ritwik Datta, Vengadeshprabhu Karuppagounder, Han Song, Zhihua Li, Thach Mai, Banmeet Anand, Colin Hislop, Priya Handa, Hanadie Yousef and Jeremy O'connell
Juvena Therapeutics.Inc, Redwood city, United States

Age-related sarcopenia is characterized by progressive skeletal muscle wasting, reduced fiber size, and loss of strength, leading to functional decline and increased frailty risk. Current therapeutic options are limited, highlighting the need for interventions that both preserve muscle mass and restore muscle function. At Juvena Therapeutics, we have developed a biologics-based drug discovery platform focused on identifying stem-cell secreted proteins capable of restoring tissue health in aged individuals. JUV-161 is a novel secreted protein engineered to promote muscle regeneration, repair, and functional recovery.

To evaluate the efficacy of JUV161 in sarcopenia, we treated aged C57BL/6 male mice (23-25 months old) with daily subcutaneous injections of JUV-161 (12 mg/kg) or vehicle control for three weeks followed by the assessment of body composition, muscle function and tissue histopathology.

JUV-161 treatment significantly improved body composition, as indicated by percent increase in lean mass from the baseline compared with vehicle-treated controls (+1.12% vs −3.23% in vehicle). Histological analysis revealed that JUV-161 reversed muscle aging in terms of fiber type composition, with increased frequency of fast-twitch fibers ($P < .01$) and a corresponding reduction in slow-twitch fibers ($P < 0.01$) compared to the vehicle-treated controls. These structural and compositional changes are closely aligned with the observed improvements in strength and functional performance. JUV161 treatment significantly improved specific forelimb grip strength (25.51 mN/g vs 23.20 in vehicle, $P < .05$) and all-limb grip strength (46.73 mN/g vs 41.21 mN/g in vehicle, $P < .01$), demonstrating meaningful gains in muscle function.

Collectively, these findings show that we successfully alleviated age-related muscle wasting, restored fiber size, and enhanced functional performance with JUV-161 in a model of sarcopenia. By simultaneously improving structural, compositional, and functional aspects of skeletal muscle, JUV-161 represents a promising therapeutic candidate for counteracting sarcopenia, mitigating muscle loss, and restoring strength in older adults. These data support further translational development of JUV-161 for clinical applications aimed at improving mobility, reducing frailty risk, and enhancing quality of life in aging populations.

Abstract citation ID: lvag096.1124

EP741 - ECE_1533 - Physician workplace health behaviors and BMI: evidence from the healthy lifestyle and personal control questionnaire and organizational implications

Dana kagansky[1], Racheli Magnezi[2], Matan Elkan[1] and Orna Tal[1]
[1]*Shamir Medical Center (Assaf Harofeh), Endocrine Institute, Affiliated to the Gray Faculty of Medical & Health Sciences, Tel Aviv University, Beer Yaakov, Israel;* [2]*Bar-Ilan University, Department of Management, Ramat Gan, Israel*

Background: Physician well-being is central to organizational performance and patient care, yet workplace demands may erode healthy behaviors.

Objective: To examine associations between self-reported health behaviors and BMI among physicians and outline implications for workplace wellness.

Methods: Cross-sectional online survey of physicians using the 26-item Healthy Lifestyle and Personal Control Questionnaire (HLPCQ). Participants were categorized into normal weight (BMI < 25) and overweight (BMI ≥ 25) groups based on their BMI. Group differences were assessed, and multivariable logistic regression was performed.

Results: Of 200 respondents, 144 complete cases were analyzed; 54.2% had a BMI < 25. Higher BMI was associated with lower adherence to health-promoting behaviors, notably Dietary Harm Avoidance ($P < .001$), Daily Routine ($P = .05$), and Organized Physical Exercise ($P = .03$). Regression analysis identified Dietary Harm Avoidance and Organized Physical Exercise as protective factors against overweight ($P < .01$). Physicians in surgical specialties reported lower health behavior scores than non-surgical peers, particularly in Daily Routines ($P < .001$) and in total lifestyle scores ($P = .01$).

Conclusions: Workplace constraints on routines and activity are associated with BMI. These findings suggest that organizational approaches addressing harm-avoidant dietary environments

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and protected time for structured exercise may be relevant to clinician health and role modeling.

Abstract citation ID: lvag096.1125

EP742 - ECE_2750 - Lifestyle behaviors and BMI among medical students: a cross-sectional study using the HLPCQ Lifestyle behaviors and BMI among medical students: a cross-sectional study using the HLPCQ

Dana kagansky[1,2], Michal Bitan[3], Ofir Vinograd[1], Noa Levi[4], Hitam Hagog Natour[5] and Orna Tal[1]

[1]Shamir Medical Center (Assaf Harofeh), Endocrine Institute, Affiliated to the Gray Faculty of Medical & Health Sciences, Tel Aviv University, Beer Yaakov, Israel; [2]Shamir medical center, Endocrine Institute, Affiliated to the Gray Faculty of Medical & Health Sciences, Tel Aviv University, Beer Yaakov, Israel; [3]The College of Management Academic Studies, School of Computer Science, Rishon LeZion, Israel; [4]Tel Aviv University, Grey Faculty of Medical & Health sciences, Tel aviv, Israel; [5]Meir Medical Center, Institute of Endocrinology, Diabetes and Metabolism, Kfar Saba, Israel

Introduction: Health-promoting lifestyle behaviors are associated with BMI and metabolic health. Among healthcare professionals, these behaviors may also influence future patient counseling practices. However, data on lifestyle patterns and BMI among medical students remain limited.

Methods: A cross-sectional online survey was conducted among medical students using the 26-item Healthy Lifestyle and Personal Control Questionnaire (HLPCQ). BMI was self-reported, and participants were categorized as normal weight (BMI < 25), overweight (BMI 25-30), or obese (BMI ≥ 30). Group differences in the total HLPCQ score were assessed, and univariable and multivariable regression analyses were used to examine associations of the total and domain-specific HLPCQ scores with BMI.

Results: The questionnaire was distributed to 2,000 medical students, of whom 516 completed the full questionnaire. Among respondents, 370 were normal weight, 113 overweight, and 33 obese. The mean age was 29 years $\pm$ 4, and 68% were female. Total HLPCQ scores differed significantly across BMI categories ($P = .019$). Among the five questionnaire subdomains, daily routine and organized physical exercise scores were significantly associated with BMI ($P = .004$ and $P = .012$, respectively). In adjusted analyses, male sex, lower BMI, and younger age were independently associated with higher HLPCQ scores.

Conclusions: In this cohort of medical students, the total HLPCQ score was significantly associated with BMI. These findings underscore the relevance of overall lifestyle patterns during medical training, a formative period that may influence future physician health and lifestyle-related counseling practices.

Abstract citation ID: lvag096.1126

EP745 - ECE_1013 - Extra-articular steroid injection induced diabetic ketoacidosis following lumbar medial branch block and radiofrequency ablation: A case report

Yotsapon Thewjitcharoen, Soontaree Nakasatien and Thep Himathongkam

THEPTARIN Diabetes, Thyroid and Endocrine Center, Vimut-Theptarin Hospital, Bangkok, Thailand

Background: Radiofrequency ablation (RFA) is an innovative procedure for managing chronic lower back pain caused by lumbar medial branch nerve irritation. Recently, clinicians prefer to inject corticosteroids into the axial space to enhance pain control and potentially limiting the size of thermal lesion. The addition of corticosteroids to RFA could lead to systemic effects as other routes of administration. However, the risks of the addition of corticosteroids must be weighed against the potential benefit. Here, we report a rare case of diabetic ketoacidosis following RFA treatment in an elderly patient with type 1 diabetes (T1D).

Clinical case: A 77-year-old man with long-standing T1D (diagnosed at age of 30) a history of alcoholism and lumbar spondylosis was brought to the emergency room with an altered state of consciousness and severe hyperglycemia as detected by continuous glucose monitoring (CGM). He denied fever, abdominal pain, or missed insulin doses. His medications included insulin degludec 10 units per day and insulin lispro 4-6 units per day. Glycemic control had been satisfactory with glycated hemoglobin (A1C) at 6.1% and time-in-range at 71% in the previous month. Upon admission, laboratory data showed random plasma glucose 452 mg/dL, A1C 7.1%, wide anion gap at 18 mEq/L, and estimated glomerular filtration rate at 64 mL/min/1.73 m^2. Further inquiry uncovered that the patient had undergone RFA treatment with Dexamethasone 8 mg injection into extra-articular lumbar facet joints 6 days earlier. The patient noticed worsening glucose level from CGM sensor but he did not increase the insulin dose due to poor appetite. The patient was diagnosed with DKA and was hospitalized in the intensive care unit. With treatments including hydration, insulin, and potassium replacement, DKA was resolved within 8 hours and renal function subsequently normalized. Additional investigations revealed no adrenal insufficiency. Insulin was increased for 2 weeks before returning to the normal dose. At the last follow-up of 6 months after DKA, his glycemic control was satisfactory at A1C $< 7.0\%$ and the patient was advised to follow “sick day rules" for diabetes self-management.

Conclusions: The possibility of adverse systemic effects of corticosteroid following extra-articular injection during RFA procedure to treat back pain should be considered among insulin-dependent patients. Spine surgeons and pain management specialists should be vigilant and consult the patient’s endocrinologist or primary physicians before performing the RFA procedure with steroid injection. Preemptive adjustments to insulin and education on sig day protocols are essential to prevent such adverse events.

Abstract citation ID: lvag096.1127

EP746 - ECE_2412 - Misdiagnosis of type 1 diabetes as gestational diabetes mellitus in pregnancy: a case report highlighting the importance of clinical vigilance

Zaiem Zarkasi[1,2], Aakansha Sinha[1] and Aye Aye Thant[1]

[1]Manchester, United Kingdom; [2]Wythenshawe Hospital, Diabetes and Endocrinology, Wythenshawe, United Kingdom

Background: Hyperglycaemia diagnosed during pregnancy is most commonly attributed to gestational diabetes mellitus (GDM), though a minority of cases represent previously unrecognized type 1 diabetes mellitus (T1DM). Distinguishing between

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

these conditions is critical for appropriate management and postpartum care. We present a case of a 20-year-old primigravida initially diagnosed with GDM whose clinical features prompted re-evaluation and subsequent diagnosis of T1DM.

Case Presentation: A 20-year-old primigravida presented to antenatal clinic at 34 + 3 weeks gestation with a prior diagnosis of GDM made at 24 weeks based on impaired fasting glucose of 5.9 mmol/L. Her HbA1c at booking was 31 mmol/mol. Despite dietary modifications and subsequent treatment with metformin modified release and insulin, her glycaemic control remained challenging. Clinical features atypical for GDM included relatively low body mass index (BMI) prior to and during pregnancy, family history of type 1 diabetes, and progressive insulin requirements. At 34+3 weeks, these features prompted testing for diabetes-related autoantibodies including glutamic acid decarboxylase (GAD), islet cell antibody (IA-2), and zinc transporter 8 (ZnT8) antibodies, along with C-peptide measurement. Results revealed negative anti-GAD and IA-2 antibodies but positive ZnT8 antibody with low C-peptide, confirming T1DM. She was transitioned to basal-bolus insulin regimen with continuous glucose monitoring. Shortly thereafter, she experienced recurrent hypoglycaemia with rapid reduction in insulin requirements, likely representing the honeymoon phase of T1DM combined with physiological decline in insulin resistance in late third trimester. Additional testing excluded adrenal insufficiency and thyroid dysfunction. Foetal growth remained appropriate (44th centile at 36+2 weeks) with normal liquor volume and Doppler studies. She underwent induction of labour at 38 weeks followed by caesarean section, delivering a healthy male infant. Postpartum, insulin doses were immediately reduced to approximately 50% of the late pregnancy requirement in line with guidance, reflecting the abrupt fall in placental insulin resistance. She was followed up in the young adult diabetes clinic, with structured education and ongoing dose titration to accommodate resumption of normal eating and reduce hypoglycaemia risk.

Conclusions: This case underscores the importance of maintaining clinical vigilance and challenging initial diagnoses when clinical features are inconsistent with typical GDM presentation. Key distinguishing features of T1DM in pregnancy include normal pre-pregnancy BMI, family history of autoimmune diabetes, and higher insulin requirements. Timely recognition through appropriate autoantibody testing enabled correct diagnosis and management, ensuring insulin continuation postpartum rather than cessation as would occur with GDM, thereby preventing potential diabetic ketoacidosis and optimizing long-term patient care.

Abstract citation ID: lvag096.1128

EP748 - ECE_2242 - Tailored prednisolone for Doege–Potter syndrome in a nonagenarian: a pattern-based approach

Hyewon Mun[1], Jang Won Son[2], Seongsu Lee[1], Sungrae Kim[1] and Soon-Jib Yoo[1]
[1]*The Catholic University of Korea Bucheon St Mary's Hospital, Bucheon-si, South Korea;* [2]*Bucheon-si, South Korea*

Background: Doege–Potter syndrome (DPS) is a rare paraneoplastic form of non-islet cell tumour hypoglycaemia (NICTH) mediated by autonomous secretion of "big" insulin-like growth factor-2 (IGF-2) from solitary fibrous tumours (SFTs). Although curative resection is definitive, it is often precluded by tumour extent or patient frailty in the extreme elderly. In such cases, glucocorticoids are commonly used; however, standard high-dose regimens are frequently poorly tolerated and optimal dosing remains unclear. We report a nonagenarian with DPS successfully managed using a tailored, relatively low-dose glucocorticoid strategy guided by glycaemic patterns and continuous glucose monitoring (CGM).

Case Description: A 90-year-old man was admitted for recurrent episodes of severe hypoglycaemia accompanied by impaired consciousness, fulfilling Whipple's triad. He had a history of type 2 diabetes but was not receiving any glucose-lowering medications. During a symptomatic episode (plasma glucose 48 mg/dL), insulin (<1.23 μIU/mL) and C-peptide (0.24 ng/mL) were suppressed, consistent with insulin-independent hypoglycaemia. Adrenal insufficiency was excluded by an adequate cortisol response to rapid ACTH stimulation. He had a biopsy-proven pulmonary SFT (12 × 18 cm) managed conservatively according to patient preference. Given the clinical context, NICTH was suspected, and a markedly elevated IGF-2/IGF-1 ratio (>29.67) strongly supported the diagnosis of DPS.

Management and Outcome: As surgical resection was not a viable option due to advanced age and comorbidities including cardiovascular disease, a medical strategy was initiated to mitigate IGF-2–mediated hypoglycaemia. To ensure sustained 24-hour glycaemic support, treatment was transitioned from intravenous hydrocortisone to oral prednisolone. Recognizing an initial nocturnal-dominant hypoglycaemia pattern, a twice-daily regimen was initiated with a higher evening dose, then titrated to a stable split-dose of 5 mg every 12 hours (10 mg/day). With structured education and consistent glucocorticoid coverage, the patient no longer required reactive, erratic carbohydrate intake. Following discharge, CGM-guided management confirmed the complete absence of hypoglycaemic episodes and improved glycaemic stability, with the coefficient of variation decreasing from 26.1% to 22.2%. Euglycaemia was maintained on this relatively low total dose without steroid-induced adverse effects.

Conclusions: In a nonagenarian with DPS who was not a surgical candidate, CGM-informed titration of a relatively low-dose, pattern-tailored split prednisolone regimen effectively prevented severe hypoglycaemia. This case suggests that aligning glucocorticoid timing with individual hypoglycaemia patterns may achieve a favourable therapeutic balance between efficacy and tolerability in frail elderly patients with NICTH.

Abstract citation ID: lvag096.1129

EP749 - ECE_1417 - Beyond glycemia: a global snapshot of multisystem comorbidities in children and adolescents with type 1 diabetes (2005-2025)

Ashraf Soliman[1], Nada Alaaraj[1], Fawziya Alyafei[1], Noor Hamed[1], Shayma Ahmed[1] and Nada Soliman[2]
[1]*Hamad Medical Center, Pediatric Endocrinology, DOHA, Qatar;* [2]*Alexandria Health Directorate, MOH, Public Health, Alexandria, Egypt*

Background: Type 1 diabetes (T1D) in children and adolescents is increasingly recognized as a multisystem disorder, with a

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

substantial burden of autoimmune, cardiometabolic, microvascular, and psychosocial comorbidities. While individual complications are well described, integrated registry-based summaries using harmonized definitions remain limited.

Objective: To summarize the point-prevalence of major comorbidities in children and adolescents with T1D over the past two decades using large international registries and validated population-based studies.

Methods: A structured synthesis of PubMed-indexed literature (≈2005-2025) was conducted, prioritizing international registries (SWEET, SEARCH for Diabetes in Youth, DPV, T1D Exchange, NPDA/ADDN) and systematic reviews. Harmonized thresholds were applied where possible: overweight/obesity (BMI ≥85th percentile, WHO/CDC), LDL-hypercholesterolemia (LDL-C ≥100 mg/dL), hypertension (blood pressure ≥95th percentile), and screen-detected microvascular or psychological outcomes. Estimates are reported as point-prevalence.

Results: Celiac disease is the most frequent autoimmune comorbidity, with a global prevalence of approximately 3-5%, ranging from ~2% in parts of Asia and the Middle East to ~7-8% in Australia and Europe. Thyroid autoimmunity is also common but variably reported. Approximately 30% of youth with T1D are overweight or obese. LDL-hypercholesterolemia affects 9-20%, and hypertension is present in 6-10%. Overall, 30-40% exhibit at least one major cardiovascular risk factor, with a smaller subset showing clustering of two or more factors. Microalbuminuria is detected in approximately 5-12%, increasing with age, diabetes duration, and glycemic exposure. Retinopathy remains uncommon in early childhood but increases in adolescents with longer disease duration. Peripheral or autonomic neuropathy is identified in roughly 7-12% by objective testing. Psychological morbidity is substantial, with 25-35% screening positive for depressive or anxiety symptoms. At diagnosis, diabetic ketoacidosis occurs in approximately 25-35%, with wide inter-country variability.

Conclusions: Children and adolescents with T1D carry a significant, multidimensional comorbidity burden. Consistent findings across international registries highlight the need for integrated screening and early preventive strategies extending beyond glycemic control.

Abstract citation ID: lvag096.1130

EP752 - ECE_2698 - Impact of basal insulin on glycaemic variability in pregnancy with focus on hypoglycaemia

Soumyabrata Roy Chaudhuri[1,2], Anirban Majumder[3], Poulomi Mukherjee[4] and Debmalya Sanyal[3]
[1]Woodlands Hospital, Kolkata, India; [2]KPC Medical College & Hospital, Endocrinology, Kolkata, India; [3]Kolkata, India; [4]Medical College Kolkata Masjid, Community Medicine, Kolkata, India

Background: Glycaemic variability is increasingly recognized as an important determinant of adverse pregnancy outcomes in women with gestational diabetes mellitus (GDM). Continuous glucose monitoring (CGM) allows detailed assessment of glucose patterns. Although GDM is primarily characterized by postprandial hyperglycaemia, many patients require basal insulin. NPH, detemir, and degludec are approved for use in pregnancy. While degludec has shown non-inferiority to detemir, there are no direct comparisons between NPH and degludec in pregnancy.

Objective: To compare glycaemic control using Time in Range (TIR), Time Below Range (TBR), and Time Above Range (TAR) in women with GDM treated with NPH versus degludec as basal insulin between 28 and 32 weeks of gestation, and to compare insulin dose requirements and nocturnal glycaemic patterns.

Methods: This was a prospective, investigator-initiated observational pilot study including 30 women with GDM. Participants received either NPH or degludec and underwent CGM using the Freestyle Libre Pro system for 14 days. All patients were prescribed a standardized diet of 30 kcal/kg/day and maintained diet diaries. CGM data, including 5-minute interval readings from midnight to 6 a.m., were analyzed. Patients unable to complete monitoring, those hospitalized during the study period, or those receiving antenatal steroids were excluded.

Results: The two groups were comparable at baseline, except that the NPH group required significantly higher total and bolus insulin doses at initiation of CGM. Patients treated with degludec had significantly higher TIR and lower TBR. By day 14, bolus insulin requirements were significantly lower in the degludec group, while basal and total daily insulin doses were similar between groups. Nocturnal hypoglycaemic events were significantly fewer in the degludec group, with more stable overnight glucose levels.

Conclusions: Insulin degludec as basal insulin during pregnancy is associated with better glycaemic stability and fewer hypoglycaemic events compared to NPH, suggesting that it may be a superior basal insulin option for managing GDM.

Abstract citation ID: lvag096.1131

EP754 - ECE_2485 - Risk of cardiovascular disease and death by LDL cholesterol level in elderly patients with diabetes

Sung Hoon Yu[1], Sang Mo Hong[1], Jung Hwan Park[1], Kye-Yeung Park[1] and Han Kyungdo[2]
[1]Hanyang University College of Medicine, Department of Internal Medicine, Seoul, South Korea; [2]Department of Statistics and Actuarial Science, Soongsil University, Seoul, South Korea

Background and Aims: Low-density lipoprotein cholesterol (LDL-C) is a well-established causal risk factor for cardiovascular disease (CVD). However, there is controversy regarding the relationship between LDL cholesterol and mortality in elderly diabetic patients. We evaluated the associations between LDL-C and cardiovascular disease or mortality in national cohort study.

Methods: We performed a retrospective observational cohort study of 249,903 older (≥65 years old) diabetes patients without CVD from 2009 to 2017 using the NHID. We divided the subjects by LDL-C category. Primary composite outcomes were stroke, myocardial infarction, and all-cause death. All outcomes were analyzed by Cox proportional hazards regression analysis while controlling for baseline covariates.

Results: During a median follow-up of 7.26 years, the incident rate of composite primary outcomes was 30.95 per 1,000 person-years. In Cox proportional hazard modeling, the risk of the primary outcome associated with a linear association with CVD. In multivariable Cox proportional hazard models with the LDL-C reference group (<85 mg/dL), the risk of primary composite outcomes was increased 1.067 times (95%CI: 1.035-1.100), 1.149 times (95%CI: 1.115-1.183) and 1.222 (95%CI: 1.185-1.261) with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

increasing LDL-C of respectively, ≥85 & <108 / ≥109 & <134, ≥134 (mg/dL) and had a linear association with LDL-C. And, these finding was consistent regardless of age, sex, smoking, chronic kidney disease, regular exercise, diabetic medications, insulin and statin. But mortality rate had inverse correlations.

Conclusions: In older patients with diabetes, increased LDL-C levels were associated with higher CVD risk, not with mortality rate.

Abstract citation ID: lvag096.1132

EP756 - ECE_3152 - Does type 2 diabetes mellitus increase the risk of major adverse cardiovascular or cerebrovascular events in long-term follow-up in patients who undergo carotid artery stenting?

Piotr Seweryniak[1], Jacek Staszewski[2], Bernadetta Kałuża[3], Jan Domański[3], Robert Gil[4], Paweł Krzesiński[1] and Edward Franek[3,5]

[1]Military Institute of Medicine, National Research Institute, Department of Cardiology, Warsaw, Poland; [2]Military Institute of Medicine, National Research Institute, Department of Neurology, Warsaw, Poland; [3]National Medical Institute of the Ministry of the Interior and Administration, Department of Internal Medicine, Endocrinology and Diabetology, Warsaw, Poland; [4]National Medical Institute of the Ministry of the Interior and Administration, Department of Cardiology, Warsaw, Poland; [5]Mossakowski Medical Research Centre Polish Academy of Sciences, Department of Human Epigenetics, Warsaw, Poland

Background: Percutaneous transluminal angioplasty with carotid artery stenting (CAS) is a revascularization method used in patients with significant carotid artery stenosis. This method is preferred in patients over 70 years old with a symptomatic stenosis of ≥50%-99% and in those with contraindications for surgery. Type 2 diabetes mellitus (T2DM), which is a risk factor of atherosclerosis and a predictor of subsequent adverse cardiovascular events, may also worsen the prognosis of CAS patients. There are no data on long-term, 5-year risk of major adverse cardiac and cerebrovascular events (MACCEs), including transient ischemic attack, major stroke, myocardial infarction, or death, after a CAS procedure.

Purpose: The purpose of the study was to answer the question if T2DM is a prognostic factor of MACCEs in patients who undergo CAS due to symptomatic carotid artery stenosis.

Methods: A total of 99 patients were included in this study; all patients underwent CAS due to symptomatic stenosis. Quantitative carotid angiography (QCA) was used to assess stenoses treated with angioplasty. To evaluate the impact of T2DM and other clinical variables on developing a MACCE over a 5-year follow-up was used Cox proportional hazards model.

Results: Patients without T2DM (n = 71, 71.72%) did not differ from those with T2DM (n = 28, 28.28%) in terms of stenosis diameter (2.13 ± 1.05 vs 1.96 ± 1.01 [mm], $P = .52$), stenosis area (4.44 ± 4.36 vs 3.82 ± 3.41 [mm^2], $P = .55$), stenosis length (17.12 ± 7.84 vs 14.12 ± 5.66 [mm], $P = .08$), percent diameter stenosis (65.65 ± 12.75 vs 66.51 ± 13.99, $P = .55$), percent area stenosis (86.74 ± 8.42 vs 86.89 ± 10.53, $P = .61$) or stenotic flow reserve (2.43 ± 1.29 vs 2.19 ± 1.37, $P = .29$), laminar flow resistance (3.39 ± 12.69 vs 2.83 ± 6.31, $P = .47$), turbulent flow resistance (4.29 ± 18.13 vs 3.43 ± 8.26, $P = .37$). Cox proportional hazards model revealed that only age increases the risk of MACCEs (HR 1.07 95% CI 1.003-1.14, $P = .003$), with no such effect exhibited by other assessed variables, namely, T2DM (1.26, 0.38-4.14, $P = .7$), hypertension (1.49, 0.49-4.61, $P = .48$), smoking (0.43, 0.14-1.33, $P = .14$), dyslipidemia (1.36, 0.47-3.90, $P = .57$), male sex (0.16, 0.02-1.23, $P = .07$), percent diameter stenosis (1.07, 0.89-1.28, $P = .49$), and percent area stenosis (0.92, 0.71-1.19, $P = .53$).

Conclusion(s): Comorbid T2DM in the evaluated group showed no significant effect on long-term prognosis of developing MACCEs in patients who underwent CAS. Therefore, comorbid T2DM is not a contraindication to this procedure.

Abstract citation ID: lvag096.1133

EP757 - ECE_3751 - Baseline phenotypic and biochemical characteristics of lipodystrophy patients at the time of diagnosis- data from a Romanian cohort

Adelina Badici[1], Iuliana Gherlan[1,2,3], Simona Galoiu[1,2], Lidia Radomir[2], Elena Braha[2], Ramona Dobre[1,2], Iulia Florentina Burcea[1,2], Iulia Grigore[2] and Catalina Poiana[1,2]

[1]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [2]"C.I. Parhon" National Institute of Endocrinology, Bucharest, Romania; [3]C.I. Parhon National Institute of Endocrinology, București, Romania

Background: Lipodystrophy syndromes are rare adipose tissue disorders, underdiagnosed despite genetic advances.

Objective: To describe the clinical, genetic and metabolic characteristics of a lipodistrophy cohort diagnosed in a Romanian tertiary endocrinology centre.

Methods: Nineteen suspected cases were identified through database search; eight were excluded due to unmet clinical and biochemical diagnostic criteria. Genetic testing was available in 4/11 reported patients. The clinical and metabolic profile, hepatic steatosis and renal involvement were analysed in 11 patients.

Results: 10/11 patients had familial partial lipodystrophy syndromes (FPLD): 6 cases - FPLD type 2, 2 FPLD type 4, 1 FPLD type 3, 1 FPLD type 6; 1 patient (POLD1/MDPL) had progeroid generalised lipodystrophy. The heterozygous LMNA c.1444C>T (p.Arg482Trp) pathogenic variant was identified in the proband of a five-member FPLD2 family and in one unrelated patient; affected relatives were diagnosed clinically. In the FPLD4 family (father–daughter), only the proband underwent genetic testing and carried the heterozygous PLIN1 c.1210-1del splice-site variant, likely pathogenic, while the father fulfilled clinical criteria. The FPLD3-compatible case harboured a heterozygous PPARG c.220 +3A>G splice-region variant classified as VUS, but fulfilled the clinical and metabolic criteria. The patient MDPL carried a heterozygous POLD1 c.1812_1814del (p.Ser605del) pathogenic variant.

Nine patients were female, 2 male. Mean age at diagnosis was 27.6 years (range 4.92-46), including 3 pediatric cases.

FPLD2 showed marked limb lipoatrophy with fat accumulation in the trunk, face and neck, muscular hypertrophy and prominent veins; acanthosis, café-au-lait lesions and hyperandrogenism occurred, with one presenting a single central maxillary incisor

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

despite normal cerebral imaging. FPLD4 displayed similar lower-limb-predominant fat loss, the FPLD3-compatible case milder limb involvement with facial hirsutism, while FPLD6 presented lower-limb fat deficiency with acanthosis and café-au-lait spots. The MDPL case showed severe progeroid features with generalised lipoatrophy, deafness, hyperpigmentation, telangiectasias, and testicular insufficiency.

Comorbidities included neuropathy, thyroid disease, PCOS, hypertension, retinopathy, and craniofacial dysmorphism.

At diagnosis, 7/11 patients recieved antidiabetic treatment (2 insulin, 5 oral). Mean glucose was 124 mg/dL (range 76-297), mean HbA1c 6.87% (4.8-11.4). In non-insulin-treated patients, mean insulinemia was 75.12 µIU/mL (5.86-339.1), and mean HOMA-IR was 12.97 (1.21-75.4). 5/11 patients were receiving lipid-lowering therapy. Mean triglycerides were 183.7 mg/dL (86-406), total cholesterol 200 (135-247), HDL 42.58 (26.8-86), LDL 130.2(61–203) and VLDL 34.8 (20.8-52.8). Hepatic steatosis was present in 9 patients; 5 had proteinuria.

Conclusions: This cohort demonstrates severe metabolic burden and phenotypic heterogeneity, emphasising the need for early diagnosis and comprehensive screening.

Abstract citation ID: lvag096.1134

EP758 - ECE_1236 - The prevalence of vitamin B12-deficiency in people living with type-1 diabetes and its associated factors: a dual-center cross-sectional study in Malaysia

Abdullah Shamshir Abd Mokti[1], Nurhanis Syazni Roslan[2], Carolina Shalini Singayar[3], Alia Nasriana Nasuruddin[1] and Raja Nurazni Raja Azwan[4]

[1]Hospital Tengku Ampuan Afzan, Kuantan, Malaysia; [2]University of Science, Malaysia, Kubang Kerian, Malaysia; [3]Hospital Selayang, Selayang, Malaysia; [4]Institut Endokrin, Hospital Putrajaya, Putrajaya, Malaysia

Background: Previous cross-sectional studies have reported association of vitamin B12-deficiency in patients with Type 1 Diabetes Mellitus(T1DM). A study in South India where vegetarianism is commonly practiced found that among 90 patients with T1DM, 45.5% had vitamin B12 deficiency.Currently there is paucity of data for B12-deficiency among T1DM patients in diverse-ethnic Malaysia.

Objectives: To determine the prevalence of vitamin B12 deficiency in patients with T1DM and its associated factors.

Method: This was a cross-sectional study which involved 104 patients at two endocrinology centers. Vitamin B12 level and anthropometric data were measured after an interview session on demographics, dietary and lifestyle, medical history and medications.

Results: 104 T1DM patients were screened and one excluded due to incomplete data. 15 out of 103 patients (14.5%) had vitamin B12-deficiency. The mean age was 29.50 years-old while BMI was 22.32 kg/m^2. Study population was female (64.1%), Malay (70.9%), non-smoker (88.3%) and non-alcoholic (96.1%). The mean duration of diagnosis was 10.59 years, with HbA1c of 10.3%, fasting blood glucose of 10.05 mmol/l. There was no significant difference between the variables except for body mass index (BMI). Patients with B12-deficiency were found to have a lower BMI (18.64 kg/m^2) as compared to patients with normal vitamin B12 (22.95 kg/m^2). In univariate analysis, we found that only BMI significantly predicted B12-deficiency with crude odds ratio: 0.493. Multivariable logistic regression analysis also found that BMI predicted B12-deficiency with adjusted OR: 0.485. With every one-unit increase in BMI, Type 1 diabetes patients were 51.5% less likely to have low vitamin B12 level

Conclusions: Results of our study shows that the prevalence of B12 deficiency among T1DM is 14.5% and with significant association with low BMI. These findings merits screening for B12-deficiency among T1DM patients with low BMI and further research is needed to explore the reasons.

Abstract citation ID: lvag096.1135

EP759 - ECE_1882 - Thyroid hormone sensitivity index in patients with type 2 diabetes mellitus and depression

Ahmed Abdelhameed Osman[1], Eman Zaky Ahmed Abdelaziz Azzam[1], Ahmed Awad Gowaid[2] and Elshimaa Ganeb[1]

[1]Endocrinology unit , Department of internal medicine, Alexandria Faculty of Medicine, Alexandria, Egypt; [2]Faculty of Medicine, Alexandria University, Department of Neurology and Psychiatry, Alexandria, Egypt

Introduction: Diabetes mellitus (DM) is a chronic debilitating disease that affects a huge number of people, disturbing their quality of life. It is a widespread disease. Depression in patients with diabetes is often unrecognized and untreated leading to poor adherence to diabetes self-care plans and resulting in potentially negative health consequences including a higher risk for diabetic complications, functional impairment, and increased healthcare expenditure. Several thyroid abnormalities have been associated with mood disorders particularly depression. However, the vast majority of patients with depression do not have biochemical evidence of thyroid dysfunction. When thyroid abnormalities exist, they consist mainly of elevated T4 levels, low T3, elevated rT3, blunted TSH response to TRH, positive antithyroid antibodies, and elevated cerebrospinal fluid (CSF) TRH concentrations. A state of brain hypothyroidism in the setting of systemic euthyroidism (10) has been suggested. This could result from a defect in the thyroid hormone-receptor, (11) or in the thyroid hormone transport and uptake into the brain and neuronal cells.

Aim: The aim of the study was to measure thyroid hormone sensitivity indices in euthyroid diabetic individuals and to correlate the sensitivity index with the presence and the degree of depression.

Methods: This study was carried out on 70 euthyroid, diabetic patients visiting endocrinology or psychiatry outpatient clinic in Alexandria main university hospital as well as matching control.

Results: The results of the present study showed that according to DSM-5 criteria, more than half of the participants were not depressed (57.1%), while 42.9% were diagnosed with depression. Based on the Hamilton Depression Rating Scale, the majority of depressed patients had mild depression (56.7%), followed by moderate depression (33.3%), whereas severe depression was observed in a smaller proportion of cases (10.0%). No significant difference between depressed and non depressed patients regarding , thyroid hormone levels and thyroid indices, on the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

other hand it was found also there was no significant association between degree of depression, thyroid indices and throid hormone levels in patients with depression. The results of this study showed that there was no significant difference between depressed and non depressed patients regarding glycemic levels, on the other hand it was found also there was no significant association between degree of depression and HbA1C, FBG and PPBG.

Conclusions: No significant association between incidence of depression and its degree with both thyroid function test and glycemic parameters though larger studies are required to confirm the results.

Abstract citation ID: lvag096.1136

EP762 - ECE_3163 - Variant of uncertain significance in IRS 2 gene in patient with diabetes mellitus—case report

Milica Jakovljevic, Sandra Stankovic, Vesna Cvetkovic, Milica Ignjatović and Tatjana Stankovic
University Clinical Centre Nis, Pediatric Clinic, Endocrinology, Nis, Serbia

Introduction: A variant of uncertain significance (VUS) is a genetic variant identified during genetic testing but whose significance to clinical presentation is not known. Insulin receptor substrate 2 (IRS2) is important for pancreatic beta-cell survival and function, reduction of peripheral insulin sensitivity and insulin signaling.

Case Report: A17 year old female patient was referred to endocrinologist because of high fasting blood glucose levels measuring up to 19 mmol/L. Her symptoms were present for two weeks and included fatigue, mouth dryness and polyuria. Prenatal and early childhood medical history were unremarkable. Her father was diagnosed with type 2 diabetes mellitus (T2DM) at the age of 40 years. Initial laboratory findings were: HbA1c 12.5%, C peptides 1.6 ng/ml. She was started with insulin therapy with oral antidiabetics (Metformin). After 3 months, HbA1c was 6.4%. She was positive for GAD (Glutamic Acid Decarboxylase) autoantibodies 26.3 U/ml, while ICA (Islet Cell Antibodies), IA-2 (Insulinoma-Associated Antigen 2) and ZnT8 (Zinc Transporter 8) autoantibodies were negative. After one year, HbA1c was 7.5% and C peptides levels were 2.6 ng/ml. Autoantibodies were negative. Since it is possible to find positive autoantibodies in 1% of MODY patients, MODY was suspected and clinical genome sequencing was requested. The result was undetermined, since one heterozygous VUS with a 67.5% probability of pathogenicity leading to diabetes mellitus was detected in the IRS2 gene. The genetic heterozygous missense variant c.4012G>A, p.(Glu1338Lys) in the IRS2 gene replaces the amino acid glutamic acid with the amino acid lysine at position 1338 of the polypeptide chain. According to the American College of Medical Genetics and Genomics classification criteria, the detected variant in the IRS2 gene is classified as VUS – class 3. This variant was not found in either the gnomAD genomes or the gnomAD exomes (PM2_Supporting) and is predicted to result in alternative splicing and loss of function in IRS2. This disease is inherited in an autosomal dominant manner and can lead to T2DM. A father and younger sister are also tested and pending results. After three years since first being diagnosed the patient is on insulin therapy with C peptide 1.6ng/ml and HbA1c 6.3%.

Conclusions: A variant of uncertain significance (VUS) can possibly lead to disease development and remains important both for carrier monitoring and for further genetic counseling. A VUS found in IRS 2 gene can lead to development of diabetes mellitus.

Abstract citation ID: lvag096.1137

EP768 - ECE_3429 - Use of tirzepatide: metabolic, functional and psychological outcomes

Khash Nikookam, Conor Bentley, Gavita Kaur, Usman Shah, Raj Tanday and Anna Hawkins
Barking, Havering and Redbridge University Hospitals NHS Trust, King George Hospital, Department of Endocrinology, London, United Kingdom

Tirzepatide is an effective treatment for weight management; however, data describing its impact beyond weight loss, on physical function, psychological wellbeing and cardiometabolic risk, remain limited. This service evaluation examined outcomes associated with tirzepatide delivered within a multidisciplinary weight management service.

A single-arm pre–post service evaluation was conducted in adults (≥18 years) receiving tirzepatide for at least three months within a multidisciplinary weight management service. Anthropometric measures, blood pressure, physical function (30-second sit-to-stand test and maximal bilateral handgrip strength), psychological wellbeing (PHQ-9 and GAD-7), dietary quality (PRIME Diet Quality Score), and cardiometabolic and nutritional biomarkers were assessed at baseline and follow-up. Data are reported as mean ± standard deviation. Paired analyses were performed with pairwise exclusion of missing data, using paired t-tests or Wilcoxon signed-rank tests as appropriate. Statistical significance was set at $p<0.05$ (two-tailed). Blood biomarker outcomes were analysed descriptively due to limited statistical power.

Eleven participants were included in the final analyses. Body mass index (BMI) decreased significantly following tirzepatide use, from 41.5 ± 5.9 kg/m^2 at baseline to 37.2 ± 4.8 kg/m^2 at follow-up ($P < .01$), accompanied by improvements in central adiposity, including a significant reduction in waist-to-height ratio and neck circumference (mean reduction 3.0 ± 1.5 cm, $P = .003$). Systolic blood pressure decreased from 137 ± 11 mmHg at baseline to 126 ± 12 mmHg at follow-up (mean change −10.9 mmHg, $P = .027$). No significant changes were observed in diastolic blood pressure or waist-to-hip ratio. Physical function improved significantly. Maximal handgrip strength increased from 32.1 ± 7.4 kg at baseline to 41.2 ± 10.8 kg at follow-up ($P < .01$). Lower-limb function also improved, with participants completing more repetitions on the 30-second sit-to-stand test (16.2 ± 4.3 vs 17.8 ± 3.9 repetitions; mean increase 1.6 repetitions, $P < .01$). Psychological wellbeing improved over the evaluation period. Mean GAD-7 scores decreased from 10.5 ± 6.4 to 3.8 ± 3.9 ($P < .01$), with parallel reductions observed in PHQ-9 scores. Dietary quality improved significantly, with PRIME Diet Quality Scores increasing from 20.4 ± 4.3 to 26.0 ± 3.1 ($P < .01$). Changes in cardiometabolic and nutritional biomarkers, including HbA1c, lipid profile, ferritin, folate and vitamin D, were directionally favourable but underpowered for formal statistical inference.**Conclusions:** within a multidisciplinary weight management service, tirzepatide use was associated with significant

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

improvements in BMI, physical function, and psychological well-being. These findings reinforce the value of an MDT approach integrating pharmacological and lifestyle interventions to improve care and outcomes.

Abstract citation ID: lvag096.1138

EP771 - ECE_1494 - When imaging misleads: diagnostic approach of hypoglycemia in non-diabetic adults

Adina-Ioana Onofrei[1], Dana Tilici[1,2], Daniela Greere[1,3], Ruxandra Costinescu[1], Ana-Maria Arnautu[1], Mirona Dinca[1,2], Beatrice Grecu[1], Claudia Nacea[1] and Diana Paun[1,2,3]
[1]Emergency University Hospital of Bucharest, Endocrinology, Bucharest, Romania; [2]Doctoral School of Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [3]Bucharest, Romania

Introduction: Nowadays, the diagnostic protocol for seemingly healthy non-diabetic adults presenting with hypoglycemic disorders mainly relies on the biochemical and imaging diagnosis of an insulinoma. Based on cases evaluated in our clinic, we propose a more biochemically oriented diagnostic approach with greater consideration for insulin autoimmune syndrome. After confirming endogenous hyperinsulinemic hypoglycemia and excluding medication-related and factitious hypoglycemia, the main etiologies include insulinoma, insulinomatosis, microinsulinomas, proinsulinoma, noninsulinoma pancreatogenous hypoglycemia and insulin autoimmune hypoglycemia.

Case Descriptions: Between July 2024 and October 2025, six patients were evaluated in our clinic for symptomatic hypoglycemia. One patient had a confirmed insulinoma, and one had suspected insulinoma with discordant imaging findings and is scheduled for GLP-1R PET/CT. Two patients were diagnosed with Hirata's disease and had conflicting imaging results, and in two cases endocrinologic causes of hypoglycemia were excluded.

Notably, the first patient with Hirata's disease experienced hypoglycemic episodes occurring randomly during both daytime and nighttime; ^{99}?Tc-tektrotyd SPECT-CT findings were suggestive of insulinoma, while MRI revealed an atypical pancreatic lesion that could not definitively exclude this diagnosis. In the second patient with Hirata's disease, symptoms occurred in both fasting and postprandial states; MRI findings suggested insulinoma, whereas endoscopic ultrasound showed no pancreatic lesions, and exploratory laparotomy failed to identify a pancreatic tumor.

The patient awaiting GLP-1R PET/CT previously underwent pancreatic MRI, which demonstrated two lesions suggestive of benign vascular lesions, along with additional pancreatic microlesions with calcified/fibrous components. However, both subsequent and prior MRIs were normal. ^{99}?Tc-tektrotyd SPECT/CT showed findings suggestive of insulinoma, and endoscopic ultrasound identified a hypoechoic lesion. Despite this, abdominal CT findings were normal, and exploratory laparotomy failed to retrieve any pancreatic tumor. The patient has a history of positive autoantibodies (rheumatoid factor, anti-SS-A, anti-Ro-52), with negative insulin and insulin-receptor antibodies. Her symptoms became severe during pregnancy but had been present for more than one year prior.

Conclusions: Although insulinoma remains the most likely diagnosis once endogenous hyperinsulinemic hypoglycemia is proven, imaging studies are often inconsistent, may yield false-positive results in real-world clinical settings and some have limited availability. As a result, attention should be directed toward excluding Hirata's disease and type B insulin resistance, despite their rarity.

We propose the following laboratory measurements at the end of the selected provocative test: insulin, polyethylene glycol precipitation, proinsulin, C-peptide, β-hydroxybutyrate, anti-insulin antibodies, anti-insulin receptor antibodies, IGF-2 and IGF-1. In addition, basal measurements of cortisol, ACTH and TSH are recommended.

Abstract citation ID: lvag096.1139

EP774 - ECE_2965 - When lipids turn lethal: acute pancreatitis from severe hypertriglyceridemia in diabetic pregnancy

Shebina Liz Mathews, Ann Francis, Kabeer Katariya and Cornelius Fernandez James
Pilgrim Hospital , Boston (United Lincolnshire Hospitals NHS Trust), Diabetes and Endocrinology, Boston, United Kingdom

Introduction: Hypertriglyceridemia-induced acute pancreatitis (HTG-AP) in pregnancy is rare and carries a significant morbidity/mortality risk to mother and fetus. This case highlights the importance of prompt diagnosis and a multidisciplinary approach.

Case Presentation: We present a 32-year-old lady (G7/P6+1) with history of gestational diabetes mellitus (GDM) in three previous pregnancies. Follow up HbA1c levels were not done after GDM pregnancies. She was non-compliant with the antenatal plans, with repeated non-attendance in the clinics. She engaged with the endocrine team only once during the current pregnancy. She stated she had been testing regularly and had glucose readings in target (pre-breakfast <5.3 and one-hour post-meal <7.8) while on diet control.

Within 4 weeks, at 35+5 weeks, she presented with abdominal/back pain with nausea. The initial blood sample could not be processed (lipemic serum). However, with point-of-care results (CBG 17.8, Ketone 2.1, pH 7.4, bicarbonate 24.5), VRIII was initiated, which helped clear the lipemia. Later blood tests revealed: eGFR >90 mL/min, amylase 259 U/L, CRP 278 mg/L, Total cholesterol 18.3 mmol/L, Triglyceride 39.5 mmol/L, HDL-cholesterol 0.5 mmol/L, Non-HDL-cholesterol 17.9 mmol/LHbA1c 88 mmol/mol, TSH 2.4 mU/L, FT4 11.6 pmol/L.

Ultrasound Abdomen: normal. Our diagnosis was: Suboptimal glycaemic control secondary to non-compliance and likely missed T2DM, severe hypertriglyceridemia and HTG-AP. Plan was to continue VRIII until triglycerides normalized, HDU bed, surgical review, emergency LSCS and CT-abdomen. CT showed focal pancreatic necrosis. She was discharged on insulin for diabetes and hypertriglyceridemia. Though lipid and diabetes clinic appointments were given, the patient repeatedly missed them.

Discussion: Hyperestrogenism and insulin resistance result in a 2-3-fold rise in triglycerides by the third trimester (gestational hypertriglyceridemia). This will be amplified in those with GDM or T2DM in pregnancy. HTG-AP usually occurs when triglycerides exceed 10 mmol/L, around six times the ULN. Diagnostic delay may occur because of assay interference from lipemic serum and the difficulty in doing a CT abdomen. Therefore, early lipid testing is essential whenever clinical suspicion persists despite lack of or

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

modest amylase/lipase results. Insulin promotes lipoprotein lipase synthesis and decreases triglyceride hydrolysis.

Conclusions: HTG-AP is a rare complication of late pregnancy, especially in those with uncontrolled diabetes mellitus. Early lipid testing is vital when suspicion persists, as pancreatic enzymes may rise only modestly in lipemic samples. Multidisciplinary management and postpartum follow-up play an integral role in optimizing maternal and neonatal outcomes in these cases.

Abstract citation ID: lvag096.1140

EP777 - ECE_2524 - Trends in overweight and obesity among children and adolescents in Uzbekistan

Marlen Ibragimov[1,2], Zulaykho Shamansurova[1] and Zulaykho Shamansurova[1]
[1]*Central Asian University, AKFA Medline University Hospital, Tashkent, Uzbekistan;* [2]*Central Asian University in Tashkent - CAU, Medical School, Medical School, Toshkent*

Background: Overweight and obesity among children and adolescents are a growing global concern. The 5-19 age group is especially important, as habits formed during these years can impact health into adulthood. Comparing national trends to global patterns helps identify vulnerable groups and contributing factors.

Aim: To assess trends in overweight (including obesity) among 5-19-year-olds in Uzbekistan between 2010 and 2022, compare with worldwide estimates, and discuss in relation to food environment changes.

Methods: An observational analysis used publicly available data on overweight (including obesity) among children and adolescents aged 5-19 years from the NCD Risk Factor Collaboration, which was chosen for its comprehensive, standardized methodology. Prevalence was calculated as the mean of three age groups (5-9, 10-14, and 15-19 years), stratified by sex. Dietary energy supply data came from FAOSTAT Food Balance Sheets, a widely used resource for international food and nutrition statistics. The analysis focused on 2010 as the baseline and 2018-2022 as the recent interval.

Results: In Uzbekistan, the prevalence of overweight (including obesity) among children and adolescents aged 5-19 years increased from approximately 15% in 2010 to 17% in 2018 and further to 19% in 2022. Worldwide estimates were consistently higher, increasing from approximately 23% to 26% over the study period.

Across all age groups, overweight prevalence was higher among boys than girls in both Uzbekistan and globally. In 2022, boys aged 5-9 years had the highest prevalence, reaching about 25% in Uzbekistan and 30% worldwide, about 1.3-1.4 times higher than girls of the same age. The lowest prevalence was among girls aged 15-19 years: 13% in Uzbekistan and 25% worldwide.

During the same period, dietary energy supply in Uzbekistan rose from 2938.5 kcal/capita/day in 2010 to 3277.0 kcal/capita/day in 2022, about 11.5% higher than in 2010 and 1.1 times the global average in 2022 (2983.5 kcal/capita/day). The increase in overweight prevalence, particularly among children aged 5-9 years, coincided with the greater availability of energy-dense foods and the expansion of international fast-food outlets in Uzbekistan since around 2018.

Conclusions: From 2010 to 2022, overweight prevalence among 5-19-year-olds in Uzbekistan increased, mostly among boys aged 5-9 years. This trend occurred alongside greater availability of energy-dense foods and the expansion of fast-food franchises since 2018. While causality is uncertain, the findings highlight the need for early prevention strategies targeting childhood nutrition and weight gain.

Abstract citation ID: lvag096.1141

EP779 - ECE_1940 - Compromised bioavailability of calcium and vitamin D following Roux-en-Y gastric bypass

Snezana Polovina[1], Mirjana Sumarac-Dumanovic[1,2], Dusan Micic[3], Danka Jeremic[4], Dusan Zivanovic[4], Nevena Radić[4], Djurdjina Lovovic[4], Danilo Lazarevski[1] and Pavle Gregoric[3]
[1]*University Clinical Center of Serbia, Belgrade, Clinic for Endocrinology, Diabetes and Diseases of Metabolism, Belgrade, Serbia;* [2]*Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Center of Serbia, Belgrade, Serbia;* [3]*University Clinical Center of Serbia, Belgrade, Emergency Center, Clinic for Emergency Surgery, Belgrade, Serbia;* [4]*University Clinical Center of Serbia, Belgrade, Clinic for Endocrinology, Diabetes and Diseases of Metabolism, Belgrade, Serbia*

Introduction: Patients with obesity undergoing Roux-en-Y gastric bypass (RYGB) are at risk for impaired calcium and vitamin D absorption. Reduced gastric acidity and the bypass of the primary sites of mineral absorption can trigger secondary hyperparathyroidism, characterized by elevated parathyroid hormone (PTH) secretion.

Methods: We evaluated serum calcium, 25-hydroxyvitamin D [25(OH)D], and PTH levels in 100 patients (33 males, 67 females; mean age 50.8 ± 11.6 years) at baseline, two years, and five years post-RYGB. Following European guidelines for bariatric surgery, patients received 1250 mg of calcium carbonate and 400 IU of vitamin D daily for the first two months. From the third month onward, supplementation was adjusted to 600 mg of calcium citrate and 2000 IU of vitamin D.

Results: Mean BMI decreased significantly from 43 ± 8.2 kg/m^2 at baseline to 29.2 ± 4.4 kg/m^2 at two years, followed by a slight increase to 31.9 ± 5.6 kg/m^2 at five years ($P < .001$). Serum calcium remained stable across all time points ($P = .83$ and .86). Baseline vitamin D levels were insufficient (52.79 ± 24.60 ng/mL) and showed a downward trend over time (46.5 ± 14.82 ng/mL at two years; 43.7 ± 22.5 ng/mL at five years; $P = .43$ and .08, respectively). Notably, mean PTH rose significantly from a baseline of 56.28 ± 25.42 pg/mL to 71.06 ± 35.4 pg/mL at two years ($P < .05$) and remained elevated at 73.05 ± 28.9 pg/mL at five years ($P < .05$).

Conclusions: These findings underscore the necessity of optimizing vitamin D status prior to surgery. Furthermore, the significant rise in PTH despite supplementation suggests that patient compliance or the adequacy of standard mineral regimens may decline after the first two postoperative years, necessitating long-term biochemical monitoring.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1142

EP783 - ECE_1325 - Glycemic control in pediatric type 1 diabetes mellitus: a meta-analysis comparing insulin glargine with neutral protamine hagedorn (NPH) insulin regimens

Ignace Claire Gamallo[1], Caridad Santos[2] and Marichu Mabulac[1]
[1]Philippine Childrens Medical Center, Pediatric Endocrinology, Quezon City, Philippines; [2]Philippine Childrens Medical Center, Section of Pediatric Endocrinology, Quezon City, Philippines

Objectives: This study aimed to compare glycemic control and complications of multiple daily insulin injection (MDII) regimen using insulin glargine with NPH as basal insulin among children with T1DM.

Materials and Methods: This is a meta-analysis of RCTs comparing glycemic control and complications of MDII regimen using insulin glargine with NPH as basal insulin among children with T1DM. A systematic search using electronic databases (MEDLib via PubMed, Google Scholar, Cochrane Library and Clinical Trials Registry) was performed using the following keywords, such as "type 1 diabetes", "insulin glargine", "intensive insulin regimen", "children", "HBA1C", "effectiveness" "RCT" "DKA". Health Research and Development Information Network (HERDIN) for applicable local articles was also done. Odds ratio was computed and Forest plot was generated to interpret the outcomes of interest.

Results: A total of 509 children aged 1 to 18 years from 5 RCTs were included in this meta-analysis. Participants had a disease duration ranging from 5 months to 1 year at the time of diagnosis. Average reduction in HbA1c is significantly better in the insulin glargine, with a mean difference of −0.30 (95% CI = −0.34 to −0.26, $P <$ .00001) compared to the NPH group with low heterogeneity ($I^2 =$ 45%) . Furthermore, this study revealed lower hypoglycemia events (OR = 0.98, 95%CI =0.62 to 1.58, $P =$.95), and nocturnal hypoglycemia (OR =0.61, 95%CI =0.37 to 1, $P =$.05) in glargine. DKA was the most common TEAE reported in both groups and one study reported that hospitalization due to DKA was significantly more frequent in the NPH group. Microvascular complications were not assessed in any of the 5 studies.

Conclusions: Results of this meta-analysis showed that insulin glargine is superior to the NPH insulin in achieving glycemic control in T1DM children on MDII. Likewise, fewer hypoglycemia events and hospitalization due to DKA were reported with glargine versus NPH. With better achievement of glycemic targets, superiority in preventing complications is implied favoring the glargine group.

Keywords insulin glargine, neutral protamine hagedorn (NPH), glycemic control

Abstract citation ID: lvag096.1143

EP784 - ECE_1864 - Demographic characteristics and glycemic profile of patients with type 1 diabetes using ypsomed HCL system at the university hospital of the Canary Islands

Selena Rodriguez Fernandez, Kevin David Díaz Gorrín, Javier Panizo Fra, Paula Pérez, Óliver Quintero Rodríguez, Ana Paola Leon Ocando, MacArena Sánchez-Gallego Alonso, Itziar Aznar Ondoño and Juan Ignacio Márquez De La Rosa
Hospital Universitario de Canarias, Endocrinology and Nutrition, San Cristóbal de La Laguna, Spain

Introduction: According to the American Diabetes Association, automated insulin delivery systems are the preferred method to improve glycemic outcomes and reduce hypoglycemia in Type 1 Diabetes Mellitus (T1DM). Currently, it is suggested that these devices should be offered at diagnosis or shortly after disease onset. In recent years, devices such as the Ypsomed AHCL system have shown increased use in clinical settings due to their integration with continuous glucose monitoring systems (CGMS) and technological improvements.

Objective: To study the demographic characteristics and glycemic profile of patients using the Ypsomed AHCL system at the University Hospital of the Canary Islands.

Materials and Methods: An observational, retrospective study including all patients using the Ypsomed AHCL system at the University Hospital of the Canary Islands in 2025.

Results: A sample of 20 patients was analyzed, 55% female (median age 47 years). The median duration of T1DM was 20 years.

Among patients using the Ypsomed AHCL system, 70% used the FSL3 sensor and 30% used Dexcom G6. Forty percent had prior insulin pump therapy (37.5% Tandem, 12.5% Medtronic, 37.5% Insight, and 12.5% Accu-Chek). Regarding initiation date, most patients started AHCL therapy in 2025.

Before AHCL initiation, patients had a median HbA1c of 6.80% and a mean of 7.05%. After AHCL implementation, median HbA1c decreased to 6.18% and mean to 6.29% (reduction of 0.59%, statistically significant). The GMI was 6.68%.

Glycemic Metrics:

Parameter	Pre-AHCL	Post-AHCL
TIR (median)	70%	78%
TAR (median)	25%	20%
TUR (median)	2%	2%
TIR (mean)	60%	78%
TAR (mean)	30%	20%
TUR (mean)	3%	2%

Statistical analysis (Wilcoxon):

- TIR: +12.65%*
- TAR: −9.8%*
- TUR: −1%

*Statistically significant results.

Only one patient experienced diabetic ketoacidosis after initiation of the Ypsomed AHCL system, and no patients reported severe hypoglycemia. Metadiabetic complications were present in 42.85% of patients (7 with retinopathy, 5 with nephropathy, 1 with neuropathy, 1 with stroke, and 1 with peripheral arterial disease). Regarding lipid control, mean LDL cholesterol was 89.45 mg/dL, and 60% of patients were above their LDL target.

Conclusions: The use of the Ypsomed AHCL system was associated with improved glycemic control (HbA1c reduction and increased TIR) without a significant increase in acute complications. These findings support the utility of this system as an effective tool in the management of T1DM. However, due

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

to the small sample size, larger studies are required to assess long-term outcomes and compare its role against other available technologies.

Abstract citation ID: lvag096.1144

EP785 - ECE_2584 - Transformative impact of continuous glucose monitoring on glycemic control through lifestyle modification in a patient with non-insulin treated type 2 diabetes

Shafik Mansour[1,2] and Khaled Baagar[1]
[1]Doha, Qatar; [2]Hamad Medical Corporation, Qatar Metabolic Institute, Doha, Qatar

Current clinical practice guidelines have endorsed Continuous glucose monitoring (CGM) primarily for individuals using multiple daily insulin injections or insulin pumps.However, emerging data suggest that CGM may also benefit patients with type 2 diabetes (T2DM) who are not treated with insulin.

A 56-year-old male with a 17-year history of T2DM was referred from the primary care center to the diabetes clinic for suboptimal glycemic control with an HbA1c of 7.6%. His medical history was significant for obesity (weight 122 Kg, BMI 45.65 kg/m^2), ex-smoker, peripheral neuropathy, and peripheral arterial disease (PAD) with bilateral lower-limb intermittent claudication, limiting his walking distance to approximately 300 meters. His medications included a combination of sitagliptin 50 mg/Metformin XR 1000 mg twice daily, aspirin, and high-intensity statin (atorvastatin 80 mg). He was not performing self-monitoring of blood glucose, primarily due to inconvenience and the finger-prick discomfort.

The patient was motivated, and while he is waiting to get his appointment with us in the diabetes clinic, he initiated FreeStyle Libre CGM by himself without making any changes in his pharmacological therapy. Within the first month of the CGM use, he began to make notable lifestyle changes. He voluntarily reduced his intake of bread and rice, incorporated more vegetables, switched to small and frequent meals, and eliminated sugary foods. He could see in real-time the impact of different foods on his glucose levels, and he changed food choices guided by the CGM. Also, he began walking as tolerated, as his mobility was affected by his PAD.

His HbA1c improved significantly from 7.6% to 5.9%. Data from the 14-day CGM ambulatory glucose profile revealed an average glucose of 128 mg/dL, a glucose management indicator of 6.4%, time-in-range (TIR) of 93%, and time below range (TBR) of 1%. Glucose variability was 23.1%.

The patient described CGM as “transformative,” noting that seeing real-time changes in glucose helped him understand the immediate impact of different food choices and exercise. This feedback loop motivated sustained changes in behavior and eliminated the need for medication intensification to achieve glycemic control.**Conclusions:** Rapid and sustained improvement in glycemic metrics, achieved solely through behavioral changes prompted by CGM feedback, reinforces its role as more than a monitoring tool. The high TIR and low variability achieved in a short duration suggest that early CGM adoption in motivated patients may minimize the need for pharmacological intensification.

Abstract citation ID: lvag096.1145

EP787 - ECE_3110 - Aflibercept as an effective alternative in anti-VEGF–resistant diabetic macular edema

Rekik Mona[1], Yoldez Ben Jemaa[1], Imene Kaibi[1], Kmar Maaloul[1], Nabila Rekik Majdoub[2] and Trigui Amira[1]
[1]Habib Bourguiba Hospital, Sfax, Tunisia; [2]Hôpital Universitaire Hédi Chaker, Sfax, Tunisia

Introduction: Diabetic macular edema (DME) remains a leading cause of visual impairment in patients with long-standing diabetes mellitus, and resistance to anti–vascular endothelial growth factor (anti-VEGF) therapy represents a significant therapeutic challenge.

Case Report: We report the case of a 63-year-old patient with a 33-year history of insulin-dependent diabetes mellitus. The patient was pseudophakic in both eyes and presented with bilateral diabetic macular edema. Despite intensive treatment with intravitreal bevacizumab, totaling 14 injections, the response was inadequate, with persistently reduced visual acuity measuring 2/10 in the right eye and 1/10 in the left eye.

Given the refractory nature of the macular edema, a therapeutic switch to intravitreal aflibercept was undertaken. The patient demonstrated a rapid and marked anatomical and functional response from after 5 aflibercept injections in each eye. Best-corrected visual acuity improved dramatically to 7/10 in both eyes and a significant reduction of macular edema on optical coherence tomography was achieved. This visual gain was accompanied by sustained anatomical stabilization, with no recurrence of macular edema observed during a follow-up period of one year.

Conclusions: This case illustrates the potential superiority of aflibercept in selected cases of bevacizumab-resistant diabetic macular edema, likely related to its broader spectrum of action and higher binding affinity for VEGF. Switching anti-VEGF agents should be considered in patients with suboptimal response to initial therapy, as it may lead to significant visual recovery and long-term disease control.

Abstract citation ID: lvag096.1146

EP788 - ECE_3157 - Efficacy and safety of semaglutide injection in type 2 diabetes mellitus: a subgroup analysis of patients with mild renal impairment

Dipesh Sonawane[1], Unnikrishnan Gopalkrishnan[2], Ameya Joshi[3], Richa Giri[4], Shalin Shah[5], Jitendra Shukla[6], Sanjiv Maheshswari[7], M.C. Rekha[8], Manish Singh[9], Aditya Bari[10], Niranjan Pathak[11], Akash Shah[12], Shweta Bhandari[13], Ambanna Gowda[14], C. Ambrish[15], Pravin Supe[16], Bharat Das[17], Prabhat Sharma[18], Mehul Virani[19], Prakash Kurmi[20], Gayatri Ghanekar[21], Mani Dasari[22], Bansidhar Sahoo[23], Sanjay Jangid[24], Manoj Srivastava[25], Prakash Shende[26], Sandesh Patil[27], Avinash Kumbhar[28], Shrikant Deshpande[29], C. Madhusudhan[30], Nitesh Patel[31], Apurva Shetty[1], Dipak Patil[1], Pravin Ghadge[1] and Suyog Mehta[1]
[1]Sun Pharma Laboratories Limited, Mumbai, India; [2]Chellaram Diabetes Institute, Pune, India; [3]Bhaktivedanta Hospital and Research, Thane, India; [4]GSVM Medical College, Kanpur, India; [5]Ratan Multi-speciality Hospital, Ahmedabad, India; [6]Motilal Nehru

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Medical College, Prayagraj, India; [7]Jawahar Lal Nehru Medical College, Ajmer, India; [8]Mandya Institute of Medical Science, Mandya, India; [9]Maya Hospital and Maternity Centre, Kanpur, India; [10]Pulse Multispeciality Hospital, Pune, India; [11]Ojas Multispeciality Hospital, Pune, India; [12]Health 1 Super Speciality Hospital, Ahmedabad, India; [13]Vincare Hospital, Bathinda, India; [14]Citizen Hospital, Bangalore, India; [15]Medstar Speciality Hospital, Bangalore, India; [16]Supe Heart & Diabetes Hospital & Research Centre, Nashik, India; [17]Sparsh Hospitals and Critical Care Private, Bhubaneshwar, India; [18]Maharaja Agrasen Superspeciality Hospital, Jaipur, India; [19]Global hospital, Surat, India; [20]Shivam Hospital, Ahmedabad, India; [21]Asian Institute of Medical sciences, Dombivali, India; [22]Rajalakshmi Hospital & Research Center, Bangalore, India; [23]Kanungo Institute of Diabetes Specialities, Bhubaneshwar, India; [24]Hi-Tech Medical College & Hospital, Bangalore, India; [25]Om Surgical Center and Maternity Home, Varanasi, India; [26]Lokmanya Medical Research Center, Pune, India; [27]Shree Siddhivinayak Maternity & Nursing Home, Nashik, India; [28]Aster Aadhar Hospital, Kolhapur, India; [29]Ashirwad Hospital and Research Centre, Ulhasnagar, India; [30]NRR Hospital, Bangaluru, India; [31]Samarpan Hospital, Ahmedabad, India

Objectives: To evaluate the efficacy and safety of Synthetic Semaglutide Injection manufactured by Sun Pharma (Test arm) with Ozempic® Injection (Reference arm) in Indian patients with type 2 diabetes mellitus (T2DM) with mild renal impairment (eGFR 60 to <90 mL/min/1.73 m^2).

Materials and Methods: This was a phase III, multicentre, randomized, open-label, active controlled study. Total 314 adults (18-65 years) with T2DM (HbA1c: 7.0-10.5%) on diet/exercise uncontrolled with stable metformin dose (≥1500 mg or maximum tolerated dose) for ≥12 weeks were enrolled. Eligible patients were randomized in a 1:1 ratio and received Test product (manufactured by Sun Pharma) or Reference product, subcutaneous injections in a weekly dose of 0.25 mg to 2 mg for 24 weeks. [CTRI Registration number: CTRI/2025/02/080592].

Results: This subgroup analysis included total 109 patients (Test arm [n=55] and Reference arm[n=54]) with mild renal impairment (eGFR 60 to <90 mL/min/1.73 m^2). HbA1c reduction (± SD) from baseline to Week 24 was comparable to comparator in this subgroup: $-1.95 \pm 0.72\%$ vs $-1.77 \pm 0.88\%$ ($P = .3920$). Significant reduction from baseline HbA1c was observed in both test arm and reference arm at Week 24. Significant reductions in post-prandial and fasting blood glucose levels at Week 24 were seen in both the study arms and the changes were comparable in this subgroup. Proportion of patients achieving HbA1c <7.0% from baseline to Week 24 were comparable between the Test arm and reference arm 42 (76.4%) vs 42 (77.8%) ($P = .7191$). One patient experienced hypoglycaemia. None of the patients required rescue medication. The incidence of treatment-emergent adverse events (TEAEs) was similar in both arms (Test arm = 66.2% and Reference arm = 69.5%). Most common TEAEs were gastrointestinal events (Diarrhoea, Nausea, Vomiting). Study medications were well tolerated.

Conclusions: Semaglutide injection (Test Product) demonstrated comparable glycaemic control to Reference product in T2DM patients uncontrolled on metformin monotherapy with mild renal impairment.

Abstract citation ID: lvag096.1147

EP793 - ECE_2553 - Association of statin therapy with cognitive function and muscle mass in postmenopausal women

Sara Anić[1,2], Anja Akmadžić[1,3], Dunja Šojat[4,5], Ivan Lekić[6,7,8], Dunja Degmečić[9,10] and Tatjana Bačun[11,12,13]

[1]Faculty of Medicine Osijek, Osijek, Croatia; [2]Health Center of Osijek-Baranja County, Osijek, Croatia; [3]Clinical Hospital Center Osijek, Osijek, Croatia; [4]Faculty of Medicine Osijek, Department of Family medicine, Osijek, Croatia; [5]Health Center of Osijek-Baranja County, Family medicine, Osijek, Croatia; [6]Faculty of Medicine Osijek, Department of Internal medicine, Osijek, Croatia; [7]Health Center Zagreb Centar, Department of Internal medicine, Zagreb, Croatia; [8]Zagreb, Croatia; [9]Faculty of Medicine Osijek, Department of Psychiatry, Osijek, Croatia; [10]Clinical Hospital Center Osijek, Department of Psychiatry, Osijek, Croatia; [11]Faculty of Medicine Osijek, Department of Internal Medicine, Osijek, Croatia; [12]Faculty of Dental Medicine and Health, Department of Clinical medicine, Osijek, Croatia; [13]Clinical Hospital Center Osijek, Internal medicine clinic, Department of Endocrinology, Osijek, Croatia

Objective: The aim of this study was to investigate the effects of statin therapy on cognitive function and muscle mass percentage in postmenopausal women, as well as to examine associations based on age, duration of menopause, statin dose and lipid levels.

Study Design: This was a prospective study.

Participants and Methods: The study included 71 postmenopausal women aged 45 to 70, patients in primary care clinics of the Osijek-Baranja County Health Center. Anamnestic data were collected, and blood samples were analyzed for lipid profile values. Cognitive function was assessed using the MMSE test, while body composition was measured by bioimpedance. Statin dose was determined according to cardiovascular risk.

Results: The study was conducted on 71 participants with a median age of 60 years (range 50-70). High cardiovascular risk was noted in 33 (46.5%) participants, and moderate risk in 15 (21.1%). A greater number of participants treated with atorvastatin achieved target LDL cholesterol values compared to those treated with rosuvastatin (Fisher's exact test, $P = 0.03$). No significant change was observed in the percentage of muscle mass between initial and final measurements (Wilcoxon test, $P = .46$). A statistically significant improvement in cognitive function according to the MMSE test was recorded at the final control (Wilcoxon test, $P < .001$). Age was negatively correlated with muscle mass percentage (Spearman's Rho = −0.264, $P < .05$). Duration of menopause, statin dose, and total cholesterol showed no significant association with cognitive tests or muscle mass percentage ($P > .05$).

Conclusions: Statin therapy is associated with improvements in cognitive function in postmenopausal women, with no significant impact on muscle mass percentage. There are significant differences in achieving target LDL cholesterol values between statins, with atorvastatin being more effective.

Keywords atorvastatin, cognitive function, lipid profile, muscle mass, postmenopause, rosuvastatin, statins

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1148

EP794 - ECE_2566 - Correlation of statin therapy with body composition and inflammation in postmenopausal women

Anja Akmadžić[1,2], Sara Anić[1,3], Dunja Šojat[4,5], Ivan Lekić[6,7,8], Aleksandar Kibel[9,10] and Tatjana Bačun[11,12,13]
[1]*Faculty of Medicine Osijek, Osijek, Croatia;* [2]*Clinical Hospital Center Osijek, Osijek, Croatia;* [3]*Health Center of Osijek-Baranja County, Osijek, Croatia;* [4]*Faculty of Medicine Osijek, Department of Family medicine, Osijek, Croatia;* [5]*Health Center of Osijek-Baranja County, Family medicine, Osijek, Croatia;* [6]*Faculty of Medicine Osijek, Department of Internal medicine, Osijek, Croatia;* [7]*Health Center Zagreb Centar, Department of Internal medicine, Zagreb, Croatia;* [8]*Zagreb, Croatia;* [9]*Faculty of Medicine Osijek, Department of Physiology and Immunology, Osijek, Croatia;* [10]*Scientific Unit for Medical Research, Priora, International Medical Center, Čepin, Čepin, Croatia;* [11]*Faculty of Medicine Osijek, Department of Internal Medicine, Osijek, Croatia;* [12]*Faculty of Dental Medicine and Health, Department of Clinical medicine, Osijek, Croatia;* [13]*Clinical Hospital Center Osijek, Internal medicine clinic, Department of Endocrinology, Osijek, Croatia*

Objective: The aim of this study was to investigate the effect of statin therapy on inflammation and body composition in postmenopausal women, as well as to examine associations based on age, lipid levels, and statin type.

Study Design: This was a prospective study.

Participants and Methods: The study included female participants aged 45 to 70 who were patients in primary care clinics of the Osijek-Baranja County Health Center. Relevant anamnestic data were collected, and blood samples were analyzed for inflammatory markers and lipid profiles. Body composition was assessed using bioelectrical impedance analysis, while the statin dose was determined based on cardiovascular risk using the SCORE table.

Results: The study included 67 women, divided into two groups based on the type of statin used. Among those who achieved target lipid levels, 20 women (57%) received atorvastatin. A statistically significant difference between the final and initial measurements was observed in body weight ($P = .001$, Wilcoxon test), body fat percentage ($P = .008$), BMI ($P = .02$), and hip circumference ($P = .001$). Positive correlations were found between triglycerides and WHR (Rho = 0.508), age and visceral fat (Rho = .334), while a negative correlation was found between total cholesterol and NLR (Rho = −0.360).

Conclusions: Although a statistically significant difference was found regarding the effect of statins on body composition, the changes were minimal and not clinically relevant. No effect was demonstrated on RDW or NLR. However, certain associations between the examined parameters were observed.

Keywords body composition, hydroxymethylglutaryl-CoA reductase inhibitors, inflammation, lipids, postmenopause

Abstract citation ID: lvag096.1149

EP796 - ECE_3585 - LMNA-related familial partial lipodystrophy type 2 complicated by severe dilated cardiomyopathy: a fatal case report and experience with metreleptin therapy

Alina Alzhaxina, Assel Issabayeva, Kristina Baikadamova, Marzhan Rakhimzhanova and Aigul Durmanova
University Medical Center, Astana, Kazakhstan

Introduction: Familial partial lipodystrophy type 2 (FPLD2) is a rare autosomal dominant disorder caused by pathogenic *LMNA* variants. It is characterized by selective loss of subcutaneous fat, insulin resistance, dyslipidemia and hepatic steatosis. Cardiac involvement, including conduction defects and dilated cardiomyopathy (DCM), can be life-threatening.

Clinical Case: A 19-year-old girl presented with progressive cardiac dysfunction and a known diagnosis of *LMNA*-related FPLD2, confirmed at age 17 by a heterozygous pathogenic *LMNA* c.1488 +1G>A variant (HGMD CS094346; PMIDs 20848652, 34240052). She had acanthosis nigricans, hirsutism, muscular extremities, and loss of subcutaneous fat from the face, abdomen, and limbs (BMI 14.06 kg/m^2). At 16 years, she underwent ovarian cystectomy, and then she suffered an ischemic stroke affecting the left anterior and middle cerebral arteries. At 17 years, she developed hypertension and arrhythmias with alternating tachycardia and bradycardia. Echocardiography showed a dilated left ventricle, LVEF 14.3%, and mild pulmonary hypertension. NT-proBNP 276 pg/mL (N<125) indicated early cardiac damage, and an ICD was implanted.

Metreleptin (0.4 mL s.c. daily) was started at the age of 18 years. Labs before therapy: fasting glucose 80.2 mg/dL (74-106), insulin 218 µIU/mL, HbA1c 6.2%, C-peptide 3.54 ng/mL (1.1-4.4); TG 1.56 mmol/L (0.44-1.4), LDL 0.67 mmol/L (0.91-1.91), low HDL; ALT 114.9 U/L, AST 93.9 U/L (N<35), indicating hepatic steatosis. Imaging revealed moderate hepatomegaly with diffuse hepatic steatosis and parenchymal changes in the pancreas and kidneys. After one year of therapy, metabolic parameters normalized: fasting glucose 98.1 mg/dL, HbA1c 5.7%, ALT 32.5 U/L, AST 39 U/L, TG 61.2 mg/dL, LDL 62.1 mg/dL. However, NT-proBNP increased to 4363 pg/mL (N<125), consistent with worsening heart failure. Despite therapy, she died approximately one year after treatment initiation due to complicated pneumonia and terminal cardiac failure.

Discussion: This case demonstrates a clear dissociation in LMNA-related FPLD2. Metreleptin reversed hepatic steatosis and normalized metabolic markers but failed to stop cardiomyopathy progression. This confirms that cardiac decline is driven by primary structural defects in the nuclear envelope rather than metabolic toxicity. The early stroke and multi-organ involvement underscore that LMNA-mutations are aggressive, systemic laminopathies. Ultimately, metabolic improvement provides a false sense of security; heart failure in these patients progresses independently of glycemic or lipid control, necessitating early and rigorous cardiac intervention.

Conclusions: Metreleptin improved hepatic and metabolic markers but failed to halt cardiac deterioration in *LMNA*-related FPLD2. Early recognition of cardiac manifestations and multidisciplinary follow-up are crucial to improving outcomes.

Abstract citation ID: lvag096.1150

EP798 - ECE_3902 - Severe nephrotoxicity after short-term multiple dietary supplements use in a type 2 old diabetic female - a case report

Daniel-Tudor Cosma[1,2]
[1]*Horezu City Hospital, Diabetes, Nutrition and Metabolic diseases Outpatient Clinic, Horezu, Romania;* [2]*Gerontohealthcare Clinic,*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Diabetes, Nutrition and Metabolic diseases Outpatient Clinic, Ramnicu-Valcea, Romania

Dietary supplements are widely used for their perceived health benefits with minimal regulation. However, they have been associated with various toxicities including kidney disease.

A 76-year-old female with type 2 diabetes mellitus (DM) controlled through diet and complicated by peripheral neuropathy, under treatment with benfotiamine + B6 + B12, presented in the emergency department of a county hospital with generalized myalgia, oligoanuria and high blood pressure (BP $\leq$ 230 mmHg) after using 5 different dietary supplements by the same company for 3 weeks. Lab exams revealed creatinine = 11 mg/dl, hyperkalemia, metabolic acidosis, GPT = 600 U/L and CK = 25000 U/L, for which hemodialysis on a central venous catheter in right femoral vein was initiated. After 20 days the patient developed thrombosis on right common femoral vein for which intravenous anticoagulation was started. 2 months after initial presentation, she was referred to a University Nephrology Department for hemodialysis cessation after partial recovery of renal function. Besides twice positive ANA screen ratio, mild anemia, creatinine = 1.99 mg/dl, leukocyturia, asymptomatic bacteriuria and albumin/creatinine ratio of 30mg/g, all the other investigations were within normal limits. The patient was reevaluated in the University Nephrology Department after one month and then every 6 months, the last creatinine being 0.95mg/dl with an estimated glomerular filtration rate of 58 ml/min/1.73 m^2.

While dietary supplements are advertised and consumed with the promise of significant health benefits without side effects, evidence suggests minimal benefits and potential harm to human health. This case illustrates the severe renal injury requiring hemodialysis, long hospitalizations and intensive follow-ups after a short period of using multiple dietary supplements. Despite significant improvement in renal function, the patient remained with stage G3aA1 chronic kidney disease.

Abstract citation ID: lvag096.1151

EP803 - ECE_2536 - Microalbuminuria as a marker of endothelial dysfunction in patients with Type 2 diabetes

Gabrijela Malesevic[1,2], Snjezana Popovic Pejicic[3] and Valentina Soldat Stankovic[1]

[1]Faculty of Medicine, University of Banja Luka, Republic of Srpska, Banja Luka, Bosnia and Herzegovina; [2]University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina; [3]Academy of Sciences and Arts of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina

Introduction: Type 2 diabetes (T2D) is associated with an increased risk of cardiovascular diseases (CVD), with endothelial dysfunction representing an early event in the development of atherosclerosis. Microalbuminuria (MAU), defined as the presence of small amounts of protein in the urine (30-300 mg/24 h), is increasingly recognized as a potential marker of systemic vascular damage and early endothelial dysfunction in patients with T2D.

Objective: The aim of this study was to investigate the role of MAU as a marker of endothelial dysfunction in patients with T2D and its significance in the early identification of patients at increased cardiovascular risk.

Methods: The study included 60 patients with T2D without symptoms or signs of cardiovascular disease (CVD). Based on 24-hour urinary albumin levels measured by immunoturbidimetry, patients were divided into two groups: with and without microalbuminuria. All participants underwent exercise stress testing.

Results: In the group of patients with confirmed CVD, 90% had MAU, while in the group without CVD, microalbuminuria was present in only 18% of participants ($P < .01$). Combinations of MAU with HbA1c values and duration of diabetes, analyzed through three binary logistic regression models, were significant predictors of CVD confirmed by exercise testing, with an increase in these parameters associated with a higher probability of a positive stress test ($P < .01$).

Conclusions: MAU in patients with T2D can serve as a valuable biomarker of endothelial dysfunction and a predictor of cardiovascular risk. Its timely detection allows for early intervention and planning of preventive strategies to reduce cardiovascular complications.

Keywords microalbuminuria, endothelial dysfunction, type 2 diabetes

Abstract citation ID: lvag096.1152

EP805 - ECE_1039 - Gut microbiome imbalance in obesity and type 2 diabetes

Hassan Heshmati[1] and Gloria Lin[2]

[1]Endocrinology Metabolism Consulting, LLC, Hassan Heshmati and Valerie Shaw Endocrine Research, Anthem, AZ, United States; [2]CG Discovery, Inc., San Diego, CA, United States

Introduction: Gut microbiome is a complex community of microorganisms living in the digestive tract (mainly in the colon). It contains up to 100 trillion microbes, mainly bacteria (several thousand species), but also fungi, protozoa, archaea, and viruses. The taxonomic ranking of gut microbiome includes species, genera, families, orders, classes, and phyla. The predominant phyla (90%) are Firmicutes and Bacteroidetes. Gut microbiome influences human physiology and susceptibility to diseases. There are important interactions between gut microbiome and metabolic and endocrine parameters. This review presents an update on gut microbiome imbalance (dysbiosis) in obesity and type 2 diabetes.

Methods: A systematic search of literature was conducted for the period 2018 to 2025 using the search terms gut microbiome, dysbiosis, obesity, type 2 diabetes, and management.

Results: Over the entire lifespan, multiple factors impact gut microbiome composition. These factors include diet, age, pregnancy, diseases, and medications. Dysbiosis is observed in several disorders including obesity and type 2 diabetes. In obesity, dysbiosis is represented by a decrease in gene richness, a higher abundance of Firmicutes phylum, a lower abundance of Bacteroidetes phylum, an increase in Firmicutes to Bacteroidetes phyla ratio, and a lower abundance of Verrucomicrobia phylum (with lower presence of *Akkermansia* genus). Obesity is a major contributor to the development of type 2 diabetes. Approximately 80% of people with type 2 diabetes have obesity and their gut microbiome profile is relatively similar to people with obesity. Gut microbiome can be modulated to change the host metabolism and manage obesity and type 2 diabetes. Potential corrective interventions include diet

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(eg, hypocaloric, low-fat, high-protein, and high-fiber diets), prebiotics (eg, oligofructose-enriched inulin), probiotics (eg, fermented milk containing *Lactobacillus gasseri* species), synbiotics (combination of prebiotics and probiotics), paraprobiotics (inactivated probiotics), postbiotics (beneficial metabolites of microorganisms), gut microbiota transplantation (addition of healthy stool), and bariatric surgery (eg, Roux-en-Y gastric bypass). The targeted gut microbiome should have high gene richness, low abundance of Firmicutes phylum, high abundance of Bacteroidetes phylum, low Firmicutes to Bacteroidetes phyla ratio (<1.0), and high abundance of Verrucomicrobia phylum (with high presence of *Akkermansia* genus).

Conclusions: Dysbiosis is associated with obesity and type 2 diabetes. Relevant gut microbiome changes include decreased gene richness, increased Firmicutes to Bacteroidetes phyla ratio, and low presence of *Akkermansia* genus. The correction of dysbiosis with different tools (eg, diet, prebiotics, probiotics, and gut microbiota transplantation) can help to manage obesity and type 2 diabetes.

Abstract citation ID: lvag096.1153

EP811 - ECE_2213 - From pathways to precision: integrating clinical and genetic data for early Risk Stratification in Type 2 Diabetes

Siobhan O' Sullivan[1], Cynthia Al Hageh[2] and Pierre Zalloua[2]
[1]*College of Medicine and Health Sciences, Abu Dhabi, United Arab Emirates;* [2]*Public Health & Epidemiology, Khalifa University, Abu Dhabi, United Arab Emirates*

Type 2 diabetes (T2D) is a multifactorial endocrine disorder driven by insulin resistance, β-cell dysfunction, mitochondrial stress, and chronic low-grade inflammation. This heterogeneity underlies substantial variability in disease onset, progression, and therapeutic response, complicating early prediction, patient stratification, and treatment optimisation. Early genetic association studies identified variants in genes central to insulin action and β-cell function, including *IRS1*, *TCF7L2*, and *CDKAL1*, and linked genetic susceptibility to clinical traits such as dyslipidaemia, hypertension, and age. While informative, these single-layer analyses offered limited insight into the dynamic, tissue-specific processes that drive disease progression.

A systems biology framework addresses these limitations by integrating molecular and clinical information to characterise the endocrine networks underlying T2D. Longitudinal and single-cell studies reveal progressive impairment of functional β-cell subpopulations, tissue-specific stress responses, and disrupted inter-organ communication between pancreas, liver, adipose tissue, skeletal muscle, and gut. These coordinated disturbances evolve over time, reflecting the transition from compensated insulin resistance to β-cell failure and highlighting the temporal nature of endocrine dysfunction in T2D.

Pathway-level molecular signatures highlight endocrine-relevant disruptions in insulin signalling, nutrient sensing, mitochondrial function, and stress-response pathways that are not captured by conventional clinical measures alone. These insights support stratification of individuals into biologically distinct T2D endophenotypes with differing glycaemic trajectories, cardiometabolic risk profiles, and responses to therapy, moving beyond glucose-centric classification toward a pathophysiology-informed understanding of disease heterogeneity.

In our recent work, we analysed population-based data to examine the contribution of genetic susceptibility, alongside established clinical risk factors, improving early identification of individuals at risk of T2D. Integrative models incorporating clinical features and T2D-associated genetic variants enabled more refined stratification of endocrine risk, particularly in younger individuals, for whom early intervention may yield the greatest long-term benefit. These endocrine risk patterns were consistent across independent population-based cohorts, supporting their generalisability.

By embedding endocrine-relevant signatures within network-based models derived from population and molecular data, this systems-level approach provides a foundation for patient-specific simulations of disease trajectories and treatment response. Such models offer a conceptual basis for the future development of digital representations of endocrine disease progression, enabling exploration of how variation in insulin sensitivity, β-cell reserve, or inflammatory burden may shape disease evolution over time. Rather than replacing clinical judgement, these frameworks aim to support physiology-informed risk stratification and clinical decision-making.

Abstract citation ID: lvag096.1154

EP814 - ECE_3766 - Semaglutide therapy in a woman with polycystic ovary syndrome and type 1 diabetes: a clinical case

Andriana Vereshchynska and Alina Urbanovych
State non-profit enterprise " Danylo Halytsky Lviv National Medical University", Lviv, Ukraine

Background: The prevalence of polycystic ovary syndrome (PCOS) among women with type 1 diabetes mellitus (T1DM) ranges from 24% to 40% regardless of body mass index, while obesity increases this risk nearly fourfold. The coexistence of T1DM, obesity and PCOS represents a complex clinical phenotype associated with a high metabolic and reproductive risk.

The pathophysiology of PCOS in T1DM is thought to be related to long-term exposure to high doses of exogenous insulin leading to systemic hyperinsulinaemia, as well as to chronic hyperglycaemia-induced impairment of peripheral insulin sensitivity. These mechanisms contribute to hyperandrogenism, disordered folliculogenesis and chronic anovulation.

In this context, glucagon-like peptide-1 receptor agonists (GLP-1), particularly semaglutide, represent a promising therapeutic strategy due to their effects on body weight reduction, insulin sensitivity improvement and potential reproductive benefits. However, clinical data in women with combined PCOS and T1DM remain scarce.

Aim: To evaluate the metabolic and reproductive effects of semaglutide in a woman with PCOS and type 1 diabetes.

Case Presentation: A 30-year-old woman with T1DM for 14 years, treated with basal–bolus insulin therapy, presented with obesity, oligomenorrhoea and hirsutism. Body mass index was 34.1 kg/m^2. Menstrual cycles occurred up to three times per year. Ultrasound examination revealed polycystic ovarian morphology.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Hormonal assessment showed elevated AMH (9.4 ng/mL), total testosterone (2.14 ng/mL) and LH/FSH ratio (3.2). Metabolic evaluation demonstrated poor glycaemic control (HbA1c 10.7%, TIR 22%), hypertriglyceridaemia (2.01 mmol/L) and elevated LDL-cholesterol (3.39 mmol/L).

After insulin therapy optimisation, GLP-1 RA treatment was initiated with liraglutide titrated to 3.0 mg daily for 12 weeks, followed by a switch to semaglutide with gradual titration to 1.0 mg once weekly for 18 weeks.

Results: After 30 weeks of treatment: body weight decreased by 15 kg (13% from baseline); total daily insulin requirement decreased by 21%; glycaemic control improved (HbA1c 7.1%, TIR 76%); triglyceridaemia (1.44 mmol/L) and LDL-cholesterol (2.13 mmol/L)$ menstrual frequency increased to one cycle every 45 days; clinical signs of hyperandrogenism diminished; AMH decreased to 6.01 ng/mL; both GLP-1 receptor agonists were well tolerated, with only mild and transient gastrointestinal adverse events.

Discussion and Conclusions: This clinical case demonstrates that semaglutide therapy in a woman with PCOS and type 1 diabetes was associated with significant improvements in metabolic control, body weight, insulin requirements and reproductive parameters. These findings support the potential role of GLP-1 receptor agonists as a pathogenetically oriented and personalised therapeutic option in this complex patient population.

Abstract citation ID: lvag096.1155

EP815 - ECE_1444 - The deceptive calm of normoglycaemia: fatal euglycaemic diabetic ketoacidosis in a case of septic cholangitis

Thaalitha Naidu Suranthiran Naidu[1], Anis Syakirah Azizol Rahman[1] and Wan Daizyreena Wan Jaafar[1,2]
[1]*Medical Department, Hospital Kemaman, Terengganu, Malaysia;* [2]*Radiology Department, Hospital Kemaman, Terengganu, Malaysia*

Euglycaemic diabetic ketoacidosis (EDKA) defined by profound ketoacidosis in the absence of marked hyperglycaemia, is an uncommon but potentially fatal metabolic emergency. It poses a diagnostic challenge and is often precipitated by infection, medications, or pregnancy.

We encountered a 67-year-old Malay woman with longstanding type 2 diabetes mellitus complicated by prior Ray's amputation of the right third to fifth toes, hypertension, bronchial asthma, and dyslipidaemia, who presented to our district hospital with a two-day history of diffuse abdominal pain and anorexia following ingestion of restaurant food. Her symptoms were accompanied by recurrent emesis and watery diarrhoea, resulting in omission of medications, including metformin, DPP-4 inhibitor, subcutaneous insulin, aspirin, statin, and antihypertensives. On admission, she appeared lethargic and septic, with hypotension (100/50 mmHg), tachycardia (97 bpm), and normothermia (36.8 °C). Capillary glucose was 4.4 mmol/L. Examination demonstrated preserved peripheral perfusion, reduced bibasal air entry, and absence of abdominal guarding or peripheral oedema.

Laboratory evaluation revealed severe high–anion-gap metabolic acidosis (pH 7.09, bicarbonate 9.8 mmol/L) with elevated serum ketones (5 mmol/L) and lactate (8.4 mmol/L). Additional abnormalities included hypalbuminaemia (32 g/L), acute kidney injury (creatinine 641 µmol/L, urea 17.2 mmol/L), anaemia (Hb 8.3 g/dL), leukocytosis (12×10^9/L), markedly elevated serum amylase (1701 U/L), with preserved hepatic function. C-reactive protein rose from 14.27 mg/L to 112.01 mg/L within 48 hours; HbA1c was 8.6%. Chest radiography showed cardiomegaly with blunted costophrenic angles, and computed tomography illustrated dilated extrahepatic biliary ducts consistent with acute cholangitis, concurrent pulmonary infiltrates but intact pancreatic parenchyma.

She was electively intubated for impending haemodynamic collapse and severe metabolic derangement. Management encompassed aggressive intravenous fluid resuscitation, vasopressor support, continuous insulin infusion with electrolyte correction, broad-spectrum antibiotics (ceftriaxone and metronidazole), and sustained low-efficiency dialysis for anuric renal failure. Blood cultures isolated *Cronobacter* species susceptible to ampicillin–sulbactam and gentamicin, prompting targeted antimicrobial therapy. Her ICU course was complicated by myocardial injury, evidenced by anterolateral ST-segment depressions and markedly elevated troponin (9.8 ng/mL). Despite transient stabilisation and extubation, she deteriorated with refractory septic shock culminating in pulseless electrical activity. Resuscitative efforts were unsuccessful, and endotracheal cultures subsequently isolated multidrug-resistant Acinetobacter baumannii.

This case underscores the imperative for heightened clinical vigilance for EDKA in diabetic patients presenting with severe infection and metabolic acidosis, even with normoglycaemia. Prompt recognition and aggressive management are critical, yet outcomes remain poor in fulminant sepsis complicated by multidrug-resistant pathogens.

Abstract citation ID: lvag096.1156

EP816 - ECE_2033 - The clinical value of routine C-peptide measurement in diabetes diagnosis and management: a two-case series

Teona Kandinashvili[1,2]
[1]*National Center of Surgery, New Life Clinic, Tbilisi, Georgia;* [2]*New Life Clinic, Ambulatory, Tbilisi, Georgia*

Case 1**Background:** Accurate classification of diabetes type at diagnosis is crucial for appropriate management. Clinical presentation alone may be misleading, particularly in young patients with weight loss and ketosis. C-peptide measurement can provide valuable information regarding endogenous insulin secretion and guide therapeutic decisions.

Case Presentation: A 33-year-old man with no prior chronic illnesses presented with unintentional weight loss of 10 kg over two weeks, polydipsia, and polyuria. His body mass index was 19.5 kg/m^2. Laboratory evaluation revealed fasting plasma glucose of 309 mg/dL, HbA1c of 11.6%, and urinary ketones of 5 mmol/L. Given the clinical picture suggestive of type 1 diabetes, further evaluation was performed to determine diabetes type.

Results: Fasting C-peptide level was 2.49 ng/mL (reference range 0.73-4.37), indicating preserved endogenous insulin secretion. Based on this finding, insulin therapy was deferred, and treatment

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

with oral hypoglycemic agents (DPP-4 inhibitor combined with metformin), along with dietary modification and increased physical activity, was initiated.

Outcome: At a 2-week follow-up visit, the patient demonstrated significant improvement in glycemic control, with fasting glucose ranging from 90-125 mg/dL and 2-hour postprandial glucose between 145-185 mg/dL. Weight loss had stabilized, and the patient reported complete resolution of symptoms.

Conclusions: This case highlights the importance of C-peptide measurement in the initial evaluation of patients with newly diagnosed diabetes. Routine assessment of C-peptide may prevent misclassification of diabetes type and allow for individualized, effective treatment strategies.

Case 2

Case Presentation: A 49-year-old woman with a 20-year history of type 1 diabetes, hypertension, and obesity (BMI 39 kg/m^2) presented with nausea, vomiting, headache, dry mouth, and polyuria. Despite adherence to insulin therapy and diet, her glycemia fluctuated between 200-500 mg/dL, with progressive weight gain and uncontrolled blood pressure. Laboratory evaluation revealed metabolic acidosis, glucosuria, and ketonuria. Fasting C-peptide was 1.79 ng/mL (normal range 1.1-4.4), indicating preserved endogenous insulin secretion.

Management and Outcomes: The patient received intravenous fluid therapy and insulin adjustment, achieving stabilization of metabolic parameters. Subsequent outpatient management included a switch to oral therapy with metformin, DPP-4, and SGLT-2 inhibitors. Within 2 weeks, glycemic control improved (fasting glucose <130 mg/dL, postprandial <180 mg/dL), blood pressure normalized, and weight decreased by 10 kg.

Conclusions: This case illustrates that routine C-peptide measurement in long-standing type 1 diabetes can inform therapeutic decisions and support transition to combination oral therapy in patients with residual insulin secretion.

Abstract citation ID: lvag096.1157

EP819 - ECE_1783 - The role of digital literacy in the prevention and management of adolescent obesity: a nursing perspective

Despoina Rizikou, Afroditi Tsalkitzi, Anastasia Ntikoudi and Eugenia Vlachou
Nursing, University of West Attica, Athens, Greece

Introduction: Adolescent obesity, recognized as a chronic disease, affected over 340 million individuals aged 5-19 globally in 2022 and is linked to persistent obesity in adulthood and early onset of type 2 diabetes. Meanwhile, over 90% of adolescents regularly use digital platforms for health information. In this evolving digital environment, nurses play a central role in supporting adolescents through digital tools and behavior change strategies. However, the effectiveness of such interventions is influenced by the level of digital literacy—the ability to access, evaluate, understand, and apply digital health information effectively, ethically, and safely, making it essential for equitable and effective nursing care.

Purpose: This study aims to explore the impact of digital literacy on the prevention and management of adolescent obesity and to emphasize the evolving role of nurses in assessing and strengthening digital competencies in young populations.

Method: A scoping review of 15 studies was conducted using PubMed, Cochrane Library and Scopus. Keywords such as digital "literacy", "adolescent obesity", "nursing interventions", "health technology" were used to identify studies published between 2019 and 2025.

Results: Recent evidence indicates that adolescents with limited digital literacy are more vulnerable to misinformation and disengagement from digital health tools and poor self-management, particularly in low and middle-income countries, where digital inequalities are more pronounced. Although the American Diabetes Association Standards of Care (2026) recommend the use of digital technologies in pediatric populations, they lack structured guidance on digital literacy. Nurses are well positioned to bridge this gap, provided they are digitally competent themselves, through validated tools such as the eHealth Literacy Scale (eHEALS) and the Digital Health Literacy Instrument (DHLI), which support assessment and education. Studies also highlight that parental digital literacy influences adolescents' ability to safely engage with online health content. Family-based digital literacy education improves outcomes in obesity prevention, particularly when guided by trained nurses. Ethical aspects such as privacy, consent, and online safety must also be considered.

Conclusions: Digital literacy is essential for effective digital health interventions in adolescent obesity care. The contribution of nurses is vital, as they play a key role in guiding, educating, and supporting adolescents and their families within the digital health landscape. Building on this role, nurses should integrate digital literacy assessment and education into everyday clinical and community practice. Future nursing frameworks should ensure that digital tools are accessible, understandable, and meaningful, with emphasis on training, valid assessment, and health equity.

Abstract citation ID: lvag096.1158

EP821 - ECE_2156 - Citrate–fluoride tubes preserve glucose concentrations under routine conditions and improve diagnostic accuracy in two-step gestational diabetes screening and diagnosis

Bernardino González de la Presa[1], Alex Barragán[2], Sandra Oms[3], Eva Fernandez[3], Susana Santamaria[1], Akemys Watts[1], Emilio Ortega[4], Irene Vinagre[4], Federico Migliorelli[5] and Gregori Casals[6]
[1]Maternity Core Laboratory, Biomedical Diagnostic Center, Hospital Clínic of Barcelona, Barcelona, Spain; [2]Department of Biochemistry and Molecular Genetics, Hospital Clínic of Barcelona, FRCB-IDIBAPS, Barcelona, Spain; [3]Phlebotomy Center, Biomedical Diagnostic Center, Hospital Clinic of Barcelona, Barcelona, Spain; [4]Endocrinology and Nutrition Department, Hospital Clinic Barcelona, Barcelona, Spain; [5]Department of Maternal-Fetal Medicine, Hospital Clinic of Barcelona, Barcelona, Spain; [6]Department of Biochemistry and Molecular Genetics, CDB, Hospital Clínic de Barcelona, FCRB-IDIBAPS, Barcelona, Spain

Introduction: The diagnostic protocol for gestational diabetes mellitus (GDM) used in our laboratory is based on the two-step approach (O'Sullivan screening test and diagnostic oral glucose

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

tolerance test [OGTT]). For glucose measurement, the use of plasma obtained in the reference fluoride–EDTA tubes kept in ice–water slurry is recommended, as this procedure stabilizes glucose concentrations after sample collection and prevents glycolysis during the preanalytical phase. However, due to the complexity of handling this tube in routine, serum is commonly used instead. More recently, collection tubes containing fast-acting glycolysis inhibitors, such as citrate buffer, have become available as an alternative to the reference fluoride-EDTA tubes and are easier to implement in routine practice. Nevertheless, the use of these tubes is not yet widespread in routine, which may significantly influence the interpretation of test results.

Materials and Methods: The aim of this prospective study was to compare glucose measurements and their subsequent clinical impact across three sample types: serum (routine clinical practice), citrate-fluoride (S-Monovetter, GlucoEXACT), and fluoride–EDTA tubes processed in ice–water slurry (reference procedure). The study included 124 women undergoing the O'Sullivan screening test and 80 women undergoing a diagnostic OGTT. Diagnostic criteria followed American College of Obstreticians and Gynecologists (ACOG) recommendations. Glucose concentrations were measured using the Gluc Dimension method (Siemens).

Results: In both groups (O'Sullivan and OGTT), serum samples systematically showed lower glucose concentrations than samples collected in either glycolysis-inhibiting tubes (serum 129 ± 33 mg/dL, citrate-fluoride 134 ± 34 mg/dL, fluoride-EDTA: 136 ± 34 mg/dL; $P < .001$). Accordingly, for the O'Sullivan test, the proportion of positive results was significantly lower in serum samples (33.3%) compared with fluoride–EDTA (41.5%) and citrate-fluoride tubes (40.7%). A similar pattern was observed for the OGTT, with a prevalence of positive results of 24.7% in serum, compared with 45.5% in fluoride–EDTA and 42.1% in citrate-fluoride samples. In both the O'Sullivan test and the OGTT, differences in the proportion of positive results were significant between serum and fluoride–EDTA ($P < .01$), but not between citrate–fluoride and fluoride–EDTA. No false-negative results were observed with serum or citrate–fluoride samples.

Discussion: Citrate-fluoride tubes handled under the same simple preanalytical conditions as routine serum samples (room temperature, without immediate cooling or centrifugation) preserve glucose concentrations comparable to those obtained using rigorously processed reference fluoride–EDTA tubes and substantially reduce the risk of glucose underestimation associated with serum samples, thereby minimizing diagnostic misclassification in two-step GDM screening and diagnosis.

Abstract citation ID: lvag096.1159

EP822 - ECE_1168 - Continuous Glucose Monitoring (CGM) technologies and Reactive Hypoglycemia (RH) management: a review of emerging clinical evidence

Pendar Farahani
NFMPC—Endocrinology Clinic, Milton, Canada

Background: Continuous Glucose Monitoring (CGM) has become a cornerstone of diabetes management, supported by robust randomized clinical trials (RCTs) and incorporated into standard care guidelines. Recently, CGM has been explored off-label for the management of Reactive Hypoglycemia (RH), a condition characterized by postprandial hypoglycemia in individuals without diabetes.

Objective: To evaluate the current clinical evidence from RCTs and observational studies regarding the use of CGM in RH management across diverse etiologies.

Methods: A systematic literature search was conducted using PubMed and Google Scholar, employing combinations of MeSH terms related to CGM, RH, postprandial hypoglycemia, and rare endocrine disorders. Studies were categorized based on RH etiology.

Results: Over 95% of published studies focused on patients with obesity or those who had undergone bariatric surgery, with or without diabetes. A limited number of cohort studies, case series, and case reports addressed CGM use in RH among patients without obesity or diabetes. These included individuals with chronic kidney disease, inborn errors of metabolism, autoimmune syndromes, cystic fibrosis, and paraneoplastic syndromes. Despite anecdotal benefits, the evidence base remains fragmented and largely observational.

Conclusions: There is insufficient high-quality clinical evidence to support CGM as a validated tool for RH management. CGM technologies are not currently approved by regulatory bodies such as the FDA or Health Canada for this indication, nor are they reimbursed by insurance programs. Future research should prioritize well-designed RCTs and longitudinal studies, particularly in rare endocrine conditions, to establish CGM's role in RH care—potentially as an "orphan indication" for "orphan diseases."

Abstract citation ID: lvag096.1160

EP823 - ECE_1873 - Current literature on the use of Probiotic and prebiotic with Glucagon like peptide- 1 receptor agonist therapy in patients with Type 2 diabetes

Thaw Htet[1,2] and Veronica Preda[3,4]
[1]*Endocrine department, Macquarie University Hospital, Sydney, Australia;* [2]*Macquarie University, Sydney, Australia;* [3]*Faculty of Medicine Health and Health Sciences, Macquarie University, Sydney, Australia;* [4]*Endocrine Department, Macquarie Hospital, Sydney, Australia*

Glucagon like peptide receptor-1 agonists(GLP-1 RAs) are commonly used in type 2 diabetes mellitus(T2DM). Gut microbiomes play an important role in human physiology and dysbiosis is associated with multiple diseases. Certain changes in the composition of gut microbiomes such *as Lactobacillus* and *Bacteroidetes* have been observed in T2DM. Gut microbiome can influence GLP-1 production via their metabolites such as short chain fatty acids(SCFA). Prebiotics and probiotics have positive influence on the gut microbiome. Prebiotics such as oligofructose and flavonoids were shown to have positive effect on GLP-1 production and glycaemic control. Probiotics such as *Lactobacillus* and *bifidobacterium* was shown to improve insulin and GLP-1 secretion. Hence, we have conducted a literature review to explore the use of probiotics and prebiotics in patients with T2DM on GLP-1 RAs.

The search strategy was based on PICOS Framework and searches were done via SCOPUS, EMBASE, Cochrane, EBSCOhost Medline and CINAHL databases from inception to

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

December 2025. Most studies exploring the use of probiotics and prebiotics in T2DM excluded GLP-1 RAs and insulin use. Only 4 studies included GLP-1 RA use. Probiotic supplementation(*bifidobacterium longum)* with dulaglutide for 12 weeks led to improvement in HbA1c, fasting plasma glucose level (FPG), inflammatory markers, blood pressure and lipid profile. Probiotic agent(*lactobacillus acidophilus, lactobacillus plantarum, bifibacterium lactis and saccharomyces boulardii*) with diabetes therapies including GLP-1 RA for 6 months showed improvement in HbA1c, FPG and total cholesterol levels compared with placebo group. However, Probiotic therapy(*lactobacillus speicies*) together with diabetes medications including GLP-1 RAs for 12 weeks showed no significant improvement in glycemic control, BMI, inflammatory markers and lipid levels. Synbiotic therapy consisting of probiotic(*lactobacillus caesi* and *bifidobacterium breve)* and prebiotic(galacto-oligosaccharide) for 24 weeks showed no significant improvement in inflammatory markers.

Our review identified that the use of probiotic and prebiotic with GLP-1 RAs has not been adequately studied despite the emerging role of gut microbiomes and GLP-1 RAs. Current evidence showed inconsistent benefits. Recent evidence showed the response to GLP-1 RAs can vary based on the diversities of the gut microbiome, and the use of probiotics and prebiotics may reduce gastrointestinal side effects of GLP-1RAs. Evolving evidence showed probiotics can be bioengineered and used as a part of targeted therapies in certain malignancies and gastrointestinal disorders .With the future direction of applying personalised and precision medicine in T2DM, further dedicated studies of the use of probiotic and prebiotics with GLP-1 RAs are needed.

Abstract citation ID: lvag096.1161

EP824 - ECE_1397 - Phased management of type 2 diabetes, obesity, and stress urinary incontinence using GLP-1 receptor agonist therapy and artificial urinary sphincter: a case report

Ivana Mickovski[1,2], Daniela Buklioska Ilievska[1,3] and Radmila Milosheska[3]
[1]*Faculty of Medical Sciences, Goce Delcev University, Stip, North Macedonia;* [2]*PZU Vasileva Kardio, Skopje, North Macedonia;* [3]*General City Hospital 8th September, Skopje, North Macedonia*

Background: Type 2 diabetes mellitus (T2DM) and obesity are frequently associated with stress urinary incontinence through metabolic, neuropathic, and mechanical mechanisms. Optimizing glycemic control and reducing body weight may improve urinary symptoms; however, severe cases often require surgical intervention.

Case Description: We report the case of a 43-year-old woman with a 10-year history of poorly controlled T2DM and obesity (BMI 39.2 kg/m^2), presenting with severe stress urinary incontinence requiring continuous diaper use. Baseline laboratory evaluation showed HbA1c 9.9%, fasting plasma glucose 200 mg/dL, dyslipidemia, and microalbuminuria. Conservative urological measures had failed.

Management: A phased treatment strategy was adopted, prioritizing metabolic optimization. The patient was treated with semaglutide 1 mg weekly, basal–bolus insulin therapy, metformin, and structured lifestyle modification. After six months, HbA1c improved to 6.7% and BMI decreased to 30.8 kg/m^2 (14% weight reduction). Despite metabolic improvement, urinary incontinence persisted. The patient subsequently underwent artificial urinary sphincter implantation.

Results: Postoperative recovery was uneventful. At three months follow-up, the patient reported complete continence with discontinuation of diaper use and significant improvement in quality of life. Glycemic control and weight reduction were maintained.

Conclusions: This case demonstrates that a stepwise approach—addressing glycemic dysregulation and obesity before surgical correction—can optimize outcomes in patients with T2DM-associated stress urinary incontinence. Combining GLP-1 receptor agonist therapy with timely surgical intervention offers effective metabolic control and durable functional recovery.

Keywords type 2 diabetes mellitus, obesity, stress urinary incontinence, GLP 1receptor agonist, metabolic control, weight loss, artificial urinary sphincter

Abstract citation ID: lvag096.1162

EP826 - ECE_3138 - Clinical management and follow-up after emergency attendance for acute glucose-related events in adults with type 1 diabetes

Víctor Siles-Guerrero, Aida Elhadri-Egea, Rosa Natalia García Pérez and Araceli Munoz-Garach
Hospital Universitario Virgen De Las Nieves, Granada, Spain

Introduction: Emergency attendance for acute glucose-related events in type 1 diabetes mellitus (T1DM) identifies a subgroup of patients with increased clinical complexity and potential gaps in ongoing diabetes management. These episodes often reflect underlying vulnerabilities that are not fully captured during routine outpatient follow-up and may be associated with recurrent emergency service utilisation. Understanding the clinical profile and outcomes of these patients using real-world data may help optimise post-event care pathways.

Objective: To describe clinical management characteristics and short- to mid-term outcomes following emergency attendance for acute glucose-related events in adults with T1DM.

Methods: A retrospective, observational, descriptive study was conducted including 66 adults with T1DM attended by prehospital emergency services between 2018 and 2022 due to acute glucose-related events. Data collected included demographic characteristics, prior diabetes-related emergency events, symptom awareness status, nocturnal occurrence of the index event, and need for subsequent emergency re-attendance during follow-up. Results are presented using descriptive statistics.

Results: The median age of the cohort was 42.5 years, with a predominance of male patients (65.2%). More than half of the cohort (54.5%) had a documented history of previous emergency attendance for similar acute glucose-related events prior to the index episode. Impaired symptom awareness was present in 43.9% of patients, suggesting reduced ability to recognise early warning symptoms. Nocturnal occurrence of the index event was reported in 53.0%, highlighting the relevance of events occurring during periods of reduced monitoring and delayed intervention. During follow-up, 22.7% of patients required at least one new emergency intervention for a recurrent acute glucose-related event. The clustering of prior emergency attendance, impaired

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

awareness, and nocturnal occurrence suggests persistence of vulnerability beyond the index emergency episode.

Conclusions: Among 66 adults with T1DM requiring emergency care for acute glucose-related events, a substantial proportion demonstrated recurrent emergency utilisation and clinical features suggestive of ongoing vulnerability. Emergency attendance may therefore represent a critical opportunity to identify high-risk individuals and to trigger structured reassessment and targeted follow-up within diabetes care pathways, with the aim of reducing recurrent emergency events and improving long-term management.

Abstract citation ID: lvag096.1163

EP830 - ECE_3318 - Association between body composition parameters and ultrasonographic abdominal fat measurements and the development of gestational diabetes mellitus

Ana Segarra Balao, María de Damas Medina and Carmen María López Pérez
Endocrinology and Nutrition, Complejo Hospitalario de Jaén, Jaén, Spain

Objectives: To investigate the relationship between body composition parameters—including anthropometric measurements, muscle ultrasound, and bioelectrical impedance analysis—and the risk of developing gestational diabetes mellitus (GDM). A secondary objective was to determine the prevalence of metabolic syndrome in the studied cohort.

Materials and Methods: This is a prospective cohort study. All pregnant women with at least one risk factor for GDM who underwent an O'Sullivan test during the first trimester of pregnancy were included. Risk factors included maternal age >35 years, body mass index (BMI) >30 kg/m^2, previous GDM or adverse obstetric outcomes, first-degree family history of diabetes mellitus, or belonging to an ethnic group with a high prevalence of diabetes.

Demographic and clinical data, along with ultrasound and bioelectrical impedance parameters, were collected to assess body composition. Statistical analysis was performed using SPSS version 25®.

Results: A total of 30 women were included. Mean age was 33.4 ± 5.4 years, mean weight 74.1 ± 16.1 kg, and mean BMI 25.0 ± 5.6 kg/m^2. Mean waist circumference was 90.7 ± 11.9 cm. Two participants had a previous history of GDM, and none had a prior diagnosis of prediabetes. A family history of diabetes was present in 70% of cases. Two women were active smokers, while ten were former smokers who had quit during pregnancy. Polycystic ovary syndrome and hypertension were present in 10% of participants each; none had dyslipidemia or metabolic-associated fatty liver disease.

The mean O'Sullivan test value was 125.2 ± 30.5 mg/dL, with 10 participants showing positive results (>140 mg/dL). Mean handgrip strength was 25.7 ± 5.0 kg.

Muscle ultrasound showed a mean cross-sectional area of 4.58 ± 1.78 cm^2 and subcutaneous fat thickness of 1.77 ± 0.44 cm. Abdominal ultrasound revealed a mean total abdominal fat thickness of 1.96 ± 0.67 cm, with superficial and preperitoneal fat measuring 1.05 ± 0.47 cm and 0.99 ± 0.80 cm, respectively.

Bioelectrical impedance analysis demonstrated a mean fat-free mass of 45.8 ± 6.1 kg, fat mass of 26.4 ± 10.2 kg, skeletal muscle mass index of 8.05 ± 1.17 kg/m^2, hydration percentage of 73.3 ± 1.6%, and phase angle of 5.5 ± 0.6°.

Conclusions: These preliminary results from an ongoing study provide a descriptive analysis of anthropometric and body composition parameters in first-trimester pregnant women, most of whom presented no associated comorbidities.

Abstract citation ID: lvag096.1164

EP832 - ECE_3865 - MASLD in diabetes mellitus: non-invasive assessment and sex-related differences

Liana Jashi[1], Tamar Shervashidze[2], Tamar Peshkova[3], Meri Beridze[3], Ketevan Dundua[4], Eter Margalitadze[3] and Maia Kobuladze[1]
[1]*Solomedi, Endocrinology, Avicenna—Batumi Medical University, Batumi, Georgia;* [2]*Avicenna—Batumi Medical University, T'bilisi, Georgia;* [3]*Batumi Shota Rustaveli State University, Batumi, Georgia;* [4]*David Agmashenebeli University of Georgia, T'bilisi, Georgia*

Background: Metabolically–dysfunction–associated steatosis liver disease (MASLD) is one of the most common metabolic comorbidities in patients with diabetes mellitus and is associated with progressive liver injury and increased cardiovascular risk. Its prevalence among patients with diabetes has reached alarming levels worldwide.

Objective: To assess the prevalence of MASLD, fibrosis risk, and sex-related differences in patients with diabetes mellitus using non-invasive diagnostic tools.

Methods: This study included 60 patients with diabetes mellitus aged 45-60 years, of whom 37 were women (61.7%), and 23 were men (38.3%). Body mass index (BMI) ranged from 26 to 36 kg/m^2. All patients were treated with metformin. Liver steatosis was assessed by abdominal ultrasound. Fibrosis risk was estimated using the FIB-4 index based on age, alanine aminotransferase (ALT), and platelet count. Data were analyzed according to sex.

Results: Hepatic steatosis was detected by ultrasound in 68.3% of patients, including mild steatosis in 41.5% and moderate steatosis in 26.8%. According to the FIB-4 index, 71.7% of patients were classified as having low fibrosis risk, 23.3% as intermediate risk, and 5.0% as high risk.

The prevalence of MASLD was 64.9% in women and 73.9% in men. Intermediate-to-high fibrosis risk was more frequent in men compared with women (34.8% vs 24.3%).

Conclusions: MASLD is highly prevalent among patients with diabetes mellitus. Non-invasive screening tools such as ultrasound and the FIB-4 index are effective for early identification of liver involvement and fibrosis risk. Consideration of sex-related differences may improve risk stratification and individualized management strategies.

Abstract citation ID: lvag096.1165

EP834 - ECE_2519 - Fat loss vs muscle loss: bioimpedance trajectories in women and men during dietary weight management

Roxana Pui[1], Stefania-Alexandra Bunceanu[1] and Stoian Dana[2]
[1]*Department of Doctoral Studies, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania;* [2]*Discipline of Endocrinology,*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Second Department of Internal Medicine, Universitatea de Medicină și Farmacie Victor Babeș, University of Medicine and Pharmacy "Victor Babes", Timișoara, Romania

Introduction: In clinical practice, dietary weight-loss outcomes are often assessed by changes in body weight and BMI, although clinically meaningful improvement depends on preferential fat loss with preservation of lean mass. Responses in routine care are heterogeneous, with marked early changes, plateaus, and occasional rebound. Objective body composition assessment may better characterize these patterns and support individualized dietary optimization and outcome evaluation. This study aimed to describe trajectories of weight and body composition during a structured hypocaloric program, focusing on sex-specific patterns and potential lean mass vulnerability, in patients managed with nutritional intervention only.

Methods: We conducted a retrospective observational study of adults with BMI $\geq$25 kg/m^2 managed between 2010 and 2020 in a specialized endocrinology and nutrition center in Timișoara, Romania. Patients received individualized hypocaloric nutritional plan with a staged energy deficit of ~1000 kcal/day below estimated energy requirements for 4-6 weeks, followed by ~750-500 kcal/day below requirements, with monthly follow-up for up to 6 months. Body composition was assessed serially using bioimpedance (Tanita BC-418), including body weight, BMI, trunk fat (%), total body fat (%), and total muscle mass (% and kg). Monthly trajectories were summarized separately for women and men.

Results: Weight and BMI decreased predominantly during early follow-up and then tended to stabilize. Trunk fat percentage showed an overall downward trend, while muscle mass fluctuated during caloric restriction, underscoring the value of monitoring beyond weight alone. Sex-stratified trajectories suggested different dynamics: men tended to show larger absolute reductions in weight and adiposity, whereas women showed patterns consistent with greater relative vulnerability to lean mass loss. In participants with paired baseline–final bioimpedance assessments, total body fat percentage decreased significantly in both sexes across all age decades ($P < .001$), indicating consistent adiposity improvement among those completing follow-up. The relationship between fat mass loss and muscle mass loss showed a variable positive trend, highlighting inter-individual heterogeneity and supporting a personalized approach.

Conclusions: Serial bioimpedance monitoring captured heterogeneous and sex-specific body composition trajectories during hypocaloric intervention. While adiposity improved significantly in participants who completed follow-up, signals of lean mass vulnerability—particularly in women—support sex-aware strategies emphasizing adequate protein intake, resistance training, and close body composition monitoring to minimize unintended muscle loss during dietary weight management.

Abstract citation ID: lvag096.1166

EP835 - ECE_3442 - Allergy to dexamethasone: a rare pitfall in endocrine practice

Rihab Khochtali, Imen Halloul, Taieb Ach, Wiem Saafi, Hamza Elfekih, Ghada Saad and Yosra Hasni
Department of Endocrinology, Farhat Hached Hospital, Sousse, Tunisia

Background: Dexamethasone is widely used in endocrinology, particularly for diagnostic suppression tests. Hypersensitivity reactions to corticosteroids are rare, with a reported frequency ranging from 0.2% to 5%. This condition may represent both a diagnostic and therapeutic challenge.

Case Presentation: We report the case of a 55-year-old woman admitted to our department for evaluation of resistant hypertension evolving for six years, complicated with a left ventricular hypertrophy. Her medical history included type 2 diabetes treated with dual therapy, obesity (BMI: 39 kg/m^2), and documented allergies to penicillin and paracetamol.

Secondary causes of hypertension were investigated. Renal artery CT angiography excluded a renovascular cause. During the low-dose dexamethasone suppression test, the patient developed a mild acute urticarial reaction a few minutes after dexamethasone administration. The reaction persisted throughout the test, and resolved spontaneously afterward. Subsequent skin prick testing confirmed an allergy to both dexamethasone and betamethasone. As the dexamethasone suppression test was uninterpretable in this context, Cushing's syndrome was excluded using alternative screening methods: Late-night cortisol and 24-hour urinary free cortisol levels were normal.

Further evaluation of contributing factors to resistant hypertension revealed severe obstructive sleep apnea syndrome (OSAS), confirmed by polysomnography. The patient was managed with lifestyle and dietary measures, GLP-1 receptor agonist therapy (semaglutide), and continuous positive airway pressure for OSAS. After six months of follow-up, she achieved a 7% weight loss, with good blood pressure control under dual therapy and improved glycemic control on GLP-1 therapy.

Conclusions: Corticosteroid allergy is a rare but clinically significant condition that can complicate endocrine diagnostic procedures. Alternative diagnostic strategies should be considered when evaluating hypercortisolism in patients with confirmed corticosteroid hypersensitivity. Late-night salivary cortisol or repeated urinary free cortisol may represent safe alternatives for Cushing's syndrome screening in these patients.

Abstract citation ID: lvag096.1167

EP838 - ECE_2208 - Cardiovascular risk factors in patients with newly diagnosed type 2 diabetes

Alla Shepelkevich[1], Diana Baalbaki[1], Alena Yurenia[2] and Yuliya Dydyshka[1]
[1]*Endocrinology, Belarusian State Medical University, Minsk, Belarus;* [2]*Minsk City Clinic Endocrinology Center, Minsk, Belarus*

Background: Type 2 diabetes (T2D) is associated with an increased risk of cardiovascular disease (CVD) and CV mortality. Additionally, multiple modifiable risk factors (obesity, dyslipidemia, hypertension) can further increase the risk of a poor outcome. Hence early identification of CVD risk factors in patients with T2D is crucial for proactive management and primary prevention.

Objectives: Assessment of cardiovascular risk factors and stratification of CVD risk in patients with newly diagnosed T2D.

Methods: A retrospective study was conducted among newly diagnosed T2D patients attending the outpatient clinic. Anthropometric measurements (BMI, WHR), biochemical

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

parameters (lipid panel, HbA1c) and past medical history were analyzed. Control group included patients matched by gender and age, without diabetes. The stratification of CVD risk was performed using SCORE2-Diabetes and SCORE2 in patients with T2D and controls respectively.

Results: 100 patients with T2D were enrolled (50F, 50M), median age 52 years [IQR 47-55]. Glycemic control was optimal with median HbA1c—7.1% [6.7-7.5]. Obesity was observed in 45% of T2D patients and 32% were overweight with BMI 30.6 [25.6-36.4] and WHR 0.95 [0.82-1.09]. Dyslipidemia was found in 61% of T2D patients with LDL—3.6 [2.97-4.1] mmol/L and triglycerides—1.76 [1.3-2.12] mmol/L that were significantly higher vs controls with LDL—2.7 [2.39-3.37] mmol/L and triglycerides—1.19 [0.93-1.49] mmol/L ($P < .5$). In addition to a higher level of HDL—1.3 [1.09-1.63] mmol/L was observed in controls vs T2D patients HDL—1.12 [0.96-1.32] mmol/L ($P < .5$). Co-occurring hypertension was present in 78% of T2D patients with systolic BP 141 [134-146] mmHg. Upon CVD risk evaluation in T2D patients—83% were at high/very high risk (41% and 42% respectively) and only 17% had moderate risk, whereas in the control group—35% had moderate risk and 65% of patients had low risk. Furthermore, none of the high and very high-risk patients had target LDL and only 23.5% of moderate risk patients were within their target LDL level.

Conclusions: Our findings show the prevalence of high/very high CVD risk (83%) and illustrate a constellation of modifiable CVD risk factors in patients with newly diagnosed T2D, which subjects them to an increased risk of major cardiovascular events. This emphasizes the significance of timely metabolic management alongside proper glucose control.

Abstract citation ID: lvag096.1168

EP841 - ECE_3287 - Mortality predictors in digestive neoplasms via morphofunctional assessment

Ana Rocío Martínez Hartmann, Carlos López-Pereira, María González-Pacheco, Maria del Mar Roca-Rodriguez and Almudena Lara Barea

Endocrinology and Nutrition Department, Endocrinology and Nutrition, Puerta del Mar Hospital, Puerta del Mar Hospital, Cadiz, Spain

Introduction: Nutritional and functional status conditions the prognosis in patients with digestive cancer. Bioimpedance, muscle ultrasound, and functional tests allow for the identification of values associated with higher mortality, facilitating risk stratification and early intervention.

Objectives:

1. To determine the cut-off points for morphofunctional parameters (bioimpedance, muscle ultrasound, dynamometry, and Up and Go test) associated with mortality, differentiated by sex, in patients with digestive tumors.
2. To identify possible morphofunctional parameters that could serve as independent predictors of survival in this population.

Materials and Methods: A retrospective observational study was conducted on a series of patients with digestive cancer (biliary tract, pancreas, esophagus, stomach, colon, or rectum), evaluated using morphofunctional assessment techniques at our center (HUPM). Descriptive analyses, sex-stratified ROC curves, and survival analyses were performed.

Results: The cohort consisted of 131 patients, obtaining a median Phase Angle (PhA) of 4.6°, Body Cell Mass (BCM) of 21.4 kg, dynamometry of 20 kg, Timed Up and Go (TUG) of 6.5 seconds, and rectus femoris muscle area of 2.88 cm^2. Overall mortality was 37%.

The cut-off points associated with mortality were as follows:

Parameter	Men	Women	*P*-value
PhA	<4.6	<4.1	<.001
BCM	<23.1 kg	<19.3 kg	<.001
Rectus Femoris Area	<2.63 cm^2	<2.18 cm^2	<.001
Dynamometry	<32.5 kg	<14.3 kg	<.001
TUG	>5.6 seconds	>6 seconds	<.001

PhA was identified as an independent predictor of mortality in the Cox regression analysis (HR = 0.59; 95% CI 0.36-0.97; $P = .038$). Patients with PhA <3.8° presented a significantly lower median survival (19.5 vs 38.5 months) and reduced survival at 12 and 24 months (50.8% and 33.9% vs 79.2% and 60.7%).

Conclusions: Morphofunctional parameters allow for the identification of sex-differential cut-off points associated with mortality in digestive cancer. A PhA <3.8° is consolidated as an independent predictor of lower survival, along with dynamometry and TUG. These findings support the integration of bioimpedance, ultrasound, and functional tests into clinical practice to optimize individualized nutritional and functional intervention.

Abstract citation ID: lvag096.1169

EP845 - ECE_2576 - Cardiovascular risk stratification and determination of lipoprotein a in patients with type 1 diabetes mellitus

Víctor Simón-Frapolli[1,2,3], Ángel López Montalbán[1], Ainoa Mallorquín Castillo[1], Teresa Campos Varela[1], Irene García Gómez[1] and Francisco José Tinahones Madueño[1,2,3]

[1]*Endocrinology and Nutrition, Hospital Universitario Virgen De La Victoria, Málaga, Spain;* [2]*Ibima Plataforma Bionand, Málaga, Spain;* [3]*Facultad de Medicina-UMA, Málaga, Spain*

Introduction: Elevated lipoprotein A, or Lp(a), is an independent risk factor for the development of atherosclerotic cardiovascular disease (CVD). Given its stability over time, the Spanish Society of Arteriosclerosis (SEA) suggests universal determination of Lp(a) coinciding with the first biochemical determination that includes the lipid profile, as it behaves as a modifier of cardiovascular risk (CVR) in the most widely used CVR stratifications to date. However, there is currently no consensus, as the European Atherosclerosis Society (EAS) recommends its measurement only in individuals with certain characteristics. In addition, in patients with type 1 diabetes mellitus (T1DM), the current criteria for CVR stratification are not specific, as they are usually extrapolated from studies conducted in patients with type 2 DM.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Objective: To assess CVR in patients with T1DM following the 2024 SEA Standards, as well as to study the frequency of Lp(a) determination in our clinical practice in these patients.

Materials and Methods: Descriptive observational study including 100 patients with T1DM reviewed in outpatient clinics at the Virgen de la Victoria Hospital between June 2023 and December 2024. Demographic, clinical and analytical variables were collected, and CVR stratification was performed. In addition, the analytical history of all patients was retrospectively explored to determine how many had had their Lp(a) level assessed at some point.

Results: The mean age of our sample was 43.91 ± 13.1 years and 61% of patients were women. 24% of patients were T1DM for <10 years, 25% for 10 to 20 years, and 51% for >20 years. 78% of patients were on multiple daily insulin (MDI) therapy and 22% on continuous insulin infusion systems (CIS), while 6% had >3 CVR factors and 32% had at least one CVR factor. 32% had target organ damage at the time of evaluation. 53% had a very high CVR, 25% had a high CVR and 22% had a moderate CVR. None of the patients had a low CVR, since the presence of DM by definition implies a moderate CVR. We note that the Lp(a) levels were determined in only one patient (1%) during follow-up.

Conclusions: The low determination of Lp(a) in T1DM patients may be due to the absence of an approved targeted treatment to date to reduce its levels. However, its measurement could be useful to reclassify CVR in primary prevention from moderate to high in approximately a quarter of patients (22%), and thus consider intensifying control targets for other CVR factors.

Abstract citation ID: lvag096.1170

EP849 - ECE_2019 - An unusual cause of postprandial hypoglycemia: impaired gastric emptying

Pavel Cee[1], Jan Cap[1], Jiří Cyrany[2], Veronika Špačková[1] and Filip Gabalec[1]

[1]*The 4th Department of Internal Medicine, University Hospital Hradec Králové, Hradec Králové, Czech Republic;* [2]*The 2nd Department of Internal Medicine, University Hospital Hradec Králové, Hradec Králové, Czech Republic*

Introduction: Hypoglycaemia in patients not treated with insulin represents a diagnostic challenge. The most common causes include endogenous hyperinsulinism or insufficient counter-regulatory hormonal response. Disorders of gastrointestinal motility are less frequently considered. We present a case of recurrent hypoglycaemia associated with impaired gastric emptying.

Case Report: We present a 77-year-old woman with no history of major internal diseases, long-term follow-up for arterial hypertension, dyslipidaemia, and diet-controlled type 2 diabetes mellitus. Her history also included laparoscopic repair of a large hiatal hernia (upside down stomach) half a year before. She was admitted to our department for evaluation of recurrent symptomatic hypoglycaemia, which appeared approximately three weeks prior to hospitalization. Episodes typically occurred in the evening, about 3-4 hours after meals, with a frequency of once every two days, and were accompanied by sweating, tremor, and marked fatigue. The patient obtained a glucose sensor, with the lowest recorded value being 2.8 mmol/L.

A 72-hour fasting test was performed and was negative, excluding organic hyperinsulinism. Comprehensive laboratory tests, including hormonal profile and Synacthen test, revealed no pituitary dysfunction or other endocrine abnormalities. Further evaluation confirmed significant impairment of gastric emptying, which had been present for about a year and was originally detected as an incidental finding during gastroscopy and verified by 99mTc gastric emptying scintigraphy (Tougass protocol) with less than 50% evacuation of stomach after 4 hours. A prolonged oral glucose tolerance test (oGTT) demonstrated an initial increase in glycemia followed by a late decline into hypoglycaemic values. After excluding hyperinsulinism, treatment with a somatostatin analogue (lanreotide) was initiated to modulate postprandial insulin secretion. Following therapy, the frequency of hypoglycaemic episodes decreased markedly and now occurs approximately once every two weeks.

Conclusions: Rapid gastric emptying is a known cause of postprandial hypoglycaemia (dumping syndrome). Hypoglycaemia that occurs in patients with delayed gastric emptying is unusual. The pathophysiological mechanism may involve dysregulation of the enteroendocrine axis. Delayed delivery to the small intestine leads to disproportionate release of incretin hormones (particularly GLP-1 and GIP), stimulating insulin secretion and inhibiting glucagon. The result is an excessive insulin response and subsequent hypoglycaemia. Clinical improvement after lanreotide therapy supports this hypothesis, as somatostatin analogues suppress insulin and incretin secretion, thus reducing postprandial insulin hypersecretion. This case emphasises the need to consider gastrointestinal motility in the differential diagnosis of hypoglycaemia, even in patients without rapid gastric emptying.

Abstract citation ID: lvag096.1171

EP850 - ECE_3354 - Evaluation of dyspnea, quality of life and lung function in Greek patients with COPD and Type 2 diabetes mellitus treated with roflumilast: a subgroup analysis of the ARGO study

Georgios Hillas[1], Christoforos Efthymiou[2], Dimitrios Zarifis[3], Maria Bertoli[4], Polyanthi Papanastasiou[4], Vasiliki Paraskeva[4], Alexandros Gkinis[4] and Paschalis Steiropoulos[5]

[1]*2nd Respiratory Medicine Department, "ATTIKON" University General Hospital, National and Kapodistrian University of Athens, Medical School, Athens, Greece;* [2]*Respiratory Medicine Department, "Papageorgiou" General Hospital of Thessaloniki, Thessaloniki, Greece;* [3]*Private Pulmonary Site, Patras, Greece;* [4]*Medical Department, ELPEN Pharmaceutical Co. Inc., Athens, Greece;* [5]*Respiratory Medicine Department, University General Hospital, Democritus University of Thrace, Medical School, Alexandroupolis, Greece*

Background: Type 2 diabetes mellitus (T2DM) is a common comorbidity in patients with chronic obstructive pulmonary disease (COPD) and is associated with increased morbidity, mortality, and disease complexity. Emerging evidence suggests that T2DM may adversely affect pulmonary mechanics, further impairing lung function. This subgroup analysis of the ARGO study evaluated the effects of roflumilast on dyspnea, health-related quality of life (HRQoL) and lung function in patients with severe COPD and concomitant T2DM in a real-world setting.

Methods: ARGO was a multicenter, non-interventional, observational study conducted in Greece (NCT05426915) that enrolled 750 patients with severe COPD. Of these, 140 patients with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

concomitant T2DM and a mean (±SD) age of 72.7 ± 7.3 years, were included in this subgroup analysis. Patients were assessed at baseline (V_0) and after 3 (V_1), 6 (V_2) and 12 (V_3) months of treatment with roflumilast. Dyspnea was assessed using the modified Medical Research Council (mMRC) scale, HRQoL using the validated Greek version of the Clinical COPD Questionnaire (CCQ) and lung function by Forced Expiratory Volume in 1 second (FEV_1) % predicted.

Results: Among patients with T2DM, roflumilast treatment was associated with a progressive reduction in dyspnea severity, demonstrated by a shift from higher (mMRC grades 4-3) to lower (mMRC grades 2-1) over time. HRQoL, as assessed by the CCQ, improved significantly at 3, 6, and 12 months compared with baseline ($P < .001$, paired t-test), exceeding the minimal clinically important difference (MCID > 0.4). Mean CCQ scores (±SD) decreased from 3.50 ± 1.07 at baseline to 2.26 ± 0.98 at 12 months. Lung function also showed clinically meaningful improvement (MCID $FEV_1 \geq 0.1$L) at 6 and 12 months, with FEV_1% predicted increasing from 47.76 ± 13.95 at baseline to 54.51 ± 16.30 at 12 months. Similar improvements in HRQoL and lung function were observed in the overall ARGO study population, indicating consistency of treatment effects irrespective of T2DM status.

Conclusions: In this real-world subgroup analysis, treatment with roflumilast was associated with reduced dyspnea severity and clinically significant improvements in HRQoL and lung function in patients with severe COPD and concomitant T2DM. These findings are consistent with those observed in the overall ARGO study population.

Abstract citation ID: lvag096.1172

EP851 - ECE_3849 - Nutritional ultrasound in the study of sarcopenia in diabetes mellitus

Maria Jiménez Aceituno, Ana de Gracia Valero, Carlos Castro Mesa and Ana Segarra Balao
Endocrinology and Nutrition, Complejo Hospitalario de Jaén, Jaén, Spain

Introduction: Diabetes is consistently associated with an increased risk of muscle mass loss and functional impairment, promoting the development of sarcopenia. In this clinical framework, nutritional ultrasound has emerged as a pivotal tool for the objective quantification of muscle architecture and adiposity.

Objectives: To evaluate muscle mass and abdominal fat distribution via nutritional ultrasound in diabetic patients, analyzing its correlation with glycemic control and comparative variances across diabetes subtypes.

Material and Methods: A prospective observational study was conducted including patients with Type 1 (T1DM), Type 2 (T2DM), LADA, and pancreatogenic diabetes. Rectus femoris ultrasound was utilized to measure cross-sectional area (CSA), circumference, and muscle axes. Additionally, abdominal ultrasound assessed preperitoneal and visceral fat layers.

Results: The study included 75 patients with a mean age of 52.84 ± 14.91 years. The sample consisted of 56.8% men and 43.2% women, with a mean 11.56 ± 3.22%. The average BMI was 27.54 ± 4.16 kg/m^2. Diagnostic distribution was: 65.3% Type 1, 17.3% LADA, 12% Type 2, and 5.3% pancreatogenic diabetes.

	DM Type 1	DM Type 2	DM LADA	DM Pancreatogenic	*P*-value
X-axis (cm)	3.76 ± 0.99	3.01 ± 0.77	3.36 ± 0.52	3.40 ± 0.73	187
Y-axis (cm)	1.57 ± 0.35	2.93 ± 5.12	1.56 ± 0.36	1.53 ± 0.47	186
Area (cm^2)	5.10 ± 2.38	3.20 ± 1.56	4.16 ± 1.33	5.16 ± 2.77	97
Preperitoneal Fat (cm)	0.59 ± 0.34	0.45 ± 0.17	0.49 ± 0.29	0.55 ± 0.23	727

A trend toward a smaller rectus femoris area was observed in patients with type 2 diabetes, with no significant differences in other ultrasound parameters across subtypes. The lack of statistical significance may be attributed to the limited sample size, particularly within certain subgroups.

Conclusions: Preliminary results suggest differences in muscle and adipose composition depending on the diabetes mellitus subtype. Expanding this cohort will be necessary to confirm these findings.

Abstract citation ID: lvag096.1173

EP852 - ECE_3334 - Pregnant women with type 1 Diabetes Mellitus on Hybrid closed-loop systems

Dimitra Pappa, Eleftheria Barmpa, Anastasia-Konstantina Sakali and Alexandra Bargiota
Department of Endocrinology and Metabolic Diseases, University Hospital of Larissa, Larissa, Greece

Background and Aims: Women with type1 Diabetes Mellitus (DM1) is important to maintain good glycemic control during pregnancy, avoiding perinatal and maternal complications. Hybrid closed-loop systems (HCLS) are widely used in diabetes management but data are restricted on using during pregnancy. Here we present two such cases of our center.

Methods: Two women with DM1 attending our outpatient clinic for 5 years, managing their diabetes with HCLS (MiniMed780), were studied during their pregnancy. CGSmetrics; time in range (TIR;63-140 mg/dl), above range (TAR;>140 mg/dl), below range (TBR;63-54 mg/dl, TBR54;<54 mg/dl) and coefficient variation (CV) were recorded on the 14th, 34th and 38th gestational week (GW), as well as gestational age at delivery (GAd), childbirth type and offspring birthweight (ofBW).

Results: WomanA; 23 years old, having diabetes for 3 years, on HCLS for 6 months, had her first pregnancy unplanned, and presented on the 14thGW with TIR = 90%, TAR = 10%, TBR = 0%, CV = 24,4%. She chose to remain on HCLS and on 34thGW had TIR = 95%, TAR = 5%, TBR = 0%, CV = 18,8%, on 38thGW TIR = 93%, TAR = 7%, TBR = 0%, CV = 21,9%.

WomanB; 29 years old, having diabetes for 17 years, on HCLS for 2 years, had an unplanned second pregnancy and presented

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

on the 14thGW with TIR = 51%, TAR = 41%, TBR = 3%, CV = 34,1%. She continued on HCLS and on 34thGW had: TIR = 71%, TAR = 28%, TBR = 1%, CV = 26,1%, on 38thGW TIR = 79%, TAR = 19%, TBR = 2%, CV = 32,2%.

Both women had caesarean section on 39th GAd, delivered healthy female babies 3600gr and 3830gr ofBW respectively, and had no maternal or perinatal complications.

Conclusions: HCLS seem to improve CGSmetrics in women with DM1 during pregnancy, improving their glycemic control, minimizing their stress for hypoglycemia.

Abstract citation ID: lvag096.1174

EP853 - ECE_2527 - The contradictory side of bariatric surgery: late dumping syndrome manifesting as hypoglycemia unawareness and bone fractures

Dominyka Suminskaite[1] and Diana Simoniene[2,3]
[1]Faculty of Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [3]Endocrinology, University of Lithuanian Health Sciences, Kaunas, Lithuania

Introduction: Late dumping syndrome is a recognized long-term complication of Roux-en-Y gastric bypass, characterized by postprandial hyperinsulinemic hypoglycemia due to rapid nutrient delivery to the small intestine and exaggerated incretin-mediated insulin secretion. Clinical manifestations range from adrenergic symptoms to neuroglycopenia, including syncope and impaired hypoglycemia awareness, affecting quality of life. Bariatric surgery is associated with increased bone turnover, reduced bone mass, and an elevated fracture risk.

Case Presentation: A 37-year-old woman with a history of morbid obesity underwent laparoscopic Roux-en-Y gastric bypass. Her preoperative body mass index (BMI) was 37.6 kg/m^2 (106 kg, height 168 cm), which decreased to 25.2 kg/m^2 (71 kg) postoperatively.

Approximately five years after surgery, she developed recurrent postprandial episodes of weakness, tremor, hunger, and progressive neuroglycopenic symptoms, including evening syncope, often triggered by meals or mild physical activity. Capillary glucose monitoring documented hypoglycemia as low as 2.4 mmol/L, while continuous glucose monitoring revealed nadirs of 1.9 mmol/L during symptomatic episodes. Fasting plasma glucose remained normal (5.2 mmol/L).

A mixed-meal tolerance test demonstrated postprandial hypoglycemia with elevated insulin and C-peptide levels, confirming hyperinsulinemic hypoglycemia and supporting the diagnosis of late dumping syndrome. Initial management consisted of dietary modification. Due to persistent symptoms, pharmacological therapy with diazoxide provided only transient improvement. Ongoing severe hypoglycemia and the development of hypoglycemia unawareness (sensory threshold 1.9 mmol/L) prompted escalation to acarbose.

Four years postoperatively, the patient sustained a non-traumatic cervical fracture, followed by a lumbar vertebral fracture associated with elevated CTX levels. Endocrine causes, including Cushing's syndrome and parathyroid dysfunction, were excluded. To address skeletal fragility, calcium citrate and high-dose vitamin D supplementation were initiated, followed by off-label intravenous zoledronate therapy.

Conclusions: Bariatric surgery remains an effective strategy for reducing obesity-related morbidity; however, clinicians must remain vigilant for paradoxical long-term complications, including dumping syndrome–related hypoglycemia and skeletal fragility. This case underscores the challenges of managing complex post-bariatric hypoglycemia and highlights the importance of multidisciplinary follow-up to prevent neuroglycopenic complications and monitor skeletal outcomes.

References

1. Abdelgadir E, Rashid F, McGowan B. The evolution in the management of postbariatric hypoglycemia: a review and comparison between international guidelines from 2017 to 2024. *J Diabetes Endocr Pract*. 2025;8:166–172. https://doi.org/10.1055/s-0045-1809367
2. Mele C, Caputo M, Ferrero A, et al. Bone response to weight loss following bariatric surgery. *Front Endocrinol*. 2022;13:921353. https://doi.org/10.3389/fendo.2022.921353
3. Scarpellini E, Arts J, Karamanolis G, et al. International consensus on the diagnosis and management of dumping syndrome. *Nat Rev Endocrinol*. 2020;16(8):448-466. https://doi.org/10.1038/s41574-020-0357-5

Abstract citation ID: lvag096.1175

EP854 - ECE_3854 - Off-label use of semaglutide (Ozempic®) for weight reduction: a real-world case series of 20 patients

Entela Puca[1,2,3], Sonila Bitri[4], Nereida Xhabija[5], Dea Puca[6] and Edmond Puca[7]
[1]Endokrinology, Western Balkans University, American Hospital, Tiranë, Albania; [2]Endocrinology, Research, Western Balkans University, Tirana, Albania; [3]Endocrinology, Western Balkans University, Tirana, Albania; [4]Western Balkans University, Tiranë, Albania; [5]Cardiology, Western Balkans University, American Hospital, Tiranë, Albania; [6]Lady of Good Counsel University, Tirana, Albania; [7]Infectious Disease, University Center Mother Teresa, Tirana, Albania

Background: Obesity is a chronic metabolic condition closely linked to insulin resistance and increased cardiometabolic risk. While semaglutide 2.4 mg is specifically approved for obesity treatment, lower doses of semaglutide (Ozempic®) are frequently used off-label for weight reduction in everyday clinical practice. However, real-world data describing outcomes with these lower doses remain scarce.

Objective: To evaluate weight loss outcomes and tolerability of off-label semaglutide (Ozempic®) in adults with overweight or obesity in a routine outpatient setting.

Methods: This real-world case series included 20 adult patients (17 women and 3 men) with overweight or obesity, with a mean age of 42 years and a mean baseline BMI of 33 kg/m^2. All patients were managed in an outpatient endocrinology clinic. Semaglutide (Ozempic®) was initiated at 0.25 mg once weekly and gradually titrated according to clinical response and tolerability; all patients reached a maximum dose of 1.0 mg weekly. The mean follow-up period was 6 months. Changes in body

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

weight and BMI were assessed using routine clinical data. Adverse events and treatment discontinuations were systematically recorded. Off-label prescribing was based on clinical judgment and informed patient consent.

Results: After 6 months of treatment, patients experienced a mean weight reduction of 9.8% from baseline, accompanied by a consistent decrease in BMI across the cohort. Gastrointestinal adverse events—primarily nausea and reduced appetite—were reported by 8 patients (40%) and were mostly mild to moderate in severity. Treatment was discontinued in 2 patients due to intolerance. No serious adverse events were observed.

Conclusions: In this real-world case series, off-label use of semaglutide (Ozempic®) at doses up to 1.0 mg weekly was associated with clinically meaningful weight loss over 6 months and an acceptable tolerability profile. These findings suggest that lower-dose semaglutide may be an effective option for weight reduction in routine clinical practice, while underscoring the need for larger prospective studies to better define long-term safety and efficacy.

Keywords Semaglutide, Ozempic®, off-label use, obesity, weight loss, real-world evidence, case series

Abstract citation ID: lvag096.1176

EP855 - ECE_2646 - Type 4 renal tubular acidosis misdiagnosed as diabetic ketoacidosis in a patient with Type 2 diabetes mellitus

Kiran Hullur, Naina Skariah and Bilal Jajah
Darlington Memorial Hospital, Darlington, United Kingdom

Background: Type 4 renal tubular acidosis (RTA) is a rare cause of hyperkalemic metabolic acidosis that can mimic diabetic ketoacidosis (DKA), especially in patients with diabetes and advanced age. Recognition is critical to avoid inappropriate management.

Case Details: A 69-year-old woman with a background of hypertension, obstructive sleep apnea, ischemic heart disease, heart failure, and poorly controlled type 2 diabetes mellitus was admitted with a left axillary abscess requiring incision and drainage. Blood tests on admission revealed raised inflammatory markers, moderate hyponatremia, mild hyperkalemia, metabolic acidosis, hyperglycaemia, and raised ketone levels. Blood cultures grew an ESBL-producing organism, and she was treated with meropenem. Her regular medications including dapagliflozin, metformin, amlodipine, losartan, and spironolactone, were withheld in view of sepsis and electrolyte abnormalities. She was managed as diabetic ketoacidosis (DKA) according to hospital protocol. However, despite six days of treatment, she remained acidotic with worsening hyponatremia and hyperkalemia.

She was subsequently referred to the endocrinology team. Adrenal insufficiency was excluded. It was noted that her anion gap remained normal throughout admission, suggesting that the metabolic acidosis was not primarily driven by DKA, raising suspicion of type 4 renal tubular acidosis (hyporeninemic hypoaldosteronism). Enoxaparin, used for venous thromboembolism prophylaxis, was identified as a likely contributing factor in addition to the longstanding diabetes.

Enoxaparin was discontinued and replaced with fondaparinux, and fludrocortisone therapy was initiated. Biochemical improvement was observed within 24 hours, with normalization of electrolytes and resolution of metabolic acidosis within six days. Fludrocortisone was subsequently discontinued.

Discussion: This case highlights type 4 RTA secondary to enoxaparin masquerading as DKA. Treatment including hypotonic fluids worsened electrolyte disturbances that only normalized after discontinuation of enoxaparin and temporary fludrocortisone therapy.

Low-molecular-weight heparin is commonly used for DVT prophylaxis in hospitalized patients. Heparin has a direct toxic effect on the adrenal zona glomerulosa cells and should be considered as a cause of Type 4 RTA in patients presenting with hyperkalemia, hyponatremia, and metabolic acidosis. Switching to fondaparinux, a synthetic selective factor Xa inhibitor, may be a safer alternative in such scenarios.

Current JBDS and NICE DKA diagnostic criteria do not include anion gap, which may contribute to misdiagnosis in atypical cases, while the American Diabetes Association guidelines recommend it in unclear or atypical presentations.

Assessment of the anion gap is crucial in atypical presentations of suspected DKA and should be emphasized in future national DKA guidelines.

Abstract citation ID: lvag096.1177

EP856 - ECE_2195 - When obesity is a symptom: hypothalamic hamartoma and panhypopituitarism—CASE REPORT

Teresa Alegria Neto[1], Mariana Agapito Fonseca[1], Miguel Duarte[1], Catarina Isabel Lopes[1], Mariana de Griné Severino[1], Marta Vaz Lopes[1], Sónia Do Vale[1,2], Rita Santos[1,2] and Ema Lacerda[1,2]
[1]Endocrinology, Diabetes and Metabolism, ULS Santa Maria, Lisbon, Portugal; [2]Lisbon, Portugal

Panhypopituitarism is a rare condition characterized by global pituitary hormone deficiency, which can present with non-specific symptoms such as weight gain, fatigue or infertility. Hypothalamic hamartomas are uncommon benign malformations that may impair hypothalamic–pituitary function, although a causal relationship is not always demonstrable.

We report the case of a 28-year-old male referred to an Obesity Outpatient Clinic for grade III obesity (BMI 48.2 kg/m^2). The patient was previously of normal weight until the age of 12, when progressive weight gain began during treatment with daily subcutaneous injections for a “growth problem” of unknown specification. He had no dysmorphic features or family history of obesity. Laboratory evaluation revealed secondary hypothyroidism [TSH 1.85 μU/mL (0.30-4.20), FT4 0.72 ng/dL (0.85-1.70)], secondary hypogonadism [FSH 2.0 U/L (1.5-12.9), LH 2.71 U/L (1.3-9.8), testosterone 48.9 ng/dL(240-830)], and low IGF-1 [41.7 ng/mL(135-271)], consistent with panhypopituitarism. Adrenal insufficiency was excluded. MRI of the sellar region showed a 7 mm hypothalamic hamartoma. Previous records confirmed childhood treatment for growth hormone deficiency and secondary hypothyroidism, with an MRI from childhood already documenting the hamartoma, stable since 2005. Multidisciplinary discussion with neurosurgery concluded that the lesion was stable and required no surgical or imaging follow-up. A direct cause-effect could not be established between the presence of the hamartoma and the panhypopituitarism.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Current therapy included levothyroxine and intramuscular testosterone, and after 6 months of levothyroxine and 2 months of testosterone, the patient reported significant clinical improvement, with more energy levels and less depressed mood, with a weight loss of 4 kg.

This case highlights the importance of thorough hormonal assessment in patients with severe obesity. The coexistence of long-standing panhypopituitarism raises diagnostic challenges regarding etiology and emphasizes the need for multidisciplinary management.

Abstract citation ID: lvag096.1178

EP860 - ECE_1154 - Enhancing transition from paediatric to adult endocrine care: a prospective study of patient experience and intervention feasibility

Vera Haidar[1] and Nilanjana Ray[2]
[1]Imperial College London, London, United Kingdom; [2]London, United Kingdom

Objectives: Transition from paediatric to adult endocrine services is a critical period during which young people with chronic conditions are vulnerable to loss to follow-up, suboptimal disease management, and long-term health consequences. Despite national recognition of the importance of high-quality transition pathways, data evaluating the existing transition experience remains limited. This study aims to assess the current transition process and analyse the feasibility of a newly developed structured transition checklist to support pathway optimisation.

Methods: A prospective evaluation was conducted using a standardised questionnaire administered to young people who had transitioned to adult services within the preceding two years. Outcomes included understanding of the transition pathway, preparedness for self-management, perceived support from paediatric and adult teams, and recommendations for improvement. Findings from this initial cycle informed development of a structured transition checklist and accompanying patient information leaflet, guided by validated transition frameworks, Ready Steady Go and the Transition Readiness Assessment Questionnaire (TRAQ).

Results: A total of eight patients completed the survey. Most participants (87.5%) transitioned at age 17, with the remaining 12.5% transitioning at age 16. Nearly two thirds of respondents (62.5%) felt that they had been transitioned too early. Understanding of the transition process was limited, with 75% rating their understanding as 3/5. Preparedness for self-management was also suboptimal, with 37.5% rating this as 2/5 and 37.5% as 3/5.Perceived support declined between paediatric and adult services (mean scores 3.75/5 and 2.9/5, respectively). Notably, no participants received supportive transition materials (including, prompt sheets, checklists, or written transition plans), despite 87.5% indicating that such resources would have been beneficial. Overall satisfaction with the transition process was moderate (mean 3.4/5).

Conclusions: Significant gaps persist in transition preparedness, perceived support, and availability of patient-centred resources within endocrine transition pathways. Young people demonstrated strong receptiveness to structured written interventions. The newly developed transition checklist and patient information leaflet appear feasible for wider implementation, with ongoing work evaluating their longer-term impact on patient experience and engagement.

Abstract citation ID: lvag096.1179

EP866 - ECE_2713 - Continuous glucose monitoring in prediabetes and newly diagnosed type 2 diabetes: a pilot case series

Ilona Rudnieva[1], Nazarii Kobyliak[1,2], Viktoriia Yerokhovych[1], Oksana Klymenko[3], Yeva Ilkiv[1] and Galyna Mykhalchyshyn[1]
[1]Bogomolets National Medical University, Kyiv, Ukraine; [2]Medical Laboratory CSD, Kyiv, Ukraine; [3]Department of Hypoxia, Bogomoletz Institute of Physiology, Kyiv, Ukraine

Introduction: Type 2 diabetes mellitus (T2DM) and prediabetes are major global health challenges due to high prevalence, asymptomatic early stages, and risk of cardiovascular and microvascular complications. By 2050, the number of people with diabetes is projected to reach 852.5 million, with 90%-95% of cases being T2DM. Early detection and glycemic control are crucial, but conventional self-monitoring provides limited insight into daily glucose fluctuations, particularly postprandial. Continuous glucose monitoring (CGM) enables detailed assessment of glycemic variability and may support personalized early management.

Aim: To evaluate the clinical and metabolic utility of CGM in patients with prediabetes and newly diagnosed T2DM.

Materials and Methods: This pilot observational case series included two patients: a 26-year-old woman with prediabetes, obesity class I, and subclinical hypothyroidism, and a 61-year-old man with newly diagnosed T2DM, obesity class I, and hypertension. Both underwent CGM for one month. CGM data were analyzed alongside anthropometrics, body composition, lipid profile, markers of carbohydrate metabolism (fasting plasma glucose, HbA1c, fructosamine, C-peptide, HOMA-2), and health-related quality of life (SF-36). Patients received standard pharmacological therapy and lifestyle guidance tailored using CGM findings.

Results: In the prediabetes patient, baseline HbA1c was 5.7% with normal fasting glucose (4.9 mmol/L). CGM revealed postprandial hyperglycemic excursions not detected by routine labs. After one month, body weight decreased from 88.5 to 85.8 kg, body fat from 46.7% to 43.7%, and visceral fat from 12 to 11. Fructosamine decreased from 225.6 to 218.7 μmol/L, HDL cholesterol increased from 0.95 to 1.1 mmol/L, and quality-of-life scores improved, particularly physical functioning (80→90) and vitality (60→80). In the T2DM patient, baseline HbA1c was 6.73% and fasting glucose 7.27 mmol/L. After one month, fasting glucose decreased to 6.77 mmol/L. Weight remained stable (89.5 kg), but waist circumference decreased from 103 to 100.5 cm, body fat from 33.5% to 31.5%, visceral fat from 20 to 17, and lean mass increased from 59.5 to 61.3 kg. Triglycerides decreased from 1.5 to 1.1 mmol/L, HDL cholesterol increased from 1.1 to 1.3 mmol/L, and emotional well-being improved from 64 to 84.

Conclusions: CGM provides clinically relevant insights into glycemic variability in prediabetes and newly diagnosed T2DM, including postprandial excursions undetected by conventional

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

labs. Even over a short period, CGM-guided management improved glycemic control, body composition, lipid profile, and quality of life. Follow-up assessments at 3 and 12 months will evaluate the durability of metabolic effects, patient motivation, and long-term prevention of disease progression.

Abstract citation ID: lvag096.1180

EP868 - ECE_3991 - Obesity and muscle health in atrial fibrillation: 6-month lifestyle intervention in the ongoing FATBEAT study

Krzysztof Glaser[1,2,3], Mikiko Watanabe[4] and Marek Ruchala[1]
[1]Poznan, Poland; [2]Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza University of Rome, Roma, Italy; [3]Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznań, Poland; [4]Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza University of Rome, Rome, Italy

Atrial fibrillation (AF), the most common sustained arrhythmia, substantially increases stroke, heart failure, and mortality risk. Obesity aggravates AF through systemic inflammation, epicardial and visceral fat accumulation, oxidative stress, and atrial remodeling. Higher BMI and central adiposity consistently associate with increased AF incidence and persistence, and reduced muscle mass and function (sarcopenia) may be an independent risk factor. On the other hand, higher adherence to the mediterranean diet seems protective. Whether muscle mass sparing weight loss achieved through higher adherence to a mediterranean pattern may lead to improved AF outcomes is underinvestigated.

A 70-year-old woman with paroxysmal AF was enrolled in FATBEAT. The patient reported 1-2 monthly AF episodes for the past 6 years; she presented with overweight and central obesity (weight 73.5 kg, height 161.5 cm, BMI 28.2 kg/m^2, waist 90.5 cm, hips 107 cm). Blood pressure 129/85 mmHg, HR 66 bmp.

Right-hand grip strength was 27.5, 24.9, 23.9 kg; sit-to-stand test 18 reps/30s, suggesting preserved muscle mass. However, the SARC-F score 2/10 indicated sarcopenia risk screening (2 points indicate low risk).

The 14-item PREDIMED questionnaire (Prevención con Dieta Mediterránea), a validated Mediterranean diet adherence tool, scored 3/14 at baseline, reflecting poor intake of vegetables, fruits, legumes, nuts, fish, and olive oil. The patient was provided with structured lifestyle counseling targeting PREDIMED improvement without pharmacotherapy, according to the study protocol she was enrolled in.

After 6 months, the patient reported 7% weight loss, with waist and hip circumference reduction (87.5 cm, and 105 cm, respectively). Blood pressure (129/86 to 125/75 mmHg), and heart rate (66 to 62 bpm) improved. Interestingly, grip strength rose markedly (right: 34, 32, 32 kg; left: 20, 29.5, 30 kg), and SARC-F dropped to 1/10, suggesting improved muscle function despite the weight loss. AF episodes totaled 1-2 over 6 months; PREDIMED improved to 8/14.

This case suggests that a structured lifestyle intervention aligning to the mediterranean diet principles may achieve muscle-preserving weight loss, strength gains, and, above all, reduced AF burden in patients with central obesity and AF.

Abstract citation ID: lvag096.1181

EP869 - ECE_2483 - Morphofunctional assessment and in-hospital complications in post-critically ill patients after covid-19 pneumonia as a function of the metabolic disease "continuum"

Víctor Simón-Frapolli[1,2,3], Isabel Mª Vegas-Aguilar[2,4], Isabel Cornejo-Pareja[2,4], Francisco José Tinahones Madueño[2,3,4] and Jose Manuel Garcia-Almeida[2,4]
[1]Hospital Universitario Virgen De La Victoria, Málaga, Spain; [2]Ibima Plataforma Bionand, Málaga, Spain; [3]Facultad de Medicina-UMA, Málaga, Spain; [4]Endocrinology and Nutrition, Hospital Universitario Virgen De La Victoria, Málaga, Spain

Introduction: Patients with elevated cardiovascular risk are a subgroup of patients at increased risk of developing severe COVID-19 disease, a condition associated with a significant in-hospital morbidity and mortality rate. Abdominal obesity (waist circumference ≥102 cm for men or ≥88 cm for women), diabetes mellitus (DM), arterial hypertension (AHT) (figures ≥135/85 mmHg or on treatment), an HDL <40 mg/dl (men) or <50 mg/dl (women) or under treatment, and hypertriglyceridemia (≥150 mg/dl or under treatment) are cardiovascular risk factors (CVRF) that correlate positively with the risk of cardiovascular disease at the population level, and that together (≥3 of them) make up the so-called metabolic syndrome. Likewise, metabolic disease is expressed morphologically as an alteration in muscle mass as well as in the proportion and distribution of body fat mass (adiposity) with a relative increase in visceral fat.

Objective: To determine whether there are differences in body composition as well as in complications during ICU stay and sequalae after admission in post-critical patients with metabolic syndrome with respect to patients without any CVRF and patients with one or more CVRF (DM, hypertension, dyslipidemia and abdominal obesity) without being part of this syndrome.

Method: Prospective observational study including 75 patients who were admitted to the ICU for severe COVID-19 pneumonia. Demographic, clinical and analytical data, medical history, and a complete morphofunctional assessment by bioimpedanciometry with phase angle, nutritional ultrasound, dynamometry and functional tests were performed 14-21 days after hospital discharge. Differences in body composition and complications during hospitalization were analyzed using ANOVA, according to the presence of metabolic syndrome, isolated CVRF or absence of CVRF.

Results: Patients with metabolic syndrome show statistically significant differences compared to patients with isolated CVRF in weight (91.1 ± 18.1 kg vs 105.3 ± 27.4 kg, respectively), BMI (29.4 ± 5.7 vs 32.9 ± 6.7 kg/m^2), as well as in FM% (30.8 ± 7.1% vs 34.7 ± 8.1%). In addition, they present statistically significant differences in ASMMI (7.4 ± 1.5 kg vs 8.4 ± 1.6 kg) and RF-Y axis (1.13 ± 0.3 cm vs 1.41 ± 0.5 cm). No statistically significant differences were observed in functional tests, analytical variables, in-hospital complications, or sequelae after admission.

Conclusions: The presence of metabolic syndrome, with respect to isolated CVRF, shows statistically significant differences in parameters related to low muscle mass (lower ASMMI and RF-Y axis), but in our sample there were no differences in parameters

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

related to visceral adiposity, analytical variables, functional tests, in-hospital complications or sequelae after admission.

Abstract citation ID: lvag096.1182

EP876 - ECE_3911 - Lipodystrophy a rare case of diabetes mellitus-clinical consideration in pediatric patient

Mihaela Kebakoska[1], Cvetanka Volkanovska Ilijevska[2], Irfan Ahmet[2], Marija Zivkovic[3], Aksinja Gabreska Kebakoska[4] and Valentina Velkoska Nakova[5]

[1]General Hospital Prilep- North Macedonia, Prilep, North Macedonia; [2]Diabetes and Metabolic Disorders, Faculty of Medicine, University Clinic for Endocrinology, Ss. Cyril and Methodius University, Skopje, North Macedonia; [3]Prilep, North Macedonia; [4]Center for Public Health, Prilep, North Macedonia; [5]Faculty of Medical Sciences, Goce Delcev University, Internal medicine, Stip, North Macedonia

Abstract: Familial partial lipodystrophy of the Dunnigan type 2 (FPLD2) is a rare autosomal dominant disorder characterized by progressive loss of subcutaneous adipose tissue in the trunk and extremities and an abnormal accumulation of adipose tissue in the face, neck and intrabdominal organs. Metabolic disorders such as insulin resistance, diabetes mellitus, hypertriglyceridemia, MAFLD, and PCOS, invariably accompany FPLD2.

Case Presentation: A 16-year-old female patient, diagnosed with type 2 DM at age 8, was referred to our clinic for endocrine care. The patient appeared athletic, with prominent muscles and veins and no subcutaneous adipose tissue in the trunk and extremities. The Cushingoid appearance was caused by abnormal facial and neck adipose tissue accumulation. Acanthosis nigricans around the neck and generalized hirsutism were present. The gynecologic history was unremarkable. Laboratory results showed hypertriglyceridemia, hyperinsulinemia, and hyperandrogenemia. An ultrasound revealed hepatic steatosis and the fibroscan estimated liver stiffness was 4 kPa. Additionally, we assessed the patient's mother. She suffered a myocardial infarction at 46 and had similar muscle phenotype and subcutaneous fat deficit. We diagnosed her with DM type 2 and dyslipidemia. Genetic validation of FPLD 2 was indicated and results are pending.

Conclusions: Our case report seeks to heighten clinician awareness of FLPD2 in pediatric and adolescent patients. Lipodystrophy typically occurs throughout puberty. A comprehensive clinical evaluation of abnormalities in fat tissue distribution is a prerequisite for clinical suspicion. Recognition of FLPD2 enable patients, and afflicted family members to be adequately screened for cardiometabolic abnormalities, thus enabling timely and targeted interventions.

Keywords familial partial lipodystrophy

Abstract citation ID: lvag096.1183

EP878 - ECE_2743 - Unusual DKA presentation secondary to Budesonide used for IgA nephropathy treatment

Ammar Ahmad and Taimoor Shafiq

Medicine and Specialties, Worcestershire Acute Hospitals NHS Trust, Worcestershire, United Kingdom

Introduction: Budesonide has become one of the most important and effective medication in management of IgA Nephropathy. With improving research and clinical trials, drugs like Budesonide have helped to make breakthrough in reducing the progression of IgA Nephropathy to ESRD and a better control of the disease. At the same time, with wider use of these Budesonide, we have come across unexpected new complications.

This case report highlights newer and unexpected complication in a patient under treatment for IgA Nephropathy with target release Budesonide

Method: I am presenting this case report about patient who presented to A&E with DKA while being on treatment with Budesonide for IgA Nephropathy.

I have used data from the clinic letters and investigations carried out for the patient during his clinic appointments and hospital admission due to DKA. I have used the data from clinics correspondence and correlated it with the investigations and events at the hospital.

Discussion: I am presenting the case of a gentleman in his 40s who was referred to OP Renal clinic for unexplained haematoproteinuria. On subsequent clinic follow ups and investigations, it was established that the patient had IgA nephropathy for which he was started on treatment with ACE inhibitors, SGLT-2 inhibitors and later, he was started on the Budesonide.

While being on treatment with Budesonide for his IgA nephropathy, he presented to A&E with DKA.

He was started on treatment for his hyperglycaemia and followed up by Endocrinology team in the clinic.

On following up the patient in the clinic, it was established that the DKA presentation was secondary to Budesonide use. After stopping Budesonide, his glycaemic control improved and subsequently, his HbA1c and glycaemic control came back to normal range.

Results: This report highlights that we are seeing advancements in clinical care and better outcomes due to the newer medications' availability. At the same time, introduction of these newer drugs like Budesonide may lead to unexpected complications.

As far as I am aware, this is first case report showing DKA secondary to Budesonide use. This case report will help to highlight and adopt better follow up strategies for patients being treated with target release Budesonide.

Abstract citation ID: lvag096.1184

EP879 - ECE_2957 - Correlation between vitamin D deficiency and hyperandrogenism in individuals with insulin resistance

Solomiia Plakhetko[1,2] and Alina Urbanovych[1]

[1]State Non-profit Enterprise "Danylo Halytsky Lviv National Medical University", Lviv, Ukraine; [2]State Non-profit Enterprise "Danylo Halytsky Lviv National Medical University", Lviv, Ukraine

Background and Aims: Vitamin D (VD) deficiency is a prognostic marker influencing the risk of insulin resistance (IR). IR plays a pivotal role in the pathogenesis of obesity, type 2 diabetes mellitus, and polycystic ovary syndrome (PCOS). Currently, the impact of VD on the course of IR is being extensively studied, highlighting its influence on total testosterone and glycated hemoglobin (HbA1c) levels.

Objective: To evaluate the correlation between VD insufficiency/deficiency and hyperandrogenism in patients with IR based on

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

body mass index (BMI) and waist circumference (WC), and to determine their association with HbA1c levels.

Materials and Methods: Our study involved 41 women aged 22 to 45 years, including 24 individuals with alimentary-constitutional obesity (BMI 35,3 ± 5,2 kg/m^2) and 17 overweight individuals (BMI 27,1 ± 2,3 kg/m^2). Laboratory parameters included HOMA-IR index, 25-hydroxyvitamin D (25(OH)D), HbA1c, and total testosterone. Anthropometric data included weight, height, and waist circumference (WC).

Results: VD deficiency was more pronounced in patients with obesity. Levels of 25(OH)D, HOMA index, HbA1c, and total testosterone achieved statistical significance in obese patients (19,8 ± 10,8 ng/mL; 7,9 ± 3,0; 5,8 ± 2,1% %; 2,3 ± 1,1 ng/mL, respectively) compared to overweight individuals (19,8 ± 10,8 ng/mL; 7,9 ± 3,0; 5,8 ± 2,1%; 2,3 ± 1,1 ng/mL, respectively). Additionally, WC was significantly higher in obese patients (102,1 ± 19 cm) compared to the overweight group (84,5 ± 16,5 cm) ($P < .05$).

Lower serum 25(OH)D levels correlated with higher BMI (r = −0,32, $P < 0,05$), whereas HOMA index positively correlated with BMI (r = −0,16, $P < 0,05$). Furthermore, decreased serum 25(OH)D levels correlated with increased HbA1c (r = −0,15, $P < 0,05$). Increased WC was associated with lower 25(OH)D (r = −0,12, $P < 0,05$), higher HOMA-IR (r = 0,39, $P < 0,05$) and elevated total testosterone (r = 0,3, $P < 0,05$).

Conclusions:

1. Patients with obesity exhibit lower VD levels; the deficiency worsens with increasing severity of obesity and HOMA-IR scores.
2. In individuals with obesity and VD deficiency, a significant increase in total testosterone levels is observed.

Abstract citation ID: lvag096.1185

EP881 - ECE_3032 - Severe glycaemic fluctuations post-high-dose glucocorticoid exposure in an adolescent female: pitfalls in diagnosis leading to the diagnosis of Wilson disease

Mariam Kobuladze[1], Shota Janjgava[1,2] and Elene Giorgadze[1]
[1]*National Institue of Endocrinology, Tbilisi, Georgia;* [2]*Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia*

Severe glycaemic fluctuations following high-dose glucocorticoid exposure in an adolescent female: diagnostic pitfalls culminating in the diagnosis of Wilson disease.

Background: Severe glycaemic variability in adolescents is most commonly attributed to diabetes mellitus, endocrine hypersecretion syndromes, or factitious disorders. Exposure to high-dose glucocorticoids may further confound diagnostic evaluation by inducing cushingoid features and accentuating metabolic disturbances. Diagnosis of other metabolic etiologies is essential when glycaemic patterns and conventional diagnostic indices do not correlate.

Case presentation: An 18-year-old female was referred for endocrinological evaluation because of rapid weight gain (12 kg), violaceous striae, facial edema, weakness, headaches, and intense carbohydrate craving following treatment with high-dose systemic glucocorticoids for acute unilateral sensorineural hearing loss. The treatment consisted of high-dose intravenous prednisolone followed by oral tapering, after which cushingoid features developed rapidly.

From early adolescence, the patient had experienced recurrent nocturnal tremor associated with documented hypoglycaemia (plasma glucose 42 mg/dL), as well as marked glycaemic variability with intermittent extreme hyperglycaemia reportedly exceeding 600 mg/dL. Glycaemic indices were markedly discordant: HbA1c values repeatedly ranged between 4.0% and 5.1%, whereas continuous glucose monitoring–derived estimates reached 7.2%. Autoimmune diabetes screening, including antibodies against GAD, IA-2, pancreatic islet cells, and ZnT8, was negative.

Early metabolic assessment demonstrated low fasting insulin (1.27 μIU/mL) and C-peptide (0.5 ng/mL), which later normalized, indicating fluctuating endogenous insulin secretion. Oral glucose tolerance testing showed normal fasting glucose, a modest post-load increase, followed by late hypoglycaemia. Biochemical evaluation revealed mildly elevated plasma noradrenaline, with normal adrenaline and glucagon concentrations. Cross-sectional imaging demonstrated structurally normal adrenal glands, preserved circadian cortisol secretion, and no pituitary or abdominal pathology.

Extended metabolic screening revealed profoundly reduced serum ceruloplasmin and markedly increased 24-hour urinary copper excretion, exceeding diagnostic thresholds for Wilson disease.

Conclusion: High-dose glucocorticoid exposure can induce cushingoid features and exacerbate extreme glycaemic variability, while mild catecholamine elevation may misdirect diagnostic evaluation toward adrenal pathology. The diagnosis of Wilson disease in this patient underscores the importance of considering disorders of copper metabolism in adolescents presenting with unexplained fluctuating glycaemia, discordant HbA1c values, and negative pancreatic autoimmunity. Wilson disease–associated bile acid dysregulation and reduced farnesoid X receptor activity may alter glucocorticoid receptor signaling and cortisol metabolism. Together with reduced cortisol clearance and increased peripheral 11β-HSD1 activity, this might predispose to tissue-specific glucocorticoid excess in the absence of overt hypercortisolism. This case highlights the need for a broad, structured diagnostic approach in complex endocrine presentations.

Abstract citation ID: lvag096.1186

EP884 - ECE_3140 - Patterns of emergency service utilisation in adults with type 1 diabetes attended for acute metabolic disturbances

Víctor Siles-Guerrero, Rosa Natalia García Pérez, Aida Elhadri-Egea and Martín López de la Torre-Casares
Hospital Universitario Virgen De Las Nieves, Granada, Spain

Introduction: Emergency service utilisation related to acute metabolic disturbances remains frequent in adults with type 1 diabetes mellitus (T1DM) and represents a relevant component of diabetes-related healthcare burden. These emergency episodes often reflect underlying clinical vulnerability, impaired symptom recognition, and challenges in day-to-day diabetes self-management. However, real-world descriptive data

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

characterising patterns of emergency utilisation and short-term outcomes in this population remain limited.

Objective: To describe patterns of emergency service utilisation and short-term outcomes in adults with T1DM attended for acute metabolic disturbances.

Methods: An observational, retrospective, descriptive study was conducted including 66 adults with T1DM attended by emergency medical services between 2018 and 2022 due to acute metabolic disturbances. Variables analysed included history of previous emergency attendance for similar events, nocturnal occurrence of the index episode, symptom awareness status, and need for emergency re-attendance during follow-up. Data were analysed using descriptive statistics and are presented without inferential comparisons.

Results: A previous history of emergency attendance for acute metabolic disturbances was present in 54.5% of patients, indicating that more than half of the cohort had experienced recurrent emergency utilisation prior to the index episode. Impaired symptom awareness affected 43.9%, suggesting reduced capacity to recognise early warning signs of acute metabolic imbalance. Nocturnal occurrence was reported in 53.0% of events, highlighting the frequency of episodes arising during periods of reduced monitoring and delayed response. Following the index emergency attendance, 22.7% of patients required at least one further emergency intervention during follow-up. Collectively, these findings illustrate a recurrent pattern of emergency service utilisation within a substantial subset of patients with T1DM.

Conclusions: Among 66 adults with T1DM, emergency service utilisation for acute metabolic disturbances frequently followed a recurrent pattern and was commonly associated with impaired symptom awareness and nocturnal occurrence. These descriptive real-world data suggest that emergency attendance may serve as an important marker of ongoing vulnerability. Systematic analysis of emergency utilisation patterns may help identify patients who could benefit from proactive follow-up, structured reassessment, and targeted preventive strategies aimed at reducing recurrent emergency interventions.

Abstract citation ID: lvag096.1187

EP889 - ECE_1624 - "Educating Families, Empowering patients: the diabetes nurse's role in self-management—a narrative review"

Afroditi Tsalkitzi[1], Despoina Rizikou[1], Anastasia Ntikoudi[1] and Eugenia Vlachou[1,2]
[1]Athens, Greece; [2]Nursing, University of West Attica, Athens, Greece

Background: Diabetes self-management constitutes a complex and demanding process that extends beyond the individual patient and is substantially influenced by the family context. Growing evidence indicates that family support plays a pivotal role in treatment adherence, psychological well-being, and long-term glycaemic outcomes. The diabetes specialist nurse is uniquely positioned to provide structured education and to actively engage family members in facilitating effective diabetes self-management.

Aim: This narrative review aims to examine the contribution of family involvement in diabetes self-management and to emphasise the role of the diabetes specialist nurse in educating and empowering family members to support patients in everyday diabetes care.

Methods: A literature search was conducted across major databases (including PubMed, Google Scholar and Scopus) to identify relevant studies published between 2017 and 2025. Search terms included *"diabetes"*, *"self-management"*, *"family support"*, *"diabetes nurse"* and *"nurse-led education"*. A total of 16 publications met the inclusion criteria and were included in the narrative synthesis.

Results: The reviewed literature consistently indicates that family involvement is associated with improved self-care behaviours, enhanced self-efficacy, better emotional well-being and improved glycaemic outcomes. Family-based diabetes self-management education programmes demonstrate positive effects on adherence to dietary recommendations, glucose monitoring, physical activity and medication regimens. Studies in paediatric populations highlight the mediating role of self-efficacy in the relationship between family support and emotional well-being, while evidence from adult and older populations confirms the value of structured family participation in self-management education. Despite these benefits, family involvement remains insufficiently and inconsistently integrated into routine diabetes care. The diabetes specialist nurse plays a pivotal role in assessing family needs, delivering individualised education, facilitating effective communication and supporting families in adopting supportive rather than controlling behaviours.

Conclusions: The diabetes specialist nurse plays a central role in translating evidence into clinical practice by educating and empowering family members to support diabetes self-management. Integrating structured family education into diabetes care pathways has the potential to improve clinical and psychosocial outcomes. However, further research is required to develop standardised, nurse-led family education models and to evaluate their long-term effectiveness.

Abstract citation ID: lvag096.1188

EP890 - ECE_3267 - Educational level and risk of severe hypoglycaemia in patients with diabetes: a clinical observational study

Aida Elhadri-Egea, Víctor Siles-Guerrero, Rosa Natalia García Pérez and Araceli Munoz-Garach
Hospital Universitario Virgen de las Nieves, Granada, Spain

Background: Effective diabetes self-management is influenced by multiple sociodemographic factors, including educational level. Limited health literacy may impair self-care skills and increase the risk of adverse metabolic outcomes, such as severe hypoglycaemia.

Objective: To evaluate the association between patients' educational level and the frequency of severe hypoglycaemic episodes.

Methods: Data from 66 patients with diabetes were analysed, including educational level and history of severe hypoglycaemia. Patients were stratified according to educational attainment, and comparisons between groups were performed using appropriate statistical tests to assess differences in the occurrence of severe hypoglycaemic events.

Results: Patients with lower educational levels showed a higher frequency of severe hypoglycaemic episodes compared with those with higher educational attainment ($P = .07$). Although this association did not reach conventional statistical

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

significance, a clear trend was observed, suggesting a potential influence of educational level on diabetes self-management and hypoglycaemia risk.

Conclusions: Lower educational level may be associated with an increased risk of severe hypoglycaemia in patients with diabetes. These findings highlight the need for tailored diabetes education programmes adapted to patients' health literacy levels to improve metabolic control and reduce the risk of hypoglycaemia.

Abstract citation ID: lvag096.1189

EP1673 - ECE_1097 - The association between type 2 diabetes and the risk of developing bronchial asthma using the Korean national health insurance service data and upper respiratory disease claims database

Heung Yong Jin[1], Jong Seung Kim[1], Jae Seok Jeong[1], Tae Sun Park[2], Jungmin Kim[3] and Jin Woo Jung[4]
[1]Endocrinology and Metabolism, Jeonbuk National University, Medical School, Jeonbuk National University Hospital, JeonJu, South Korea; [2]Endocrinology and Metabolism, Jeon Ju Hospital, Jeon Ju, South Korea; [3]St.Carollo Hospital, Suncheon, South Korea; [4]Endocrinology and Metabolism, Wonkwang University, School of Medicine, Iksan, South Korea

Background/Aim: Although it has been suggested that diverse chronic diseases besiedes well known micro-/macrovascular complications, including chronic obstructive pulmonary disease (COPD) and bronchial asthma, may be more prevalent among people with type 2 diabetes mellitus (T2DM), the precise causal relationship remains unclear between these chronic diseases and T2DM. Therefore, we investigated the incidence of bronchial asthma or asthma exacerbation in individuals with T2DM compared with those without diabetes using data from the National Health Insurance Service (NHIS) and asthma cohort.

Methods: We conducted a retrospective cohort study using two nationwide databases: (1) a 3.5 million-patient upper respiratory disease claims database (2008-2022) and (2) a 1 million-person cohort from the NHIS (2015-2021). People with T2DM were identified and matched 1:1 to non-diabetic controls using full propensity score matching.

Results: After matching, the cohort included 142 662 T2DM and 142 662 non-diabetic controls (non-DM). During follow-up, people with T2DM exhibited significantly increased risk for bronchial asthma and asthma exacerbation events compared with non-DM (Bronchial asthma-HR 1.08 (95% CI 1.04-1.13), asthma exacerbation-HR 1.97 (95% CI 1.48-2.61) in T2DM vs non-DM). The risk of bronchial asthma and exacerbation tended to increase in people with T2DM irrespective of diabetic peripheral neuropathy (DPN) as follows (bronchial asthma: HR 1.1 (95% CI 0.99-1.22) vs HR 1.12 (95% CI 1.08-1.17) in DM with DPN and DM without DPN vs non- DM in each; asthma exacerbation: HR 2.08 (95% CI 1.1-3.93) and HR 2.06 (95% CI 1.54-2.75) in DM with DPN and DM without DPN vs non- DM in each). However, the risk of both bronchial asthma and exacerbation showed a significant decreasing trend in diabetic patients treated with GLP-1 receptor agonists (GLP 1RA) or with sodium-glucose cotransporter-2 inhibitors (SGLT2Is) as follows (Bronchial asthma HR 0.7 (95% CI 0.6-0.82) in DM treated with SGLT-2Is and HR 0.42 (95% CI 0.1-1.67) in DM treated with GLP-1 RA vs non-DM in each).

Conclusions: Our study showed that the incidence of bronchial asthma tended to be higher and the occurrence of asthma exacerbations was even more common in people with T2DM irrespective of complications such as DPN. Therefore, in addition to the well-known complications of T2DM, further research is warranted to elucidate the potential associations between T2DM and various other chronic diseases that may develop in diabetic patients.

Abstract citation ID: lvag096.1190

EP1678 - ECE_1322 - Maternal exposure and re-exposure at adulthood to a high-fat diet induce long-term alterations to the pancreatic beta-cell morphometry and secretory function in male offspring

Daniele Sales, Adriana Zanella, Carolina Carvalho and Carla Collares-Buzato
Department of Biosciences, Federal University of São Paulo (UNIFESP), Santos, Brazil

Maternal nutrition can influence the metabolism and health of offspring through a process known as metabolic programming, which can lead to lifelong endocrine and metabolic disorders. The cellular and tissue mechanisms involved in metabolic programming are not fully understood, with limited studies addressing the endocrine pancreas. This study investigated the morphometric and functional alterations in pancreatic beta-cells in male offspring from dams fed a high-fat diet (HFD) during pregnancy and lactation, as well as after 30-day re-exposure to this diet in adulthood. C57BL/6 adult mice were mated, and from the first day of pregnancy, dams received either a standard diet (SD) (4.5% fat) or HFD (35% fat). After weaning (day 21), male offspring were maintained on SD until 90 days old and, then, subdivided by diet until euthanasia at 120 days: CON/CON (continuous SD), CON/HF (SD until 90 d, HFD for the last 30 d), HF/CON (HFD during gestation/lactation, SD until euthanasia) and HF/HF (HFD during gestation/lactation and last 30 d). Male offspring aged 12 and 21 days from the HF/CON group exhibited a significant postprandial hyperglycemia, with 21-day-old mice also showing increased body weight compared to the CON/CON group. In contrast, 120-day-old offspring from the HF/CON group displayed decreased body weight and postprandial glycemia, without significant differences in visceral fat, insulinemia, or responses to glucose and insulin tolerance tests compared to the CON/CON group. Meanwhile, the HF/CON adult offspring exhibited marked changes in islet structure, some already detected as early as 12 days of age, including reduced islet area and number per pancreas section, decreased total beta-cell area, smaller beta-cell size, and a lower beta-to-non-beta cell ratio. These islet morphometric alterations in HF/CON mice were accompanied by impairment of the beta-cell cytoskeletal F-actin organization and diminished glucose-stimulated insulin secretion (GSIS) in vitro. Adult HFD exposure induced overweight, increased adiposity, hyperglycemia, hyperinsulinemia, glucose intolerance, insulin resistance, and compensatory beta-cell area expansion, which were similar between the CON/HF and HF/HF groups. HF/HF offspring, however, displayed a more pronounced decrease in GSIS compared to CON/HF and HF/CON groups, suggesting an interaction between

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

early metabolic programming and adult diet. In conclusion, HFD consumption by mothers during pregnancy and lactation induces long-term changes in islet structure and beta-cell secretory capacity in offspring, which may influence their response to further metabolic challenges.

Abstract citation ID: lvag096.1191

EP1680 - ECE_3969 - Statin tolerability in postmenopausal women: influence of SLCO1B1 polymorphism and vitamin D status

Romana Marušić[1,2], Dunja Šojat[3,4], Tatjana Bačun[5,6,7], Nenad Nešković[8,9], Željko Debeljak[10,11], Mirna Glegj[12], Melita Vukšić Polić[13,14] and Saška Marczi[12,15]

[1]Faculty of Medicine Osijek, Osijek, Croatia; [2]National Memorial Hospital "Dr. Juraj Njavro" Vukovar, Vukovar, Croatia; [3]Faculty of Medicine Osijek, Department of Family Medicine, Osijek, Croatia; [4]Health Center of Osijek-Baranja County, Osijek, Croatia; [5]Faculty of Medicine Osijek, Department of Internal clinic, Osijek, Croatia; [6]Faculty of Dental Medicine and Health, Department of Clinical Medicine, Osijek, Croatia; [7]Department of Endocrinology, University Hospital Centre Osijek, Internal Medicine Clinic, Osijek, Croatia; [8]International Medical Center Priora, Čepin, Croatia; [9]Faculty of Medicine Osijek, Department of Anesthesiology and Intensive Care Medicine, Osijek, Croatia; [10]Faculty of Medicine Osijek, Department of Pharmacology, Osijek, Croatia; [11]Clinical Institute of Laboratory Diagnostics, University Hospital Centre Osijek, Osijek, Croatia; [12]Department of HLA Typing and Genomic Diagnostics, University Hospital Centre Osijek, Clinical Institute of Transfusion Medicine, Osijek, Croatia; [13]Faculty of Medicine Osijek, Department of Dermatology, Osijek, Croatia; [14]Department of Dermatology and Venereology, University Hospital Centre Osijek, Osijek, Croatia; [15]Faculty of Medicine Osijek, Department of Medical Chemistry, Biochemistry and Clinical Chemistry, Osijek, Croatia

Background: Variability in statin response and tolerability represents a major challenge in cardiovascular prevention among postmenopausal women. Genetic variation in hepatic statin transport and metabolic factors may contribute to differences in treatment outcomes. This study explored the clinical relevance of the SLCO1B1 c.521T > C variant and baseline vitamin D status in relation to LDL-cholesterol (LDL-C) target attainment and statin-related adverse effects during atorvastatin or rosuvastatin therapy.

Methods: A cohort of 145 postmenopausal women initiating statin therapy was prospectively followed for up to 16 weeks with monthly dose titration to achieve guideline-recommended LDL-C targets. Lipid parameters, liver transaminases, and creatine kinase were monitored throughout follow-up, and treatment-related adverse effects were systematically recorded. SLCO1B1 c.521T > C genotyping and baseline vitamin D assessment were performed, and their associations with treatment response and tolerability were analyzed.

Results: Overall LDL-C target attainment was significantly higher in women treated with rosuvastatin compared with atorvastatin ($P = .02$), accompanied by greater reductions in LDL-C and other atherogenic lipids. SLCO1B1 genotype did not influence lipid-lowering efficacy or dose requirements. In contrast, carriers of the T/C genotype experienced a higher incidence of statin-related adverse effects, particularly during atorvastatin therapy ($P = .008$). Baseline vitamin D status was not independently associated with LDL-C target attainment or adverse effects, although women with severe deficiency tended to show attenuated LDL-C reduction.

Conclusions: In postmenopausal women, SLCO1B1 c.521T > C polymorphism appears to be more relevant for statin tolerability than for lipid-lowering efficacy. Rosuvastatin demonstrated superior overall lipid control and a more favorable safety profile compared with atorvastatin. These findings highlight the potential clinical relevance of pharmacogenetic information for statin selection, particularly in relation to treatment tolerability.

Keywords atorvastatin, pharmacogenetics, postmenopausal women, rosuvastatin, SLCO1B1

Abstract citation ID: lvag096.1192

EP891 - ECE_2921 - Immune checkpoint inhibitor–induced type 1 diabetes mellitus in a patient with breast cancer

Katerina Stefanaki[1,2], Olympia Michalopoulou[3], Vasiliki Marinou[2], Vasiliki Kotsini[3], Sofia Pegka[4], Melpomeni` Moustaki[1,2] and Stavroula A. Paschou[1,2]

[1]Department of Clinical Therapeutics, Endocrine Unit and Diabetes Center, School of Medicine, National and Kapodistrian University of Athens, Alexandra Hospital, Athens, Greece; [2]Department of Clinical Therapeutics, Alexandra Hospital, Medical School of the National and Kapodistrian University of Athens, Athens, Greece; [3]Third Internal Medicine Clinic, Metropolitan General Hospital, Athens, Greece; [4]Endocrinology Department, Amalia Fleming General Hospital, Athens, Greece

Background: Immune checkpoint inhibitors (ICIs) have become an integral part of modern oncological treatment. Despite their clinical efficacy, ICIs are associated with immune-related adverse events, including endocrine complications. New-onset type 1 diabetes mellitus (T1DM) is a rare but severe complication, often characterized by abrupt onset and presentation with diabetic ketoacidosis (DKA). Given the increasing use of ICIs across multiple cancer types, recognition of this complication is of growing clinical relevance for endocrinologists and oncologists alike.

Case Report: We report the case of a 52-year-old woman with no previous history of glucose intolerance who was diagnosed with poorly differentiated breast carcinoma. The patient received neoadjuvant chemotherapy followed by immunotherapy with the anti–PD-1 agent pembrolizumab. Two months after initiation of immunotherapy, she presented to the emergency department with polyuria, polydipsia, and general weakness. Clinical examination was remarkable for rapid heart rate, signs of extracellular volume depletion (dry skin and mucosa) and breath smell of acetone. Initial laboratory work-up revealed severe hyperglycemia (plasma glucose 671 mg/dL), high anion gap metabolic acidosis (arterial pH 7.25, bicarbonate 11.6 mmol/L), and marked ketonuria (+++), confirming the diagnosis of DKA. Of note, glycated hemoglobin was only mildly elevated (HbA1c 6.3%), indicating recent onset of hyperglycemia. C-peptide levels were markedly reduced (0.13 ng/mL), consistent with absolute insulin deficiency, while anti–glutamic acid decarboxylase (anti-GAD) antibodies were positive (80.5 IU/mL), indicating an autoimmune pathophysiological mechanism. Therefore, immune-mediated T1DM related to pembrolizumab was diagnosed. The patient was treated with intravenous fluids, continuous insulin infusion,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and potassium replacement, followed by transition to a basal–bolus insulin regimen.

Conclusions: Immune checkpoint inhibitor–induced T1DM is a rare but serious endocrine adverse event, most commonly associated with PD-1 inhibitors. It is characterized by rapid β-cell destruction and frequently presents with DKA. Glucose monitoring and vigilance are essential for early diagnosis and prompt management of patients receiving immunotherapy.

Abstract citation ID: lvag096.1193

EP892 - ECE_1971 - Occult parathyroid carcinoma presenting as thyroid cystic lesion with cutaneous tract seeding after robotic surgery

Chun-Jen Hsiao and Wei-Yih Chiu
National Taiwan University Hospital, Taipei City, Taiwan

Introduction: Parathyroid carcinoma is a rare endocrine malignancy that may closely mimic benign thyroid disease or thyroid carcinoma, particularly when classic biochemical features of primary hyperparathyroidism are absent. Misclassification at presentation may lead to an inappropriate surgical approach. While minimally invasive and robotic techniques are increasingly used for thyroid disease, their implications in undiagnosed parathyroid carcinoma remain uncertain.

Case Presentation: A 59-year-old woman presented to a local hospital with a progressively enlarging left neck mass and throat discomfort. Neck computerized tomography (CT) scans demonstrated a large cystic lesion in the left thyroid lobe extending into the anterior mediastinum with tracheal deviation, initially suspected to be a thyroid neoplasm. She subsequently underwent robotic bilateral axillo-breast approach thyroidectomy. Histopathologic examination unexpectedly revealed parathyroid carcinoma. Three to four months following surgery, she developed locoregional recurrences in the supraclavicular and contralateral cervical regions, which were treated with repeated excisions. Nine months after surgery, she was referred to our hospital with progressive hypercalcemia and elevated parathyroid hormone levels. Imaging identified recurrent disease in the anterior mediastinum and cutaneous/subcutaneous metastases involving the right breast and chest walls. The anatomic distribution of these metastatic lesions corresponded to the prior robotic surgical access pathway, suggesting cutaneous tract seeding. Despite aggressive surgical debulking, the patient developed recurrent hyperparathyroidism with refractory hypercalcemia, requiring repeated hospitalizations and intensive medical therapy. Tissue genomic analysis identified PTEN loss and a TP53 mutation, neither of which are targetable with available therapies. Ultimately, distant metastases to bone and liver were detected, rendering further curative surgery unfeasible. Given the extent of disease progression and the lack of effective therapeutic options, management focused on controlling hypercalcemia and exploring chemotherapy or immunotherapy as potential treatment approaches.

Conclusions: This case demonstrates how parathyroid carcinoma can mimic a thyroid cystic lesion and remain unrecognized until after robotic surgery performed for presumed thyroid disease. Cutaneous tract seeding emerged as an early recurrence pattern, underscoring the importance of preoperative suspicion and careful selection of the initial surgical approach.

Abstract citation ID: lvag096.1194

EP893 - ECE_2333 - When prostate meets thyroid: incidental follicular thyroid carcinoma detected by PSMA PET/CT—a case report

Ionela-Madalina Gherghe[1], Cristina Capatina[1,2], Medeea Georgescu[1] and Catalina Poiana[1,2]
[1]*'C.I. Parhon' Institute of Endocrinology, Bucharest, Romania;* [2]*Bucharest, Romania*

Background: Prostate-specific membrane antigen (PSMA) PET/CT has become an essential tool in the staging of prostate cancer due to its high sensitivity and specificity. While PSMA expression is often associated with prostate malignancies, increasing evidence has documented its presence in other tumor types, including thyroid carcinomas. The synchronous occurrence of prostate and thyroid cancers remains extremely rare, with only a few cases reported to date, and the putative molecular/pathophysiological links between these malignancies remain largely unexplored.

Case Presentation: We report the case of a 65-year-old man recently diagnosed with poorly differentiated acinar prostate adenocarcinoma (G3, Gleason grade 9), referred for thyroid evaluation following PSMA-PET/CT performed for disease staging. PSMA-PET/CT revealed expected tracer uptake in the prostate and focal uptake in the thyroid. Thyroid ultrasonography demonstrated a $2.2 \times 2.5 \times 3.28$ cm nodule in the inferior pole of the left lobe with iso- and hypoechoic components, classified as TI-RADS 4. Fine needle aspiration biopsy (FNAB) cytology was highly suggestive of poorly differentiated carcinoma (Bethesda VI).

The patient underwent total thyroidectomy and histopathological examination confirmed an encapsulated follicular thyroid carcinoma with angioinvasion and minimal capsular invasion. The initial treatment for prostate cancer included radiotherapy combined with androgen deprivation therapy using Goserelin. Postthyroidectomy, he remains under careful multidisciplinary follow-up, including both urological and endocrinological surveillance, and is scheduled for adjuvant radioiodine therapy.

Conclusions: This case highlights the potential benefit of PSMA-PET/CT not only for prostate cancer staging but also for the incidental detection of other clinically significant pathologies, such as thyroid carcinoma. Clinicians ought to be watchful when interpreting incidental PSMA uptake outside the prostate, further studies being required to evaluate the clinical significance and feasibility of targeted thyroid screening in patients with prostate cancer.

Abstract citation ID: lvag096.1195

EP894 - ECE_3699 - Highly-differentiated follicular carcinoma of ovarian origin: a case report of a rare disease

Renato Diana[1], Claudio Cusini[2] and Livio Luzi[1,2]
[1]*Department of Biomedical Sciences for Health, University of Milan, Milan, Italy;* [2]*Department of Endocrinology, Nutrition and Metabolic Diseases, IRCCS Multi Medica, Sesto San Giovanni, MI, Italy*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Highly-differentiated follicular carcinoma of ovarian origin (HDFCO) is an extremely rare neoplasm consisting of a struma ovarii with extra-ovarian extension.

Clinical case: A 50-year-old woman presents to the gynecology clinic complaining of abdominal pain. On abdominal examination, a mass was palpable in the left iliac fossa. An abdominal CT scan showed an ovarian mass measuring 10 cm. A left hysteroannessiectomy and multiple peritoneal biopsies were performed. Histological examination revealed a mature teratoma with features of struma ovarii, showing an immunophenotype positive for thyroglobulin, TTF-1, synaptophysin and alpha-actin; periuterine fibroadipose tissue showed microlocalizations of well-differentiated thyroid-type follicular structures, consistent with the diagnosis of HDFCO. Thyroid function tests were within normal limits. Thyroid ultrasound revealed three subcentimetric nodules without suspicious features. Thyroglobulin levels in the following months remained within the normal range (3.1 ng/mL), consistent with the presence of a normal volume thyroid. Whole-body Iodine-131 scintigraphy showed physiological uptake in the thyroid bed and multiple focal areas of uptake in the abdominopelvic region. Whole-body 18F-FDG PET/CT scan showed no areas of increased glucose metabolism. Adjuvant radiometabolic treatment with I-131 was indicated following total thyroidectomy. Blood tests performed prior to thyroidectomy confirmed normal thyroid function and slightly increased thyroglobulin levels (9.9 ng/ml) however still consistent with the presence of a normal volume gland. Levothyroxine replacement therapy was introduced after thyroidectomy. Histological examination of the thyroid revealed features of nodular follicular disease. The patient underwent radioiodine therapy (5550 MBq of I-131 administered after levothyroxine withdrawal). At that time, TSH was 51.8 mU/L, thyroglobulin 10.6 ng/mL, and anti-thyroglobulin antibodies 13 U/mL (normal values <115 mU/L). The post-therapy whole-body scan showed increased radioiodine uptake in the thyroid bed consistent with thyroid remnant tissue, and multiple focal areas of radioactive iodine uptake throughout almost all abdominal quadrants, findings compatible with peritoneal disease localization. Six months after radioiodine therapy, the patient, while on levothyroxine replacement therapy at 112 mcg daily, showed suppressed TSH (0.02 mU/L) and undetectable thyroglobulin, indicating a successful response to radioiodine treatment. Given the undetectable thyroglobulin levels, no further whole-body scintigraphy was performed. The patient underwent a contrast-enhanced abdominal CT scan, which showed no pathological findings in the abdominopelvic region. Thyroglobulin levels remained undetectable. Three years after left adnexectomy and one year after radioiodine therapy the patient is disease-free and continues the periodic follow-up. Given the rarity of the disease, there is no shared consensus regarding the optimal therapeutic strategy nor follow-up approach.

Abstract citation ID: lvag096.1196

EP895 - ECE_1555 - Incomplete radiofrequency ablation promotes tumor growth and angiogenesis in thyroid cancer

Chi-Yu Kuo[1], Shih-Ping Cheng[1], Yi-Chiung Hsu[2], Ying-Syuan Li[1] and Shao-Chiang Chang[1]
[1]MacKay Memorial Hospital, Taipei, Taiwan; [2]National Central University, Taoyuan, Taiwan

Background: Radiofrequency ablation (RFA) has emerged as a treatment option for low-risk papillary thyroid cancer, but concerns remain regarding incomplete ablation and its uncertain oncologic consequences. This study investigated the biological effects of sublethal heat exposure on thyroid cancer cells following incomplete RFA.

Methods: NOD/SCID mice with xenograft tumors underwent RFA or sham ablation. Tumor growth was monitored, and histological analyses, including the Ki-67 labeling index and microvessel density, were performed. Additionally, papillary thyroid cancer cell lines were subjected to transient heat treatment. Colony formation, thyrosphere formation, wound healing, invasion assays, and VEGF secretion were assessed.

Results: Following incomplete RFA, xenograft tumors exhibited accelerated growth with scattered viable PAX8-positive cells in necrotic areas. The RFA group demonstrated significantly higher Ki-67 labeling indices and microvessel density compared to the controls. In vitro, transient heat treatment significantly increased colony formation, thyrosphere size, cell migration, and invasion across all cell lines. Heat-treated cells exhibited upregulated expression of cyclin D1, CDK1, ZEB1, N-cadherin, and heat shock proteins. VEGF secretion and HIF-1α expression were elevated, promoting endothelial tube formation. Low-dose ganetespib, an HSP90 inhibitor, effectively mitigated these pro-tumorigenic effects.

Conclusions: Incomplete RFA induces heat stress responses that promote proliferation, migration, invasion, and angiogenesis in thyroid cancer cells. These findings highlight the importance of achieving complete tumor ablation during RFA procedures. Long-term clinical studies are warranted to establish the oncologic safety of RFA for thyroid cancer treatment.

Abstract citation ID: lvag096.1197

EP896 - ECE_2307 - An isolated ovarian tumor tentacles reaches the heart and brain

Tomer Saad, Akirov Amit, Hiba Masri and Ilan Shimon
Kiryat Ono, Israel

Case Report: A 55-year-old woman without any known cardiac history was hospitalized duo to ongoing exercise intolerance. We performed a TEE following a TTE demonstrating massive tricuspid regurgitation and moderate pulmonic, aortic and mitral regurgitation with a patent foramen ovale. Considering the findings and the clinical presentation, we completed a urine collection test showing an elevated 5-hydroxyindoleacetic acid (5-HIAA) level of 95 mg/24 hours. A Gallium-68 PET/CT revealed an isolated pathologic uptake in the left pelvic originating from the ovary. The patient started Somatuline injections and after further imaging and a multidisciplinary discussion, she was scheduled for laparoscopic bilateral salpingo-oophorectomy. During the operation, despite commencing an Octreotide infusion 48 hours prior to the procedure, she underwent a carcinoid crisis. In addition, a brain CT scan showed multiple cardio-embolic ischemic strokes. The patient 5-HIAA and nt-pro-BNP levels are improving and she is recuperating prior to her valve replacement surgery.

Introduction: While Carcinoid Syndrome usually arises from intestinal neuroendocrine tumors, ovarian NETs represent a

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

distinctive group with unique implications on clinical presentation and cardiac involvement. Carcinoid Heart Disease (CHD) occurs in approximately 20%-50% of patients with Carcinoid Syndrome and has a significant impact on prognosis and survival. Ovarian NETs, bypass the portal system and hepatic metabolism, and are associated with CHD even in the absence of liver metastases.

The disease primarily effects right-sided cardiac valves, resulting in regurgitation, stenosis, and eventually right heart failure. Left-sided involvement is less common but may occur in the presence of a patent foramen ovale or extremely high hormone levels. Somatostatin analogues have a key role in the treatment, aiming to control symptoms, reduce serotonin secretion, and prevent cardiac disease progression. In patients with severe symptoms, valves replacement surgery is essential and has demonstrated symptomatic improvement and increased survival.

Conclusions: This case emphasizes how an isolated ovarian carcinoid without any dissemination can lead to severe CHD with right and left side involvement and multiple cardioembolic strokes in the presence of a patent foramen ovale. The decision regarding the optimal timing and order of the tumor removal and valve's replacement is a complex dilemma that should be tailored individually for each patient.

Abstract citation ID: lvag096.1198

EP897 - ECE_1384 - The relevance between mortality in prostate cancer patients receiving androgen deprivation therapy and 5α-reductase inhibitors

Yu-Tang Chen[1], Dai-Wei Liu[2] and Ren-Jun Hsu[3]
[1]*Buddhist Tzu Chi Medical Foundation, Hualien Tzu Chi Hospital, Hualien City, Taiwan;* [2]*Department of Radiation Oncology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien City, Taiwan;* [3]*Hualien City, Taiwan*

Background: Benign prostatic hyperplasia is often treated with 5α-reductase inhibitors (5-ARI), which might affect androgen activity.

Objective: To investigate the association between 5-ARI use and androgen deprivation therapy (ADT) in patients with prostate cancer.

Materials and Methods: This retrospective cohort study linked National Health Insurance (NHI) data with data from the Taiwan Cancer Registry (TCR) and Taiwan Death Registry (TDR) between 1997 and 2016. Prostate cancer patients who received ADT were classified into 5-ARI users and non-users. Inverse probability of treatment weighting (IPTW) was adopted for the primary analysis. The outcomes were overall mortality and prostate cancer-specific mortality. IPTW was used for the sensitivity analysis.

Results: A total of 55 744 patients with prostate cancer were enrolled in this study. Among 44 566 who received ADT, 3332 used 5-ARI, and 35 489 did not, with a mean follow-up of 5.5 years. Compared with non-5-ARI users, 5-ARI users showed no increased risk of all-cause mortality (hazard ratio [HR]: 0.96; 95% confidence interval [CI]: 0.89-1.04) and prostate cancer-specific mortality (HR: 0.96; 95%: CI 0.87-1.06) in the matched analysis. Dutasteride users showed a decreased prostate cancer-specific mortality risk when combined with gonadotropin-releasing hormone (GnRH) agonists and oral antiandrogens (HR: 0.85; 95% CI: 0.73-0.99) in the subgroup analysis.

Conclusions: 5-ARIs were not associated with an increased risk of mortality in prostate cancer patients receiving ADT. This finding provides clinical evidence for the potential safety of 5-ARI use in ADT patients.

Abstract citation ID: lvag096.1199

EP899 - ECE_1632 - Hypoglycemia of tumoral origin: diagnostic challenge of the role of IGF-2

Susana Mallea-Gil, Leyla Vivana Flores Rios, Yamila Sanchez, Bibiana Coca, Cindhy Castro and Carolina Ballarino
Endocrinology, Hospital Militar Central, Buenos Aires, Argentina

Hypoglycemia is a potentially life-threatening condition in which identifying the underlying etiology is essential for therapeutic management. On rare occasions, it may present as a paraneoplastic syndrome associated with the secretion of aberrant forms of insulin-like growth factor 2 (IGF-2) by extra-pancreatic tumors, which exerts insulin-mimetic effects. An elevated IGF-2/IGF-1 ratio constitutes a key biochemical finding.**Clinical Case:** A 49-year-old man with six-month history of lung carcinoma undergoing treatment with pembrolizumab, pemetrexed, and carboplatin presented to Emergency Room with profuse diaphoresis, fever and altered mental status. On admission, severe hypoglycemia was documented: 28 mg/dL, corrected with 25% dextrose. Physical examination: blood pressure 90/60 mmHg, heart rate 97 bpm, temperature 38 °C, oxygen saturation of 96%, bilateral rhonchi and distension with non-tender hepatomegaly. The patient reported unquantified weight loss and night sweats over recent weeks. Laboratory findings: hematocrit 35%, hemoglobin 11 g/dL, leukocytes 15 600/mm^3, neutrophils 75%, sodium 130 mEq/L and potassium 4.3 mEq/L. During dextrose infusion, glucose reached 99 mg/dL. C-peptide levels were normal.

Chest CT revealed bibasilar pneumonia, prompting initiation of ampicillin–sulbactam. Abdominal MRI showed multiple hepatic lesions suggestive of metastases and a 10 × 14 mm nodular lesion in the left adrenal gland compatible with a lipid-rich adenoma.

Due to suspicion of adrenal insufficiency, intravenous hydrocortisone was initiated with clinical improvement, tapering was continued to 30 mg/day; however, the patient again developed symptomatic hypoglycemia, including one episode of 47 mg/dL with insulin levels of 0.75 µUI/mL (2.6-24.9), ruling out endogenous and exogenous hyperinsulinism.

Pituitary profile: cortisol 19.4 µg/dL, IGF-1 <15 ng/mL (90-130 ng/mL), total testosterone 0.22 ng/mL (2.41-8.27 ng/mL), FSH 2.1 mIU/L (1.4-18 mIU/L), LH 1.7 mIU/L (1.5-9.3 mIU/L), and normal thyroid function tests.

In the context of persistent hypoglycemia with suppressed insulin levels, markedly low IGF-1, and positive response to glucocorticoids, aberrant IGF-2 secretion from a non-islet cell tumor was considered the most likely etiology. Fractionated meals and methylprednisolone 20 mg every 12 hours were prescribed, achieving glycemic stability and allowing hospital discharge. The patient died six months after discharge.

Conclusions: IGF-2–mediated paraneoplastic hypoglycemia is a rare, underdiagnosed entity with poor prognosis in Argentina,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

largely due to the unavailability of IGF-2 measurement. Ruling out common etiologies of hypoglycemia, suspecting a paraneoplastic syndrome, integrating the biochemical findings, and observing the favorable response to glucocorticoids were key to establishing a presumptive diagnosis, which proved essential for appropriate management.

Abstract citation ID: lvag096.1200

EP900 - ECE_3120 - Clinical characteristics of medullary thyroid carcinoma according to RET mutation status

Dusan Ilic, Sanja Ognjanovic, Bojana Popovic, Valentina Elezovic Kovacevic, Milica Opalic Palibrk, Lena Radic, Katarina Krstic, Natalija Dragicevic and Djuro MacUt
Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Centre of Serbia, Department for Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia

Background: Medullary thyroid carcinoma (MTC) is a rare neuroendocrine malignancy arising from parafollicular C cells of the thyroid gland. Activating mutations of the RET proto-oncogene play a central role in the pathogenesis of hereditary MTC and MEN2 syndromes and are also detected in a subset of apparently sporadic cases. Although RET mutations are known to influence the clinical and biochemical features of medullary thyroid carcinoma, their impact on disease presentation, tumor burden, and biochemical phenotype at diagnosis varies across reported cohorts and clinical series.

Objective: To compare demographic, clinical, pathological, biochemical, and MEN2-associated characteristics of RET-positive and RET-negative patients with medullary thyroid carcinoma.

Methods: We retrospectively analyzed 433 patients with histologically confirmed MTC who underwent genetic testing for RET mutations. The mean age at diagnosis was 49.3 ± 16.3 years. Age at diagnosis, nodal (N0 vs N+) and distant metastatic status (M0 vs M1), preoperative serum calcitonin levels, and MEN2-associated manifestations, including pheochromocytoma and primary hyperparathyroidism (PHPT), were compared between RET-positive and RET-negative patients. Analyses of nodal and distant metastases were restricted to cases with available staging data.

Results: RET-positive patients were diagnosed at a significantly younger age compared to RET-negative patients ($P < .001$). Among patients with available nodal status ($n = 248$), RET-positive patients had a significantly lower prevalence of nodal metastases at diagnosis compared to RET-negative patients (29.4% vs 44.2%, $P = .024$). Among patients with available distant metastatic status ($n = 187$), the prevalence of distant metastases did not differ significantly according to RET mutation status (8.1% vs 14.2%, $P = .21$). Preoperative serum calcitonin levels tended to be lower in RET-positive patients, although this difference did not reach statistical significance ($P = .074$).

MEN2-associated manifestations were strongly associated with RET positivity. Pheochromocytoma was observed exclusively in RET-positive patients (53.3% vs 0%, $P < .001$), while primary hyperparathyroidism was more frequent in the RET-positive group (16.3% vs 7.7%).

Conclusions: RET-positive medullary thyroid carcinoma represents a distinct clinical phenotype characterized by earlier age at diagnosis, a significantly lower prevalence of nodal metastases, and frequent MEN2-associated manifestations, without an increased burden of distant metastatic disease at presentation. These findings likely reflect earlier detection of disease in genetically predisposed individuals and further support the importance of routine RET genetic testing in all patients with medullary thyroid carcinoma.

Abstract citation ID: lvag096.1201

EP901 - ECE_2369 - Insulin signaling activity in women with breast and endometrial cancer in the setting of type 2 diabetes: the role of obesity and insulin resistance

Tamara Vatseba[1], Liubov Sokolova[2] and Volodymyr Pushkarev[2]
[1]*Endocrinology Department, Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine;* [2]*V.P. Komisarenko Institute of Endocrinology and Metabolism of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine*

Introducion: Recent studies indicate an increased risk of breast cancer (BC) and endometrial cancer (EC) in women with type 2 diabetes mellitus (T2DM). The mechanisms underlying the association between cancer and diabetes include the effects of obesity, hyperinsulinemia, cytokine imbalance, dysbiosis, hyperglycemia, and oxidative stress. These factors exert their effects through intracellular signaling pathways, particularly the insulin signaling PI3K/Akt/mTOR. PRAS40 is a component of this pathway and a physiological inhibitor of mTORC1; its phosphorylation promotes mTOR activation. **The aim** of this study was to assess PI3K/Akt/mTOR pathway activity by measuring phosphorylated PRAS40 (pT246) in women with breast and endometrial cancer diagnosed in the setting of T2DM, and to analyze its association with obesity and insulin resistance.

Methods: Phospho-PRAS40 content in peripheral blood mononuclear cells were measured by enzyme-linked immunosorbent assay (ELISA) using kit KHO0421 (Invitrogen, USA) on a Bio-Tek Instruments microplate reader at 450 nm. Serum insulin and IGF-1 levels were determined using a Stat Fax 303+ automated analyzer with Insulin ELISA EIA-2935 and IGF-1 600 ELISA EIA-4140 kits (DRG, Germany). Insulin resistance was assessed using HOMA-IR. Differences were assessed using Student's t-test. Correlations were analyzed using Pearson's correlation coefficient (r).

Results: Women with T2DM and cancers of both localizations exhibited obesity, insulin resistance, and significantly elevated IGF-1 levels compared with the control group ($P < .05$). Compared with controls, phospho-PRAS40 content were significantly lower in women with T2DM and BC ($t = 9.67$; $P < .001$) and in those with T2DM and EC ($t = 8.26$; $P < .001$). In women with BC, phospho-PRAS40 positively correlated with BMI ($r = 0.738$; $P < .05$) and HOMA-IR ($r = 0.696$; $P < .05$). In women with EC, phospho-PRAS40 positively correlated with insulin ($r = 0.789$; $P < .05$).

Conclusions: Reduced PRAS40 phosphorylation in women with breast and endometrial cancer and T2DM may reflect suppression of PI3K/Akt/mTOR pathway activity, potentially due to

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

competition between signaling pathways and insulin signaling inhibitors. The positive correlation of BMI, HOMA index, insulin, and phospho-PRAS40 supports the role of obesity in PI3K/Akt/mTOR activation involved in oncogenesis.

Abstract citation ID: lvag096.1202

EP903 - ECE_2515 - Peptide receptor radionuclide therapy (PRRT): response assessment and novel approaches

Calin Cristiana[1,2], Iulia Florentina Burcea[1,2], Ramona Dobre[1,2], Teodor Constantin[2] and Catalina Poiana[1,2]

[1]*Endocrinology Department, Carol Davila University of Medicine and Pharmacy, INE C.I. Parhon, București, Romania;* [2]*Endocrinology, Endocrinology I, Institutul National de Endocrinologie C. I. Parhon București, București, Romania*

Introduction: Peptide Receptor Radionuclide Therapy (PRRT) is an advanced systemic treatment with targeted action used for neuroendocrine tumors (NETs), a rare and diverse group of malignancies that arise from neuroendocrine cells. Many of these tumors overexpress somatostatin receptors, allowing PRRT to selectively deliver radiation to tumor cells while minimizing damage to healthy tissues.

Methods: We conducted a retrospective study on 93 patients diagnosed with NETs, of whom 54 (58%) had metastatic disease. Additionally, 15 patients (16.1%) underwent PRRT, including 11 gastroenteropancreatic NETs, 2 lung NETs, and 2 extra-adrenal paragangliomas.

Results: All patients who underwent PRRT had metastatic disease, with liver metastases being the most common (11 patients). They received an average of 3.8 PRRT cycles (±1.46).

Among them, 14 out of 15 patients (93.3%) received PRRT with beta emitters ([177]Lu), while 1 patient (6.7%) underwent treatment with both beta ([177]Lu) and alpha emitters ([225]Ac). Moreover, 12 out of 15 patients (80%) received PRRT with somatostatin receptor agonists, while 3 (20%) underwent combination therapy with both a somatostatin agonist (DOTATOC) and an antagonist (DOTA-JR11 or DOTA-LM3). Regarding treatment response, 8 out of 15 patients (53.3%) had stable disease, 4 (26.7%) achieved a partial response, 2 (13.3%) experienced progressive disease, and 1 patient (6.7%) had a complete response, according to RECIST criteria. The progression-free survival (PFS) was 23.25 months (±27.2 months). Among these patients, 5 died (33.3%), with a median overall survival (OS) of 17.8 months (±10.9).

Conclusions: In conclusion, the efficacy of PRRT in treating patients with metastatic NETs, according to this study, was notable, with 53.3% of patients experiencing stable disease and 26.7% achieving a partial response. Furthermore, combination therapies, including the use of somatostatin receptor agonists and antagonists, as well as the administration of alpha emitters in one case, suggest additional potential in improving therapeutic responses and overcoming tumor resistance.

Abstract citation ID: lvag096.1203

EP905 - ECE_3681 - The picture of adrenocortical carcinoma recurrence upon mitotane in adjuvant setting in a cohort from Central Europe Center

Agnieszka Kotecka-Blicharz[1], Kornelia Hasse-Lazar[1], Jordi Gras-Ozimek[1], Alexander Cortez[2], Tomasz Gawlik[1], Aleksandra Sygula[3], Magdalena Wyciślik[1], Łukasz Kluczyński[1], Barbara Jarząb[1] and Daria Handkiewicz-Junak[1]

[1]*Department of Nuclear Medicine and Endocrine Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice, Poland;* [2]*Department of Biostatistics and Bioinformatics, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice, Poland;* [3]*Gliwice, Poland*

As adrenocortical carcinomais the malignancy known for its preponderance to relapse, adjuvate therapy is a crucial issue in patient management.The clinical justification for the use of adjuvant therapy is to reduce the risk of local and distant recurrenceand/or improve survival. Mitotane is the mainstay of adjuvant treatmentin adrenocortical carcinoma.

The main objective of the study was to assess the characteristics oradrenocortical recurrence upon adjuvant mitotane treatment depending on known risk factors.

We retrospectively reviewed medical recordsfrom the Department of Nuclear Medicine and Endocrine Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, atertiary center in Poland. We identified 88 patients treated with mitotane in the adjuvant setting between 2002 and 2024. The exclusion criteria wereENSAT stage IV andR2 resection. The date of recurrence was defined as the date ofradiological evidence of a new neoplastic lesion.Recurrence-free survivalwas calculated from thetime of initial surgeryto the first radiological evidence of recurrence. The risk of recurrence was assessed according to ENSAT stage, Ki67, and hormonal activity.

Among the 88 patients, 22 (25%) patients were in the ENSAT IIIstage. Ki67 above 10% was confirmed in 39 patients (44%). In 17 patients (19%), resection was evaluated as R1.Recurrence was confirmed in 50% of patients receiving adjuvant mitotane treatment. However, in the subgroup of patients with Ki 67 between 10 and 20% recurrence rate was 66,7% and in Ki67 >20% reached70%. Regardingthe ENSAT stage,the relapse occurred in11,1% patients withENSAT I stage, 52,4% with the ENSAT II, and 45,4% in the ENSAT III stage.The median time to recurrence was 28 months (range 1-258).66% of recurrences occurred within 24 months. The median follow-up timewas 42 months (range 2-288). In both univariate and multivariate analyses, Ki67 andENSAT stage were factors significantly influencing the risk of recurrence. A significant effect of tumor hormonal activity on the risk of recurrence was confirmed only in univariate analysis.

Reported data show a stillhigh recurrence rate in adrenocortical carcinomapatients with with Ki 67 >10% despite mitotaneadjuvant treatment.The results raisethe need for more individualized and maybe more aggressive adjuvant treatmentin adrenocortical carcinoma patients with high Ki67.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1204

EP906 - ECE_2666 - Surgical management of ectopic Cushing syndrome from a pulmonary carcinoid supported by intraoperative ACTH monitoring

Agata Pokrzywa[1], Janusz Pachucki[2], Jan Domański[2,3], Zuzanna Roszkowska[4], Lukasz Koperski[5], Dariusz Wąsowski[6], Malgorzata Bobrowicz[2] and Urszula Ambroziak[2]

[1]Department of Internal Medicine and Endocrinology, University Clinical Center of the Medical University of Warsaw, Warsaw, Poland; [2]Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland; [3]Doctoral School of the Medical University of Warsaw, Medical University of Warsaw, Warsaw, Poland; [4]Student Scientific Club "Endocrinus" Affiliated to the Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland; [5]Department of Pathology, Medical University of Warsaw, Warsaw, Poland; [6]Department of Thoracic Surgery, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland

Introduction: The crucial element in the management of Cushing's syndrome (CS) is the establishment of the source of hormonal excess, thus enabling proper treatment. In cases of ectopic CS, however, this task is challenging as illustrated by the present case.

Case Presentation: A 36-year-old man was referred to the Endocrinology Department for the evaluation of hypercortisolemia. On admission he reported 15-kg weigh gain and muscle mass loss, and presented with overt cushingoid features (facial rounding and plethora and violaceous striae on the abdomen and upper limbs) and hypertension (180/110 mmHg). Biochemical testing confirmed hypercortisolemia with elevated urinary free cortisol (UFC): 3623 ug/24 h, elevated night salivary cortisol: 2.84 ug/dL, morning serum ACTH 115.5 pg/mL and borderline hypokaliemia 3.51 mmol/L. The dynamic testing including high-dose dexamethasone suppression test (HDDST), overnight single-dose metyrapone test and desmopressin stimulation test were performed. In the HDDST there was partial suppression of serum cortisol (to 18.6 ug/dL) and supression of UFC to 130 ug/24 h, in the metyrapone test 80% decrease in serum cortisol and 33% rise in serum ACTH, and in the desmopressin test 13% rise in serum cortisol and 44% rise in serum ACTH. Taking into consideration the results of dynamic tests, the Cushing's disease (CD) was suspected, however no focal abnormality was detected on contrast-enhanced pituitary MRI. Chest CT revealed an irregular 8×6 mm contrast-enhancing nodule in segment 3 of the left lung. The decision was made to apply visible tumor resection strategy, assuming that the lung lesion is the source of the hormonal excess. Intraoperative ACTH level monitoring was performed to support the diagnosis. The patient underwent thoracoscopic wedge resection of a suspicious lesion. A marked ACTH surge instead of decline was observed after excision, and intraoperative pathology revealed a neuroendocrine tumor near the resection margin. The procedure was therefore extended to an upper lobectomy, after which ACTH levels showed a rapid and sustained decline. After surgery, the patient experienced weight loss and normalization of arterial blood pressure with biochemical normalization consistent with remission.

Conclusions: This case highlights the diagnostic challenges associated with ectopic CS, particularly in situations in which endocrine test results mimic those of CD and imaging studies are non-definitive. Intraoperative ACTH measurement may serve as an excellent tool to navigate the location of a tumor and confirm the total resection.

Abstract citation ID: lvag096.1205

EP907 - ECE_1299 - Predominantly noradrenaline-producing adrenal phaeochromocytoma in a 24-year old presenting with neurological and cardiovascular symptoms

Nicholas Lo and Zhi Wen Loh

Department of Endocrinology, Tan Tock Seng Hospital, Singapore, Singapore

A young man presented to the Emergency Department with a thunderclap headache, described as the worst headache of his life. He did not have any significant past medical history but had a strong family history of young hypertension, with his brother and father having been first diagnosed with hypertension at a young age. Physical examination was unremarkable but vitals monitoring showed paroxysms of hypertension with systolic blood pressure >200 mmHg.

Secondary hypertension work up showed a right suprarenal mass first noted on an ultrasound renal artery doppler scan. CT adrenals showed 2 nodules of the right adrenal, one 4.3 cm and the other 2.5 cm in diameter. The left adrenal was normal. Hormonal evaluation with 2 samples of 24-hour urine catecholamines and metanephrines showed raised noradrenaline and normetanephrines more than 10 times the upper limit of normal. Urine adrenaline levels were normal and urine metanephrine levels were mildly elevated only in the first sample. A Gallium 68-DOTATATE scan was performed to evaluate for metastases and other sources of noradrenaline secretion, which showed tracer avid right adrenal nodules suspicious for phaeochromocytoma and no evidence of distant metastases. The diagnosis of a solitary right adrenal pheochromocytoma was made.

The patient was treated with pre-operative alpha blockade with phenoxybenzamine, and atenolol was added later on due to reflex tachycardia the patient experienced. The right adrenal gland was resected with an open right adrenalectomy and repeat 24-hour urine catecholamines and metanephrines showed normalization post-operatively.

Noradrenaline-producing adrenal phaeochromocytomas such as in this case are an unusual presentation as phaeochromocytomas originating from the adrenal medulla usually primarily secrete metanephrines. This is due to the presence of the enzyme phenyl ethanolamine N-methyltransferase (PNMT) exclusively located in the adrenal glands, regulated by cortisol, which converts noradrenaline to adrenaline. Moreover the clinical presentation of this patient was atypical showing paroxysms of hypertension. Noradrenaline-producing phaeochromocytomas typically show sustained hypertension, while adrenaline-producing tumours typically show paroxysms of hypertension.[1]

Reference

1. Ito Y, Fujimoto Y, Obara T. The role of epinephrine, norepinephrine, and dopamine in blood pressure disturbances in patients with pheochromocytoma. *World J Surg*. 1992;16(4): 759-763; discussion 763-4. doi: 10.1007/BF02067379.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1206

EP908 - ECE_2080 - Aggressive multisystem MEN2A due to a RET p.Cys634Trp mutation: recurrent pheochromocytoma, metastatic medullary thyroid carcinoma, and primary hyperparathyroidism

Ana Khvedelidze[1], Mariam Bardadze[2], Lika Tetradze[2], Nino Gvajaia[2], Nikoloz Tepnadze[2] and Tamaz Mgaloblishvili[1]

[1]*American MD (USMD) Program, Tbilisi State Medical University, Tbilisi, Georgia;* [2]*Endocrinology, Tbilisi State Medical University, Tbilisi, Georgia*

Background: Multiple Endocrine Neoplasia type 2A (MEN2A) caused by pathogenic RET mutations is associated with medullary thyroid carcinoma (MTC), pheochromocytoma, and primary hyperparathyroidism. Mutations affecting RET codon 634 are linked to a particularly aggressive phenotype with early onset, metastatic disease, and recurrence. We report a genetically confirmed MEN2A case illustrating the multisystem, recurrent nature of codon 634-associated disease.

Case Presentation: A 55-year-old woman presented with episodic hypertensive crises. Imaging revealed bilateral adrenal masses consistent with pheochromocytoma, supported by markedly elevated plasma metanephrines. Right adrenalectomy confirmed pheochromocytoma with moderate proliferative features; left adrenal disease was managed conservatively. Subsequent longitudinal follow-up demonstrated persistent adrenal lesions and a stable pulmonary nodule.

Biochemical evaluation later revealed hypercalcemia with inappropriately elevated parathyroid hormone levels, hypercalciuria, and nephrolithiasis, consistent with primary hyperparathyroidism. Genetic testing identified a heterozygous RET c.1900C>G (p.Cys634Trp) mutation, confirming MEN2A.

Total thyroidectomy with lymph node dissection demonstrated medullary thyroid carcinoma with lymph node metastases and lymphovascular invasion, alongside incidental papillary thyroid microcarcinomas. Postoperatively, calcitonin and carcinoembryonic antigen levels remained persistently elevated. Functional imaging showed uptake consistent with recurrent pheochromocytoma and probable parathyroid adenomas.

Discussion: This case highlights the aggressive and persistent clinical course associated with RET codon 634 mutations, characterized by bilateral and recurrent pheochromocytoma, metastatic MTC, and biochemical primary hyperparathyroidism. Persistent postoperative calcitonin elevation and recurrent functional imaging findings emphasize the need for vigilant long-term surveillance. Incidental papillary thyroid microcarcinomas may coexist with MEN2A-associated MTC and should not distract from the dominant disease biology.

Conclusions: MEN2A associated with RET p.Cys634Trp mutations can manifest as an aggressive, multisystem, and recurrent endocrine neoplasia syndrome. Lifelong biochemical monitoring, periodic functional imaging, and early genetic screening of relatives are essential to optimize outcomes in affected patients.

Abstract citation ID: lvag096.1207

EP909 - ECE_2236 - RNA-exosome dysregulation: core and PAXT complexes as novel mediators of MASLD-HCC oncogenesis

María Isabel Pozo-Relaño[1,2,3,4], Víctor J. Fernández-Ramírez[1,2,3,4], Samanta Lozano de la Haba[1,2,3,4], Manuel Rodriguez-Peralvarez[1,5,6], Raul M. Luque[1,2,3,4], Juan Luis López-Cánovas[1,2,3,4] and Manuel D. Gahete[1,2,3,4]

[1]*Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Cordoba, Spain;* [2]*Cordoba, Spain;* [3]*Department of Cell Biology, Physiology and Immunology, University of Cordoba, Cordoba, Spain;* [4]*Reina Sofia University Hospital Cordoba, Spain;* [5]*CIBER Obesity and Nutrition (CIBERobn), Madrid, Spain;* [6]*Department of Hepatology and Liver Transplantation, Reina Sofia University Hospital, Cordoba, Spain*

Metabolic-associated steatotic liver disease (MASLD) has emerged as the primary chronic liver dysfunction worldwide, frequently culminating in the development of hepatocellular carcinoma (HCC). Emerging evidence underscores the critical importance of RNA metabolism and surveillance in liver pathophysiology, where the RNA-Exosome complex plays a decisive role. Nevertheless, the precise molecular mechanisms and the specific contributions of this machinery during the pathological transition from metabolic steatosis to malignancy remain to be fully elucidated.

Our objective was to characterize the dysregulation of various RNA-Exosome complexes across the MASLD-HCC spectrum and to explore their subsequent clinical and functional implications. To this end, we evaluated the expression profile of the RNA-Exosome machinery across 18 independent cohorts (2 retrospective and 16 *in silico*) of MASLD, Metabolic Dysfunction-Associated Steatohepatitis (MASH), MASH-related HCC, HCC and control (normal or adjacent tissue) samples. To identify the most relevant alterations, we employed VIP-score (Variable Importance in Projection) ranking, selecting those complexes that exhibited the most significant dysregulation within tumor samples (Top-10 VIP-score). Clinical associations and Gene Set Enrichment Analysis (GSEA) were complemented by extensive *in vitro* and *in vivo* functional assays through the targeted molecular modulation of representative complex components.

Our results demonstrate a profound and progressive dysregulation of the RNA-Exosome machinery, with a generalized overexpression from early MASLD to HCC. Specifically, the Core and PAXT complexes emerged as the most altered machineries across all cohorts. High expression of these complexes, represented by key components such as EXOSC4 (Core) and ZFC3H1 (PAXT), significantly correlated with poor overall survival, increased invasiveness, and the enrichment of oncogenic pathways like MYC targets and mTOR signaling. In vitro silencing of these specific components significantly reduced tumor aggressiveness parameters (cell proliferation, migration, colony formation, and sphere-forming capacity), whereas their overexpression promoted a more malignant phenotype. Crucially, in vivo studies confirmed the pro-tumorigenic potential of the machinery, where silencing Core components inhibited tumor growth, while its induction significantly increased tumor volume and progression.

In conclusion, our findings demonstrate that the RNA-Exosome machinery, driven by its Core and PAXT complexes, is a critical

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

regulator of the MASLD-HCC axis. This study highlights the entire RNA-Exosome machinery as a promising source of prognostic biomarkers and a novel therapeutic vulnerability in the context of metabolic dysregulations and, specifically, MASLD-HCC.

Funding: ISCIII (PI23/00652, co-funded by the European Union), JdA (PI-0046-2024, BIO-0139), FSEEN, CIBERobn and CIBERehd.

Abstract citation ID: lvag096.1208

EP910 - ECE_2626 - Predictors of malignancy in pheochromocytoma and paraganglioma

Mirjana Đukić[1], Ivana Kraljevic[2,3], Mirsala Solak[2], Annemarie Balaško[2], Anja Barac Nekic[2], Tanja Skoric Polovina[2], Karin Zibar Tomsic[2], Hrvoje Popovac[2], Tina Dusek[2,3] and Darko Kastelan[2,3]

[1]Department of Endocrinology, General Hospital „Dr. Ivo Pedišić", Sisak, Croatia; [2]Department of Endocrinology, University Hospital Centre Zagreb, Zagreb, Croatia; [3]School of Medicine, University of Zagreb, Zagreb, Croatia

Background: Pheochromocytomas and paragangliomas (PPGL) are rare neuroendocrine tumours lacking definitive histopathological criteria for malignancy. About 15-20% of PPGLs show malignant potential, necessitating long-term follow-up. This study aimed to identify clinical and biochemical predictors of malignant PPGL.

Methods: A total of 94 patients with PPGL were included. Malignancy was defined by the presence of metastatic disease at initial diagnosis or during follow-up. Tumour size, age at diagnosis, and urinary metanephrines were compared between patients with benign and malignant disease. Time-to-event outcomes were analysed using Kaplan–Meier estimates.

Results: Malignant PPGL was identified in 14/94 (14.9%) patients, with a median follow-up of 77.5 months (IQR 25.5-129.5). Malignant tumours were significantly larger compared to benign (median 77.5 mm vs 50 mm, $P < .001$), and tumour size demonstrated good discriminatory performance for malignancy (ROC AUC 0.810). A tumour size ≥68 mm predicted malignancy with 71% sensitivity and 84% specificity. Patients with malignant PPGL also had higher urinary normetanephrine levels (median 84.28 µmol/dU vs 12.1 µmol/dU; ROC AUC 0.875), with a cut-off of 34.1 µmol/dU corresponding to 82% sensitivity and 83% specificity. No significant difference in age at diagnosis was observed between benign and malignant PPGL.

Conclusions: Large tumour size and markedly increased urinary normetanephrines may serve as predictive markers of malignant PPGL, warranting closer follow-up.

Abstract citation ID: lvag096.1209

EP911 - ECE_2884 - Anti-secretory and anti-proliferative actions of next-generation dual subtype 2 and 5 somatostatin receptor ligands in neuroendocrine tumor models

Margarita Bistika[1], Francesco Fedeli[1], Francesco Ascione[1], Alessandro Marangelo[2], Fabio Guzzi[1], Joerg Schrader[3], Alan Harris[4] and Natalia Pellegata[1]

[1]1Department of Biology and Biotechnology "L. Spallanzani", University of Pavia, Pavia, Italy; [2]Helmholtz Munich, Neuherberg, Germany; [3]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [4]Grossman School of Medicine, New York, United States

Introduction: First-generation somatostatin receptor ligands (SRLs) mainly target SSTR2, whereas neuroendocrine tumors (NETs) often express multiple SSTR subtypes, frequently SSTR5. Dual SSTR2/SSTR5 targeting may enhance anti-hormonal and antiproliferative effects. We evaluated five novel dual SSTR2/SSTR5 agonists (SMTR-001 to SMTR-005) in preclinical NET models to assess their anti-secretory and anti-proliferative effects in representative preclinical NET models.

Methods: The human insulinoma-derived NT-3 cell line and the murine AtT-20 corticotroph cell line, both expressing SSTR2 and SSTR5, were treated with 1-50 nM of the novel SRLs or reference agents (octreotide, pasireotide). Insulin and ACTH secretion were quantified by ELISA and cell viability was measured after 72 h (AtT-20) or 5 days (NT-3). A putative lead compound, SMTR-002, was further tested in 3D spheroid cultures of NT-3 cells. Intracellular cAMP modulation was evaluated after forskolin stimulation in AtT-20 cells.

Results: In NT-3 cells, all dual SRLs inhibited insulin secretion (−65% to −95%), with SMTR-002, SMTR-004, and SMTR-005 showing significantly greater inhibition than octreotide at 10 nM. Each compound also reduced cell proliferation (−30% to −44%). In 3D cultures of NT-3 cells, SMTR-002 reduced insulin secretion to a degree comparable to octreotide but, unlike octreotide, significantly decreased cell proliferation. In AtT-20 cells, four novel SRLs significantly reduced ACTH secretion (-11% to -69%), with SMTR-001 and SMTR-004 showing efficacy comparable to pasireotide. SMTR-002 and SMTR-003 demonstrated the greatest antiproliferative effects (−53% and −48% at 10 nM). In AtT-20 cells, SMTR-002 also suppressed forskolin-induced cAMP accumulation more strongly than reference SRLs.

Conclusions: Dual SSTR2/SSTR5 agonists exhibit antisecretory and antiproliferative activity in NET models that was similar or even superior to reference SRLs. These findings support their further development as next-generation SRLs for SSTR2/5-expressing tumors.

Abstract citation ID: lvag096.1210

EP912 - ECE_3058 - Multianalyte or multiple monoanalytes? A comparison of serum visfatin and chromogranin A as diagnostic biomarkers in neuroendocrine tumors

Paweł Komarnicki, Jan Musiałkiewicz, Adam Maclejewski, Michalina Czupińska, Elżbieta Wrotkowska, Paweł Gut and Marek Ruchala

Department of Endocrinology, Metabolism and Internal Diseases, Poznan University of Medical Sciences, Poznan, Poland

Background: Chromogranin A (CgA) remains the most widely used Neuroendocrine Tumor (NET) biomarker, despite its suboptimal sensitivity and specificity. Initial reports about serum visfatin, an adipocytokine involved in inflammation and metabolic regulation, demonstrate moderate diagnostic performance in NETs versus healthy controls. However, its performance has not been directly compared with established NET biomarkers.

Aims: To compare the diagnostic performance of serum visfatin and chromogranin A in pancreatic and small intestinal

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

neuroendocrine tumors, and to evaluate whether their combined assessment improves diagnostic discrimination.

Methods: Serum visfatin and CgA levels were analyzed in 77 patients with NETs (33 pancreatic NETs, 44 small intestinal NETs) and 29 healthy controls. Group comparisons were performed using Mann–Whitney U tests. Diagnostic performance was evaluated using receiver operating characteristic (ROC) curve analysis. Paired ROC curves were compared using DeLong's test, and classification performance between biomarkers was assessed using McNemar's test.

Results: Median visfatin and CgA concentrations were significantly higher in all NET patients compared with controls ($P = .007$ and $P = .018$, respectively) as well as in pancreatic NETs ($P = .019$ for visfatin; $P = .018$ for CgA). In small intestine NETs, only visfatin showed a significant increase ($P = .007$), while CgA did not ($P = .062$). Visfatin and CgA demonstrated comparable diagnostic performance for NETs versus controls (AUC 0.68 [95% CI 0.57-0.78] vs 0.65 [0.55-0.75]), with no significant difference in DeLong's test ($P = .72$). Similarly, no differences in ROC performance were observed between biomarkers in panNETs ($P = .96$) or siNETs ($P = .57$). A combined visfatin–CgA model improved discrimination compared with standalone biomarkers (AUC 0.75), although with borderline statistical significance ($P = .08$).

Conclusions: Serum visfatin demonstrates diagnostic performance directly comparable to chromogranin A in NETs and provides more performanceacross tumor subtypes. The improved performance of combined biomarkers suggests a complementary rather than competing role, supporting further evaluation of visfatin as NET biomarker.

Abstract citation ID: lvag096.1211

EP916 - ECE_1781 - Large symptomatic simple hepatic cysts as the presenting feature of primary neuroendocrine tumor: a diagnostic pitfall

Hitam Hagog Natour[1], Nadim Abu Rashed[2], Pnina Rotman-Pikielny[1,3], Feda Fanadka[2] and Michal Kasher Meron[1,3]

[1]Meir Medical Center, Institute of Endocrinology, Diabetes and Metabolism, Kfar Saba, Israel; [2]Department of Radiology, Meir Medical Center, Kfar Saba, Israel; [3]Gray Faculty of Medical and Health and Sciences, Tel Aviv, Israel

Primary hepatic neuroendocrine tumors (pHNET) represent an exceedingly rare neuroendocrine neoplasm that may present with nonspecific symptoms or be incidentally discovered as a large hepatic mass during imaging for unrelated reasons. We report the case of a 46-year-old woman who presented to the emergency department with persistent abdominal pain and unintentional weight loss. Cross-sectional imaging demonstrated two large cystic lesions (largest measuring 14 cm) involving both hepatic lobes, without apparent solid components, mural nodularity, or radiologic features suggestive of malignancy. Given the benign radiologic appearance, conservative management with clinical surveillance was recommended. However, the patient was lost to follow-up and re-presented one year later with worsening abdominal pain and mild elevation of liver enzymes. Repeat imaging demonstrated slight interval increase in the size of the cystic lesions, prompting surgical unroofing for symptomatic relief.

Histopathological examination and immunohistochemical analysis revealed a Grade 2 neuroendocrine tumor, Ki67 of 3%. Ga-68 DOTATATE PET/CT staging demonstrated widespread metastatic disease involving multiple lymph nodes and osseous sites, without identification of an extrahepatic somatostatin receptor-expressing lesion. She was treated with somatostatin analog therapy, showing stable disease on 6-month follow-up imaging. The patient remained clinically asymptomatic for carcinoid syndrome throughout the disease course.

This case highlights a diagnostic pitfall: pHNET may present as predominantly cystic lesions that mimic benign entities on conventional imaging, potentially delaying diagnosis. Maintaining a low threshold of suspicion for malignancy in large or symptomatic hepatic cysts is essential for timely diagnosis and appropriate management.

Keywords primary hepatic neuroendocrine tumors, liver cyst

Abstract citation ID: lvag096.1212

EP917 - ECE_2843 - Primary thyroid lymphomas—from suspicion to confirmation

Andreea-Cristina Stanciu, Ionela Baciu, Dan Alexandru Niculescu, Dumitru Alina Maria, Daniela Balosache, Anda Dumitraşcu, Dana Cristina Terzea and Catalina Poiana

Bucuresti, Romania

Introduction: Primary thyroid lymphoma (PTL) is a rare malignancy of the thyroid gland, accounting for less than 5% of all thyroid cancers. Due to its rapid growth and compressive symptoms PTL often mimics aggressive thyroid carcinomas, particularly anaplastic thyroid carcinoma, making early diagnosis challenging but crucial, given its significantly better prognosis when treated appropriately.

Objectives: To highlight the diagnostic challenges, clinical presentation, and therapeutic outcomes of primary thyroid lymphoma through a case series, emphasizing the importance of appropriate biopsy techniques and multidisciplinary management.

Methods: We present a case series of three elderly patients (two males aged 78 and 85 years, and one female aged 75 years) admitted into our clinic in the last 3 years for rapidly enlarging cervical thyroid masses associated with compressive symptoms such as dysphagia, dysphonia, and dyspnea. All patients had biochemical and imaging features suggestive of autoimmune thyroid disease. Diagnostic workup included thyroid function tests, autoantibody assessment, neck ultrasound, computed tomography or magnetic resonance imaging, fine-needle aspiration biopsy (FNAB), core needle biopsy, histopathology and immunohistochemistry. Treatment regimens and outcomes were documented.

Results: Clinical presentation with rapid onset of compressive symptoms was highly suggestive of anaplastic thyroid carcinoma and FNAB was non-diagnostic or misleading in all cases, showing either low cellularity or raising suspicion for undifferentiated carcinoma. Definitive diagnosis was established only after core needle biopsy or surgical lymph node excision with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

immunohistochemically confirmation of the diagnosis. Corticosteroid administration led to rapid symptomatic improvement regarding the compressive symptoms. All patients were referred to hematology and treated with chemotherapy regimens (CHOP or R-CHOP) with favourable clinical and imagistic responses, despite advanced local disease at diagnosis. At the time of this analysis all patients were alive, one of them being in complete remission.

Conclusions: Primary thyroid lymphoma should be suspected in patients presenting with rapidly enlarging thyroid masses especially on a background of autoimmune thyroiditis. FNAB alone is often not sufficient for diagnosis, and core needle biopsy with immunohistochemistry represents the gold standard. Early recognition is essential, as PTL responds well to chemotherapy, even in advanced stages, and unnecessary extensive surgery can be avoided. Multidisciplinary collaboration is key to optimizing outcomes in this rare but treatable condition.

Abstract citation ID: lvag096.1213

EP918 - ECE_2056 - Correlation of loss of ATRX expression with scintigraphic imaging studies in pancreatic neuroendocrine neoplasms

Marina Tsoli[1], Maria Panagaki[1], Christina Papadima[1], Georgios Kyriakopoulos[2,3] and Gregory Kaltsas[1]
[1]*Endocrine Unit, 1st Department of Propaedeutic Internal Medicine, Laiko Hospital, National and Kapodistrian University of Athens, Athens, Greece;* [2]*Department of Histopathology, Evagelismos General Hospital, Athens, Greece;* [3]*Athens, Greece*

Background: Somatic inactivating mutations of ATRX (α thalassemia/mental retardation syndrome X-linked) in pancreatic neoplasms (panNENs) are associated with aggressive phenotype and are considered an independent prognostic factor of poor overall survival.

Aims: The aim of this study was to evaluate the correlation of ATRX loss, as assessed by immunohistochemistry, with scintigraphic imaging data in patients with panNENs.

Materials and Methods: We collected retrospectively the data of patients with panNENs in whom immunohistochemistry for ATRX loss was performed and we evaluated the relationship of genetic alterations with nuclear imaging studies.

Results: We analyzed the data of 81 patients (31 female) with mean age (±SD) at diagnosis 56.6 ± 11.8 years. 17 patients had grade 1 panNEN, 55 grade 2 and 9 well-differentiated grade 3 panNEN. 38 (46.9%) patients suffered from stage IV disease. 26 (32.1%) patients presented loss of ATRX. 76 patients (34.2% with loss of ATRX) had positive somatostatin receptor scintigraphy. No significant difference was observed, regarding the SRS positivity, in patients with loss or retain of ATRX ($P = .112$). 47 patients (8 with loss of ATRX) underwent an FDG-PET/CT. Significantly higher percentage of patients with grade 3 pNEN had positive FDG-PET/CT compared to patients with grade 1 or 2 pNEN ($P = .01$). No significant difference was observed, regarding the FDG-PET/CT positivity, in patients with loss or retain of ATRX ($P = .337$). No significant correlation was observed between the loss of ATRX and FDG-PET/CT positivity (r-0.14, $P = .347$).

Conclusions: The loss of ATRX does not seem to affect the results of scintigraphic imaging studies in patients with panNENs.

Abstract citation ID: lvag096.1214

EP919 - ECE_3814 - Therapeutic challenges in medullary thyroid carcinoma with paraneoplastic Cushing syndrome

Stanescu Laura-Semonia[1,2], Andrei Muresan[2], Teodor Constantin[2], Dumitru Ioachim[2] and Corin Badiu[1,2]
[1]*Endocrinology, Endocrinology IV, "C Davila" University of Medicine and Pharmacy, Bucharest, Romania;* [2]*Research Department, Endocrinology IV, C.I. Parhon National Institute of Endocrinology, București, Romania*

Introduction: Medullary thyroid carcinoma is a rare neuroendocrine malignancy, and in fewer cases associates paraneoplastic Cushing's syndrome (PCS) through ectopic secretion of ACTH. Severe hypercortisolism drives rapid clinical deterioration, substantial morbidity, and often reflects aggressive tumor biology. We describe four cases that illustrate the heterogeneous presentation, complex biochemical evolution, and demanding multimodal management.

Case 1: A 70-year-old woman was referred with metastatic MTC diagnosed after biopsy of a left axillary lymph node. She presented with dyspnea, proximal muscle weakness, and marked hypokalemia, with calcitonin 174 000 pg/mL, CEA > 1000 ng/mL, ACTH 156 pg/mL, cortisol 58 µg/dL. Imaging revealed extensive cervical, mediastinal, hepatic, and pulmonary metastases, hyperplastic adrenal glands, and a normal pituitary. Germline RET testing was negative. After thyroid surgery, tumor immunostaining confirmed ectopic ACTH production, then vandetanib was initiated to 300 mg/day, resulting in biochemical improvement (calcitonin 82 000 pg/mL, ACTH 28 pg/mL, cortisol 13 µg/dL).

Case 2: A 53-year-old man presented with a rapidly enlarging cervical mass, hypertension, hyperglycemia and cushingoid habitus. Initial biochemical evaluation demonstrated MTC with PCS: calcitonin 1950 pg/mL, CEA 97.9 ng/mL, ACTH 115 pg/mL, elevated urinary free cortisol (>1590 µg/24 h). Imaging revealed an invasive right-sided thyroid mass, normal adrenals and pituitary. He underwent total thyroidectomy with extensive neck dissection; Immunohistochemical examination confirmed ectopic ACTH and somatic RET M918T mutation identified. Vandetanib was initiated for persistent MTC and PCS, with improvement of biochemical markers (calcitonin 58.3 pg/mL, CEA 13.7 ng/mL, ACTH 15.07 pg/mL, cortisol 10.46 µg/dL).

Case 3: A 20-year-old man initially underwent left adrenalectomy for presumed adrenal Cushing syndrome, but ACTH-dependent hypercortisolism soon recurred with a new pituitary micronodule, leading to pituitary radiotherapy and later right adrenalectomy. Six months later, a thyroid and mediastinal mass were detected, and biopsy confirmed MTC, presumed to be the ectopic ACTH source. He underwent cytoreductive thyroidectomy with mediastinal mass resection, with preoperative calcitonin >900 pg/mL and ACTH 88 pg/mL.

Case 4: A 53-year-old woman presented with metastatic MTC and PCS, calcitonin >2000 pg/mL, ACTH 153.8 pg/mL, morning cortisol 49.81 µg/dL, and marked hypokalemia. CT imaging revealed an invasive right-lobe thyroid mass with cervical lymph-node, hepatic, and bone metastases, hyperplastic adrenal glands, and a normal pituitary. Medical stabilization was unsuccessful, necessitating bilateral adrenalectomy as rescue therapy.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: MTC-associated PCS remains a rare, life-threatening presentation marked by severe biochemical instability and complex management. Early recognition and rapid cortisol control are essential, but outcomes improve significantly when targeted systemic therapies are available.

Abstract citation ID: lvag096.1215

EP920 - ECE_3044 - Improving thyroid nodule malignancy prediction on ultrasound through contrastive learning and curriculum-based fine-tuning

Ana-Silvia Corlan[1,2,3], Costi Flavia[4] and Darian Onchis[2]
[1]*Internal Medicine, Endocrinology, University of Medicine and Pharmacy Timisoara, Timisoara, Romania;* [2]*Faculty of Sciencies, PhD student, Computer Science, West University of Timisoara, Timisoara, Romania;* [3]*Artificial Intelligence, Endocrinology, West University of Timișoara, University of Medicine and Pharmacy Timisoara, Timișoara, Romania;* [4]*Faculty of Sciencies, Computer Science, West University of Timisoara, Timisoara, Romania*

Background: Ultrasound is the first-line imaging modality for thyroid nodules, yet malignancy risk stratification remains challenging due to inter-observer variability and the limited availability of biopsy-proven annotated datasets. We aimed to evaluate whether contrastive self-supervised learning, combined with confidence-based curriculum fine-tuning, can improve data-efficient thyroid nodule classification on ultrasound.

Methods: We implemented a contrastive learning framework using a SimCLR-style architecture with a ResNet encoder to learn ultrasound-specific feature representations without labels. Self-supervised pretraining was performed using ultrasound-appropriate augmentations (ROI-based cropping, horizontal flipping, noise injection, and intensity scaling). The pretrained encoder was subsequently fine-tuned for malignancy classification on the publicly available TN5000 dataset (5000 thyroid nodules with cytological or histopathological confirmation).

To further improve training stability and generalization, we incorporated **confidence-based curriculum learning**, whereby training samples were progressively introduced from high-confidence ("easy") to low-confidence ("hard") cases based on model-predicted malignancy probabilities. Model performance was evaluated on a held-out test set and compared with a baseline convolutional neural network trained from scratch.

Results: Contrastive self-supervised pretraining substantially improved feature quality, yielding clearer separation between benign and malignant nodules in the learned embedding space. On the TN5000 test set, the SimCLR-initialized model with staged fine-tuning achieved a higher discriminative performance than the baseline CNN (AUROC 0.905 vs 0.880).

Incorporation of confidence-based curriculum learning further stabilized optimization and improved the sensitivity–specificity trade-off. At a fixed decision threshold of 0.5, the contrastive model demonstrated fewer false-positive classifications among benign nodules while maintaining high sensitivity for malignancy detection. Overall, the combined approach resulted in a more favorable clinical error profile compared with conventional supervised training.

Conclusions: Contrastive self-supervised learning enables robust feature extraction from unlabeled thyroid ultrasound data and significantly enhances malignancy risk stratification when combined with large annotated datasets such as TN5000. The addition of confidence-based curriculum learning further improves training efficiency and generalization in this noisy imaging domain. This data-efficient strategy may complement existing structured reporting systems and support more consistent AI-assisted decision-making in thyroid imaging.

Limitations: The study is limited by reliance on a single public dataset for labeled fine-tuning and the absence of prospective multi-center validation.

Abstract citation ID: lvag096.1216

EP922 - ECE_1974 - Efficacy and tolerability of fezolinetant administration after current diagnosis of prostate cancer in an elderly man with acquired childhood-age hypergonadotropic hypogonadism

Massimo Giusti[1,2,3,4] and Giulia Graziani[5]
[1]*Endocrine Unit, Centro Clinico Diagnostico Priamar, Savona, Italy;* [2]*Department of Internal Medicine, University of Genoa, Genoa, Italy;* [3]*Centro Clinico Diagnostico Priamar, Endocrine Unit, Savona, Italy;* [4]*Centro Clinico Diagnostico Priamar, Savona, Italy;* [5]*Endocrine-Metabolic Unit, ASL2 Savonese, Savona, Italy*

Background: Vasomotor symptoms (VMS) are the most frequently described effects of androgen withdrawal in men. Testosterone (T) is the standard treatment for VMS, but suspected or diagnosed prostatic cancer often limit its use.

Case Presentation: An 88-year-old man came to our attention for uncomfortable VMS, mainly nocturnal sweating. VMS were long-standing and had been alleviated by oral/transdermal T. The man had undergone surgery for cryptorchidism at the age of 6 years; at 18 years of age he was deemed fit for military service, and at 25 years of age was married. Male infertility was subsequently documented. After 2013, he was unavailable for endocrinological examination, and T was discontinued.

Objective and Clinical Data: Normal male behaviour, glabrous facies and few pubic hairs. Empty scrotal sac and no evidence of testes on imaging. Low serum T (0.25 ng/mL), high FSH (31 mIU/mL) and normal-for-age PSA (3.86 ng/mL) were found.

Intervention: In November 2023, the patient started monthly (250 mg i.m.) T administration, which relieved VMS. After 3 months, plasma T was 2.0 ng/mL, but PSA had risen to 17.5 ng/mL. T was stopped. Multi-parametric MRI, followed by prostate fusion needle biopsy (July 2024) were diagnostic for prostate cancer (Gleason score 3+4). Leuprolide acetate and bicalutamide were started.On anti-androgenic drugs, plasma T was < 0.1 ng/mL, PSA 0.8 ng/mL, LH <1 mIU/mL, and FSH 22 mIU/mL. In July 2025, the patient provided written consent to start fezolinetant (45 mg/day orally), an NK3R-antagonist. He was asked to register relevant VMS daily, have liver function and hormones checked, and fill in the self-rating Kellner Symptoms Questionnaire (KSQ).

Results: On fezolinetant, liver function remained normal and FSH decreased to 3 mIU/mL, while PSA (<0.1 ng/mL), plasma T (<0.1 ng/mL) and LH (<1 mIU/mL) remained unchanged.The median number of major VMS decreased from 9/week to 0/week. During brief discontinuation of the drug, due to its temporary unavailability, VMS did not exceed 3/week.All KSQ scales (anxiety,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

depression, somatization, hostility) improved. The greatest improvement was in somatization, with a 78% reduction. No structural progression of prostate cancer was observed.

Comment: Fezolinetant was well tolerated and efficacious in this man, now 91 years old. VMS, particularly nocturnal sweating disappeared and quality of life improved markedly. Interestingly, fezolinetant seems to increase the suppression of the hypothalamus-pituitary-gonadal axis (FSH) due to anti-androgen treatment. Long-term follow-up will be necessary in order to ascertain the impact of fezolinetant on prostate cancer progression.

Abstract citation ID: lvag096.1217

EP924 - ECE_3201 - Thyroid metastasis from renal cell carcinoma: an uncommon clinical presentation

Carlos Lopez Sarmiento, Maria Elena Jerez Arzola, Pablo Delgado Moya, Jonay Rodríguez Morales, Virginia Collantes Alcalá, Diego García Gonzalez, Bárbara Alonso Moreno, Covandonga Rodríguez Mangas and Said Mohamed Said
Hospital Universitario Doctor José Molina Orosa, Arrecife, Spain

Introduction: Clear cell renal cell carcinoma (ccRCC) most frequently metastasizes to the lungs, bones, and liver, with thyroid involvement being rare.

Case Description: A 64-year-old woman with a history of arterial hypertension, migraine with aura, allergic asthma, scoliosis, and spondyloarthrosis, as well as a left hemithyroidectomy in 2000 for a benign nodule and Hashimoto's thyroiditis. She had multiple drug allergies and a history of severe intolerance to octreotide. In December 2015, she was diagnosed with G2 ccRCC, stage pT2aNx, and underwent right radical nephrectomy with laterocaval lymphadenectomy.

In March 2019, she developed oligometastatic gastric recurrence, treated with subtotal gastrectomy with Roux-en-Y reconstruction, D1 lymphadenectomy, and cholecystectomy. Subsequently, she developed severe dumping syndrome and malabsorption, resulting in severe caloric-protein malnutrition requiring multiple admissions to Endocrinology, prolonged parenteral nutrition support, and close follow-up due to sarcopenia risk. After a slow initial course, her nutritional status progressively improved, allowing discontinuation of home parenteral nutrition in 2020.

During oncological follow-up, imaging studies between 2019 and 2021 showed no evidence of active disease. However, in April 2024, the patient noticed the sudden appearance of a painful, rapidly enlarging right cervical mass, associated with compressive symptoms (dyspnea, orthopnea, and dysphagia). Cervical ultrasound revealed a nodular right thyroid with a predominantly cystic dominant lesion (TIRADS 2) and two solid nodules (TIRADS 4). Fine-needle aspiration (FNA) of the solid nodules was benign, but core needle biopsy of the cystic lesion confirmed thyroid metastasis from clear cell renal carcinoma, with immunohistochemistry positive for vimentin, CD10, and cyclin D1, and negative for thyroglobulin.

The case was evaluated by a multidisciplinary head and neck tumor board, and palliative decompressive surgery was recommended due to compressive symptoms. In November 2024, a right hemithyroidectomy was performed, confirming histopathologically a 2×1.5 cm thyroid metastasis from ccRCC with free surgical margins. Concomitant pulmonary micrometastases were also identified and confirmed by biopsy.

Given stage IV disease and an intermediate IMDC score, first-line systemic therapy with sunitinib was initiated, with dose adjustments for hematologic and gastrointestinal toxicity. At subsequent follow-up, the patient shows partial response with clinical stability, continuing joint monitoring by Oncology and Endocrinology.

Conclusions: Thyroid metastases from ccRCC typically appear years after the initial diagnosis and can mimic benign thyroid disease. This case highlights the rare thyroid localization of renal cell carcinoma metastasis and the associated nutritional management challenges.

Abstract citation ID: lvag096.1218

EP925 - ECE_2224 - When obesity masks hypoglycaemia: insulinoma presenting with rapid weight gain

Arfa Ahmed Assad, Shahroz Azhar, Huriya Siddique, Muhammad Murtaza Shafqat, Hira Irfan and Ayesha Amin
Endocrinology, Internal Medicine & Endocrinology, Pakistan Kidney And Liver Institute & RC, Lahore, Pakistan

Background: Insulinomas are rare pancreatic neuroendocrine tumors, occurring in 1-4 per million individuals and accounting for 1-2% of pancreatic neoplasms. Diagnosis is often delayed due to their variable and nonspecific presentations. Patients may present with hypoglycemia or neuroglycopenic symptoms, which are frequently misattributed to neuropsychiatric, cardiac, or neurological disorders, prolonging the time to diagnosis. We report a case in which rapid, unexplained weight gain was the predominant presenting feature, ultimately leading to the diagnosis of a pancreatic insulinoma.

Case Presentation: A 35-year-old male presented to an obesity clinic with a 40 kg weight gain over two months, resulting in a body mass index of 43.8 kg/m^2. He had no known comorbidities, and initial evaluation including thyroid function tests, cortisol, and routine metabolic panels was unremarkable. On further history, he reported intermittent dizziness, tremors, palpitations, and two episodes of transient loss of consciousness. Laboratory evaluation during symptomatic episodes revealed hypoglycemia with a plasma glucose of 42 mg/dL. Further testing showed a low HbA1c of 3.5%, with inappropriately elevated insulin (163 pmol/L) and C-peptide (10.6 ng/mL), confirming endogenous hyperinsulinemic hypoglycaemia. Sulfonylurea screening was negative and a supervised 72-hour fasting test reproduced hypoglycemia with adrenergic and neuroglycopenic symptoms, fulfilling Whipple's triad. Contrast-enhanced MRI revealed a 2.8 cm well-circumscribed lesion in the pancreatic tail, hypointense on T1 and hyperintense on T2 sequences, with homogeneous arterial enhancement, initially raising suspicion for a solid pseudopapillary neoplasm. Endoscopic ultrasound localized a hypervascular mass consistent with insulinoma. Evaluation for multiple endocrine neoplasia type 1 was negative, with normal serum calcium, parathyroid hormone, prolactin, and pituitary hormone levels.The patient underwent laparoscopic enucleation, and histopathology confirmed a well-differentiated

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

benign pancreatic neuroendocrine tumor with strong immunopositivity for insulin, chromogranin A, and synaptophysin. Postoperatively, hypoglycemia resolved completely, body weight decreased from 113 kg to 84 kg over four months, and HbA1c normalized to 5.4%, with transient mild hyperglycemia resolving conservatively. He continues routine follow-up with fasting glucose monitoring and imaging surveillance.

Conclusions: This case highlights the importance of comprehensive diagnostic evaluation in patients presenting with rapid weight gain, including the consideration of neuroendocrine tumors when clinical history or associated symptoms suggest hypoglycemia. Meticulous history-taking and attention to subtle neuroglycopenic or adrenergic features can prevent delayed diagnosis and avoid potentially life-threatening complications.

Abstract citation ID: lvag096.1219

EP927 - ECE_1191 - The spectrum of endocrine paraneoplastic syndromes in neuroendocrine neoplasms: real-world data from a tertiary referral center

Christina Papadima[1,2], Maria Evangelia Koloutsou[1,2], Marina Tsoli[1,2], Maria Panagaki[1,2], Georgios Kyriakopoulos[3,4], Aggeliki Karapanagioti[1,2], Anna Angelousi[1,2] and Gregory Kaltsas[1,2]

[1]European Reference Network on Rare Endocrine Conditions (ENDO-ERN), Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece; [2]First Department of Propaedeutic and Internal Medicine, Athens, Greece; [3]Evangelismos Hospital, Athens, Greece; [4]Department of Pathology, Athens, Greece

Introduction: Endocrine paraneoplastic syndromes (EPNS) are rare but clinically relevant manifestations of neuroendocrine neoplasms (NENs), resulting from ectopic hormone secretion, complicating diagnosis, delaying tumor identification, and adversely affecting patient management and morbidity. Although EPNS have been reported in up to 8-15% of patients with NENs, real-world data regarding the prevalence of clinically overt EPNS, timing of presentation, and impact on management across several NEN subtypes remain limited.

Methods: Retrospective analysis of 1218 patients with histologically confirmed NENstreated at our center. The cohort comprised 767 pancreatic NENs, 214 thoracic NENs (lung and thymus), 153 NENs of unknown primary origin (UOP), and 84 pheochromocytomas/paragangliomas. Demographic characteristics, histologic features, type and timing of EPNS onset, therapeutic strategies, and follow-up outcomes were systematically collected and analyzed.

Results: EPNs were identified in 21/1218 patients (1.7%), all with well-differentiated NENs (mean age 65 years; 16 males). Ectopic adrenocorticotropin (ACTH) secretion was observed in 15 (71%), parathyroid-hormone-related-peptide (PTHrP) secretion in 4 (19%), and calcitonin secretion in 2 patients (9%) respectively.

The most frequent primary tumor site was pancreatic NEN in 10 patients (48%, 1.3% of pancreatic NENs), followed by thoracic primaries in 9 patients (42%, 4.2% of thoracic NENs) (6 lung and 3 thymus). One patient had a pheochromocytoma, while another had a tumor of UOP. EPNS-related clinical features preceded tumor diagnosis and prompted further diagnostic evaluation in 9 patients (42.9%), were synchronous to diagnosis in 5 patients (23.8%) and developed meta-chronously in 7 patients (33.3%).

First-line surgical treatment was performed in 11 patients (52%). Patients with unresectable or metastatic disease (15 patients, 71%) required multimodal non-surgical management, including molecularly targeted therapies, systemic chemotherapy, peptide receptor radionuclide therapy, and radiotherapy. Despite optimized medical treatment, 5 patients (24%) ultimately underwent bilateral adrenalectomy for refractory Cushing's syndrome. During follow-up, 2 patients (10%) remained disease-free after first-line surgery, while 9 patients (43%) died, reflecting the high morbidity associated with EPNS.

Conclusions: EPNs are associated with high clinical complexity and heterogeneous outcomes. ACTH secretion and pancreatic neuroendocrine tumors predominated in this cohort. Compared with the existing literature, the lower prevalence observed likely reflects the inclusion of clinically overt endocrine paraneoplastic syndromes only, excluding subclinical hormone secretion and isolated immunohistochemical hormone expression.Early recognition, prompt hormonal control, and multidisciplinary management are essential to optimize patient outcomes. Real-world data from specialized centers provide valuable insights into these rare conditions.

Abstract citation ID: lvag096.1220

EP928 - ECE_2155 - Outcomes and prognostic factors in ectopic cushing syndrome: the experience of two tertiary referral centers

Gustaw Laskowski[1], Zuzanna Roszkowska[2], Lukasz Dzialach[1], Malgorzata Bobrowicz[2], Urszula Ambroziak[2] and Przemysław Witek[1]

[1]Department of Internal Medicine, Endocrinology, and Diabetes, Warszawski Uniwersytet Medyczny, Warszawa, Poland; [2]Department of Internal Medicine and Endocrinology, Warszawski Uniwersytet Medyczny, Warszawa, Poland

Ectopic Cushing syndrome (ECS) is an uncommon cause of ACTH-dependent Cushing syndrome associated with high morbidity and mortality. Systemic inflammation-based scores (SIBS) are accessible prognostic tools in oncology, but their value in ECS remains uncertain.

We performed a retrospective observational study of patients with ECS managed at two tertiary endocrinology referral centers in Warsaw, Poland, between February 2004 and October 2025. Demographic, tumor-related, clinical, and biochemical variables at diagnosis were extracted from a dedicated database. SIBS (neutrophil-to-lymphocyte ratio [NLR], platelet-to-lymphocyte ratio [PLR], lymphocyte-to-monocyte ratio [LMR], and systemic immune-inflammation index [SII]) were calculated from baseline laboratory parameters. To minimize confounding by acute inflammation, patients with C-reactive protein (CRP) >5 mg/L were excluded from SIBS analyses. The final cohort included 30 patients.

Primary tumor sites were the lung (60%), pancreas (10%), thymus (3%), bladder (3%), adrenal gland (3%), and occult origin (20%). Metastatic disease was present in 65% of patients. Survival was markedly heterogeneous, with a median survival of 50.61 days. Tumor resection was performed in 45% and was associated with improved survival compared with non-surgical management (log-rank test, $P = .0119$; HR = 0.225, $P = .0230$). Higher ACTH, morning cortisol, and late-night cortisol

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

concentrations were associated with increased mortality risk (HR = 1.002, $P = .0014$; HR = 1.023, $P = .0003$; HR = 1.027, $P = .0037$). Interestingly, patients who developed metastatic disease demonstrated significantly higher ACTH levels compared to those without metastases ($P = .0015$). After excluding CRP-elevated cases, NLR correlated with ACTH (r = 0.575; $P = .0157$) and morning cortisol (r = 0.658; $P = .0041$), while PLR correlated inversely with ACTH (r = −0.607; $P = .0098$). Notably, none of the evaluated SIBS predicted survival, although the strongest non-significant trend was observed for NLR ($P = .0994$).

ECS is characterized by frequent metastatic disease, severe hypercortisolism, and poor early survival. Surgical resection, when feasible, is associated with significantly better outcomes. Baseline ACTH concentration and the severity of hypercortisolism may have prognostic relevance for overall survival. Hormonal state correlates with inflammatory indices, but SIBS did not independently predict survival in this cohort. However, larger datasets are required to clarify their prognostic significance.

Abstract citation ID: lvag096.1221

EP932 - ECE_3520 - Initial clinical presentation differs substantially between ectopic Cushing's syndrome and Cushing's disease and could be the reason for the diagnostic delay. ERCUSYN Krakow database

Aleksandra Gamrat-Żmuda[1,2], Mari Minasyan[1], Alicja Hubalewska-Dydejczyk[1] and Aleksandra Gilis-Januszewska[1]
[1]*Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland;* [2]*Doctoral School of Medical and Health Sciences, Jagiellonian University Medical College, Krakow, Poland*

Background: Cushing's syndrome (CS) is often diagnosed with delay due to nonspecific initial symptoms. Clinical presentation differs across CS etiologies with ectopic Cushing's syndrome (ECS) showing often the most nonspecific initial presentation.

Objectives: To identify differences in initial clinical presentation between patients with ECS and Cushing's disease (CD) to facilitate earlier recognition and appropriate diagnostic pathways.

Methods: A retrospective analysis was performed using data from the Kraków ERCUSYN registry and included 34 patients with ECS and an equal number of age- and sex-matched patients with CD (hospitalized 2000-2025). Initial symptoms were identified based on medical records and retrospective patient history obtained at the time of diagnosis. Patients with small cell lung cancer were excluded due to severe general condition, rapidly progressive disease course, and the inability to obtain a reliable retrospective clinical history.

Results: The sources of ECS were predominantly neuroendocrine tumors (23), most commonly pulmonary carcinoids (7) and gastroenteropancreatic neuroendocrine tumors(9), with less frequent involvement of other malignant (6) and benign (2) neoplasms; in 3 cases, the source of ACTH secretion remained unidentified. Time to diagnosis from first symptoms was significantly shorter in the ECS than in the CD (2 vs 12 months, $P < .001$). In 21 (62%), ECS was diagnosed at a metastatic stage, including distant organ metastases in 19. The most frequent initial symptoms among patients with ECS were hypokalemia (52.9%), muscle weakness (38.2%), and edema (35.3%). Hypokalemia as an initial symptom was markedly more frequent in ECS patients than in those with CD (52.9%vs 5.9%,$P < .001$). However, on laboratory evaluation at diagnosis, hypokalemia was observed in 94.1% of patients with ECS and with 44.1% of patients with CD ($P < .001$). Weight loss occurred more often in ECS, whereas weight gain was significantly more common in CD (14.7% vs 59.0%,$P = .003$). Striae were observed exclusively in CD (17.6% vs 0%, $P = .03$). Muscle weakness was common in both groups, with similar prevalence. Edema and diabetes mellitus tended to be more frequent in ECS, although these differences did not reach statistical significance. Other features such as plethora, hypertension, headache, and visual disturbances were more often reported in CD but were not discriminatory at presentation.

Conclusions: ECS and CD differ substantially in their initial clinical presentation. ECS is characterized by more nonspecific and predominantly catabolic first manifestations, with hypokalemia as the most frequent initial symptom. However, hypokalemia as an initial symptom is less frequent than that observed during laboratory evaluation at the diagnosis, suggesting that early hypokalemia is underrecognized.

Abstract citation ID: lvag096.1222

EP933 - ECE_1728 - A care report of a calcitonin secreting pancreatic neuroendocrine tumour—a rare tumour entity

Umesha Wijenayake[1,2], Aisha Naseer[1], Zahir Soonawalla[1], Christine May[1] and Bahram Jafar-Mohommadi[1]
[1]*Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom;* [2]*Postgraduate Institute of Medicine, University of Colombo, Colombo, Sri Lanka*

Abstract

(A 59-year-old man without relevant past medical history presented with a history of chronic diarrhoea for 6 years. He experienced intermittent episodes of profuse watery diarrhoea and weight loss without associated flushing or abdominal pain. He was extensively evaluated in the past, where infective and inflammatory causes were excluded. Laboratory analysis, including a colonoscopy, did not help in establishing a diagnosis

His condition was progressively worsening over time, resulting in a hospital admission with profuse diarrhoea complicated by acute kidney injury.

Cross-sectional imaging revealed a 10 × 7.5 cm mass on the tail of the pancreas. His calcitonin level was markedly elevated at a value of 2480 ng/L (<11.8), while his carcinoembryonic antigen level and thyroid imaging were within normal limits.

He underwent an endoscopic ultrasound and biopsy of the pancreatic lesion. The histology confirmed a well-differentiated (G2) pancreatic neuroendocrine tumour (Ki-67-10%).

A 68-Gallium-DOTATATE PET CT scan demonstrated the pancreatic lesion to be SSTR-avid with no SSTR-avid lesions elsewhere.

Following discussion at the neuroendocrine tumour multidisciplinary team meeting, he was started on somatostatin analogue therapy and underwent a curative resection (distal subtotal pancreatectomy and spleenectomy).

Post surgery, his calcitonin level normalised and his symptoms completely resolved with no residual disease in his post-surgical scans. Currently, he is on routine surveillance.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Calcitonin-secreting pancreatic neuroendocrine tumours are very rare and often overlooked in the evaluation of chronic diarrhoea. In the presence of suggestive symptoms and negative preliminary investigations, consideration of functional pancreatic NET syndromes in chronic diarrhoea evaluation would be indicated, as timely interventions may improvesurvivaland morbidity.)

Abstract citation ID: lvag096.1223

EP934 - ECE_3189 - Integrated transcriptomics and beta-cell modelling of pancreatic cancer–associated new-onset diabetes

Klaus Brusgaard[1,2], Erol Eyüpoğlu[3], Havva Eyüpoğlu[4], Mustafa Akkiprik[4], Nedime Serakinci[3,5] and Can Erzik[3]

[1]Department of Regional Health Research, University of Southern Denmark, Odense, Denmark; [2]Departement of Regional Health Research, Universitet of Southern Denmark, Odense, Denmark; [3]Department of Medical Biology and Genetics, Marmara Universitesi, İstanbul, Türkiye; [4]Department of Medical Biology and Genetics, Marmara Universitesi, İstanbul, Türkiye; [5]Faculty of Art and Sciences, Moleculear Biology and Genetics, Cyprus International Unniversity, Lefkosa, Türkiye

Introduction: New-onset diabetes (NOD) can precede pancreatic ductal adenocarcinoma (PDAC) and may reflect a paraneoplastic effect on pancreatic islets. The signalling mechanisms driving beta-cell dysfunction in PDAC-associated NOD remain poorly defined.

Purpose: We test whether PDAC-derived factors induce a Notch-biased program in beta-cells, leading to dysfunction and reduced viability, and whether pharmacological Notch inhibition can partially reverse these effects.

Material and Methods: Public transcriptomic datasets from PDAC cohorts with NOD and long-term diabetes were analysed for pathway enrichment and candidate signatures. For experimental validation, conditioned medium (CM) from KPCY pancreatic cancer cells was applied to MIN6 beta-cells under chronic exposure, with or without the gamma-secretase/Notch inhibitor DAPT. Readouts included bulk RNA-seq to quantify Notch target gene expression (HES1, HEY1/HEY2) and broader beta-cell response programs; beta-cell viability (CellTiter-Glo); apoptosis (Caspase-Glo 3/7); and Western blot for HES1 as a marker of Notch activation.

Results: Notch-related pathway enrichment was observed in PDAC-associated NOD across patient comparisons. In MIN6 cells, chronic exposure to KPCY-conditioned medium reduced beta-cell viability compared to controls. This reduction was partially reversed by DAPT.

Conclusion/Perspective: These findings support a model in which PDAC-to-beta–cell communication activates Notch-associated programs that may contribute to PDAC-associated NOD. Ongoing RNA-seq and Western blot analyses will further characterize Notch target activation and broader beta-cell stress and dedifferentiation responses. RNAseq data will be presented. These results will help guide future biomarker development and identify potential intervention targets.

Abstract citation ID: lvag096.1224

EP935 - ECE_3721 - A Case of Parathyroid Carcinoma Presenting with Mild Hypercalcemia

Selin Celik[1], Ozge Sahin Kimyon[1], Necmettin Ozkanbas[2], Bahar Atasoy[3], Sema Ciftci[4] and Hamide Piskinpasa[1]

[1]Department of Endocrinology and Metabolism, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Research and Training Hospital, İstanbul, Türkiye; [2]Pathology, Sağlık Bilimleri Üniversitesi Bakırköy Doktor Sadi Konuk Eğitim Ve Araştırma Hastan, Bakırköy, Türkiye; [3]Radiology, Sağlık Bilimleri Üniversitesi Bakırköy Doktor Sadi Konuk Eğitim Ve Araştırma Hastan, Bakırköy, Türkiye; [4]Endocrinology and Metabolism, Sağlık Bilimleri Üniversitesi Bakırköy Doktor Sadi Konuk Eğitim Ve Araştırma Hastan, Bakırköy, Türkiye

Introduction: Parathyroid carcinoma is a rare endocrine malignancy, accounting for less than 1% of primary hyperparathyroidism cases. Despite typically being associated with markedly elevated serum calcium and parathyroid hormone levels, definitive diagnosis is usually made postoperatively by histopathology. We report a rare case of parathyroid carcinoma presenting with only mild hypercalcemia.

Case: A 44-year-old male with no history of chronic disease or medication use was referred to our clinic after incidental detection of hypercalcemia. Laboratory evaluation showed a euthyroid state with a serum calcium level of 12.2 mg/dL, albumin of 4.4 g/L, and PTH of 178 pg/mL. Physical examination was unremarkable and the patient had a history of surgery for nephrolithiasis. There was no history of fractures or family history of hyperparathyroidism. Ultrasonography demonstrated a TIRADS3 nodule measuring 43 × 36 × 28 mm occupying the entire right thyroid lobe, as well as a lesion measuring 19 × 26 × 26 mm inferior to the left thyroid lobe, consistent with a parathyroid adenoma. No pathological lymph nodes were observed. Tc-99msestamibi scintigraphy showed focal uptake in the inferior aspect of the left thyroid lobe, compatible with a parathyroid adenoma. Bone densitometry was normal. Fine-needle aspiration biopsy of the thyroid nodule was reported as benign.The patient was diagnosed with PHPT accompanied by a benign solitary thyroid nodule, and right lobectomy with left inferior parathyroidectomy was planned. Two months after the initial diagnosis, preoperative tests revealed a serum calcium level of 12.5 mg/dL and a markedly elevated PTH level of 643 pg/mL. Intraoperatively, the parathyroid gland was firm, gray and fixed to the surrounding muscles. Frozen section demonstrated invasion into adjacent muscle tissue, raising suspicion for parathyroid carcinoma. Therefore, left central lymph node dissection, left thyroid lobectomy, and wide excision of the parathyroid lesion including strap muscles were performed. Histopathology showed benign thyroid tissue, while the parathyroid specimen exhibited features suggestive of carcinoma, including cytological atypia, fibrous bands, and skeletal muscle invasion. No lymphovascular or perineural invasion was detected, surgical margins were negative, and the Ki-67 proliferation index was <5%. The patient was normocalcemic at one month postoperatively, and genetic mutation analysis was planned.

Discussion: Differentiating parathyroid carcinoma from adenoma based on clinical and biochemical findings is challenging, and diagnosis is usually made postoperatively. Although severe hypercalcemia (>14 mg/dL), markedly elevated PTH (>500 pg/

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

mL), large tumor size (>3 cm), and invasive imaging features may suggest carcinoma, they are not diagnostic. Our case demonstrates that parathyroid carcinoma can occur despite mild hypercalcemia and small tumor size.

Abstract citation ID: lvag096.1225

EP936 - ECE_1975 - G-protein coupled estrogen receptor (GPER) modulates melanin prodution

Giada Mercanile[1,2], Carmela Perri[1,3], Clara Lazzaretti[1], Samantha Sperduti[1,4], Manuela Simoni[1,4,5], Cristina Magnoni[2] and Livio Casarini[1,4]

[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [2]Unit of Dermatology, Department of Medical and Surgical Sciences, University of Modena and Reggio Emilia, Modena, Italy; [3]International PhD School in Clinical and Experimental Medicine (CEM), University of Modena and Reggio Emilia, Modena, Italy; [4]Center for Genomic Research, University of Modena and Reggio Emilia, Modena, Italy; [5]Department of Medical Specialties, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy

Melanin is produced by melanocytes to protect skin from UV radiation-mediated DNA damage. Melanogenesis is induced by α-melanocyte-stimulating hormone (α-MSH), which binds to melanocortin-1 receptor (MC1R) and requires the allosteric modulation by melanocortin receptor accessory protein (MRAP) to activate the cyclic adenosine monophosphate (cAMP) pathway. However, melanin excess occurs in pregnancy, during use of hormonal contraceptive pills, melanoma and melasma, suggesting that other hormones could be involved in melanogenesis. Our preliminary data demonstrated that skin hyperpigmentation may be due to overexpression of G protein-coupled estrogen receptor (GPER), another GPCR detected in skin cells and displaying MRAP-like allosteric behaviour.

We aim to assess whether GPER may act as an allosteric partner for MC1R, leading to α-MSH-mediated melanin hyperproduction.

Experiments were performed using skin tumour Sk-Mel-2 and Sk-Mel-28 cell lines, and human primary melanocytes over/under-expressing GPER. Cells were treated 48 h with 100 nM α-MSH, in the presence or in the absence of increasing doses (0-50 nM range) of estradiol and progesterone. *MC1R*, *MRAP* and *GPER* gene expression levels were evaluated by droplet-digital PCR, while the GPER-MC1R interaction by proximity ligation assay (PLA). Intracellular cAMP levels and melanin production were measured by bioluminescence resonance energy transfer (BRET) and spectrophotometric analysis. 5 independent experimental replicates were performed and statistically analysed by Kruskall-Wallis test and Dunn's post-test ($P < 0.05$).

In transfected MC1R-expressing Sk-MEL-2 and -28 cell lines, α-MSH increases cAMP levels compared to untreated cells ($P < .05$), regardless of GPER and MRAP co-expression. Control experiments demonstrated that sex steroids failed to induce cAMP increase ($P \geq .05$). Under GPER/MC1R and MRAP/MC1R co-expression, α-MSH leads to higher cAMP level increase than MC1R-expressing cells ($P < .05$). In primary melanocytes, nM progesterone concentrations induced GPER expression and melanin production in a steroid dose-dependent manner. Under progesterone exposure, melanocyte treatment with 100 nM α-MSH enhances the melanogenesis compared to progesterone-untreated cells ($P < .05$), while no effects were found under cell exposure to estradiol ($P \geq .05$).

Cell exposure to progesterone increases GPER expression, which replaces MRAP-specific allosteric functions and triggers marked response to α-MSH, as a mechanism leading to hyperpigmentation in melasma and skin cancer.

Abstract citation ID: lvag096.1226

EP937 - ECE_2462 - Cost effectiveness and efficacy of cinacalcet in patients with hypercalcaemia

Furhana Hussein, Bhavini Bhatt, Hafsah Hussain, Mariana Dram, Godwin Simon, Belayet Hossain and Gideon Mlawa

Barking Havering andRedbridge Hospitals NHS Trust, London, United Kingdom

Introduction: Cinacalcet is a highly effective agent for controlling hypercalcaemia in patients with parathyroid carcinoma, secondary hyperparathyroidism on dialysis or primary hyperparathyroidism (PHPT) who cannot undergo parathyroidectomy surgery due to comorbidities and risk of anaesthesia.

Symptoms of hypercalcaemia include lethargy, confusion, constipations, renal stones, depression, osteoporosis leading increased risk of fractures. These complications can lead to hospital admissions.

Cinacalcet works as a calcimimetic by increasing the sensitivity of the calcium-sensing receptor on parathyroid gland cells to extracellular calcium leading to inhibition of parathyroid hormone (PTH) secretion, thus lowering serum calcium levels.

Aim: Looking at management of hypercalcaemia with cinacalcet and the cost effectiveness and efficacy on the NHS.

Methods: Retrospective single-centre study looking at patients started on cinacalcet for hypercalcaemia and their response to treatment and comparing cost effectiveness in the NHS.

19 patients were identified at Queen's Hospital, London, UK (BHRUT–Barking, Havering and Redbridge University Hospitals NHS Trust) in 2025.

Results: 19 patients were identified as being started on cinacalcet for hypercalcaemia.

63% were female

Majority of the patients were in the age group 71-80 years old (37%) then followed by over 80 years of age at 26%

100% had serum calcium levels reduced after starting cinacalcet.

In total there were 18 hospital admission for these 19 patients. Research has showed that the average cost of admission in the NHS cost approximately £500. Therefore, this is equivalent to approximately £9000. However, the longer the hospital stay the more it would cost. The average cost of cinacalcet 30 mg, 28 tablets pack on the NHS is £5.08.

5 patients eventually underwent parathyroidectomy surgery

Conclusions: Hypercalcaemia can be treated with cinacalcet to maintain serum calcium levels and avoid complications and admissions to hospital. The implications of not diagnosing and treating hypercalcaemia in timely manner with cinacalcet can result in more complications in patients that may lead to multiple hospital admissions costing the NHS more money. 1 year supply

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

of 30 mg cinacalcet once daily can cost approximately £60.96 under the NHS compared to an average hospital admission costing £500. Our study showed that using cinacalcet to manage hypercalcaemia is cost effective and has good efficacy for treating hypercalcaemia the NHS by reducing complications, need for surgery and avoiding multiple hospital admissions.

Abstract citation ID: lvag096.1227

EP938 - ECE_2657 - Beyond the classic triad: an unusual presentation of MEN2A with salivary gland carcinoma and papillary thyroid cancer

Elaine Saugar, Deciara Jacome Torres M. Mesquita, Pascual De Santis and Angel Alejandro
Miami, United States

Introduction: Multiple endocrine neoplasia type 2 (MEN2) is an autosomal dominant syndrome caused by germline gain-of-function mutations in the RET proto-oncogene on chromosome 10q11.21, affecting neural crest-derived tissues including the thyroid, adrenal, and parathyroid glands. It is classified as MEN2A or MEN2B, with MEN2A accounting for 70-80% of cases. Presentation typically occurs before age 35. Medullary thyroid carcinoma develops in nearly 98% of patients and is often the initial manifestation. Pheochromocytomas occur in about 50% of cases and are frequently bilateral, while primary hyperparathyroidism affects about 25% of patients, usually later in life. We report a unique case of MEN2A with atypical late presentation and rare associated malignancies.

Case Presentation: A 60-year-old Hispanic male presented with abdominal pain and sepsis secondary to acute cholecystitis, complicated by NSTEMI and newly diagnosed non-ischemic cardiomyopathy. The patient was undergoing outpatient evaluation for MEN2A due to known RET mutations in his three children. CT imaging revealed bilateral adrenal nodules suspicious for pheochromocytomas in the setting of elevated plasma free metanephrine (520 pg/mL). Following alpha and beta blockade, he underwent right total and left partial adrenalectomy with cholecystectomy. Pathology confirmed bilateral low-grade pheochromocytomas, and postoperative adrenal function remained intact. Subsequent thyroid ultrasound demonstrated bilateral highly suspicious nodules in the setting of elevated plasma calcitonin (4,451 pg/mL). Total thyroidectomy revealed medullary thyroid carcinoma (T2N1a) and incidental papillary thyroid carcinoma, follicular variant (pT1aN0a). He never developed hyperparathyroidism. Five years later, routine surveillance imaging identified a left parotid mass. Biopsy confirmed salivary duct carcinoma. He received neoadjuvant trastuzumab/pertuzumab followed by parotidectomy, neck dissection, and reconstruction. Tumor sequencing identified pathogenic PIK3CA and RET mutations on exons 10 (p.Q546R) and 11 (p.C634S), respectively, without RET fusion. He is currently receiving adjuvant radiation therapy.

Discussion: This case demonstrates an expanded MEN2A phenotype with delayed presentation, pheochromocytoma as the initial manifestation, coexisting papillary thyroid carcinoma, and subsequent salivary gland carcinoma. Although RET fusions are implicated in subsets of papillary thyroid and salivary gland tumors, these represent somatic events distinct from germline RET mutations in MEN2A. Several case reports have documented the unusual association between MEN2A and papillary thyroid carcinoma; however, there appear to be no prior reports linking MEN2A with salivary gland carcinoma. This case highlights the importance of recognizing atypical and late-onset manifestations of MEN2A and underscores the role of genetic and molecular evaluation in guiding lifelong surveillance and individualized management.

Abstract citation ID: lvag096.1228

EP939 - ECE_2703 - When you hear hoofbeats think horses but remember zebras: a case of life-threatening VIPoma

Maja Wróblewska[1], Agata Belińska[1,2], Maria Kałas[3,4], Jacek Szypenbejl[3,4], Anna Lewczuk-Myślicka[1,2], Mariusz Siemiński[3,4] and Renata Świątkowska-Stodulska[1,2]
[1]*Department of Endocrinology and Internal Medicine, University Clinical Centre, Gdańsk, Poland;* [2]*Department of Endocrinology and Internal Medicine, Faculty of Medicine, Medical University of Gdańsk, Gdańsk, Poland;* [3]*Department of Emergency Medicine, University Clinical Centre, Gdańsk, Poland;* [4]*Department of Emergency Medicine, Faculty of Medicine, Medical University of Gdańsk, Gdańsk, Poland*

Introduction: Vasoactive intestinal peptide-secreting tumor (VIPoma) is a rare neuroendocrine neoplasm (NEN), with an annual incidence of 1 per million. It is usually located in the pancreatic tail. VIPoma syndrome, caused by excessive unrestricted VIP secretion, presents as severe fasting-persistent watery diarrhea, hypokalemia, and achlorhydria, known as “WDHA syndrome” or Verner-Morrison syndrome. Management of VIPoma includes symptom-oriented pharmacotherapy, conservative treatment options such as somatostatin analogs (SSAs), and surgery.

Case Report: A 69-year-old woman was admitted to the emergency department (ED) in hypovolemic shock due to massive watery diarrhea up to 10 liters per day. The physical examination revealed generalized flushing and marked dehydration, with an initial blood pressure of 80/38 mmHg and a heart rate of 122 beats per minute. Venous blood gas showed metabolic acidosis with pH of 7.12 and hypokalemia of 2.8 mmol/L. The gastroenteritis PCR panel was negative. After initial treatment (intravenous fluids, hydrocortisone, vasopressors) and stabilization of vital parameters in the ED, the patient was transferred to the Department of Endocrinology for suspected rare WDHA syndrome. Continuous infusion of octreotide resulted in resolution of diarrhea; the patient also started lanreotide. Blood tests confirmed elevated VIP—180 pmol/L ($N < 24$ pmol/L), calcitonin—941 pg/mL ($N < 11.5$), and chromogranin A 253.8 ng/mL ($N < 102$). Approximately 2 months earlier, the patient was hospitalized due to similar symptoms associated with hyperglycemia and hypercalcemia. A CT scan of the abdomen showed a solitary, irregular, polycystic mass measuring $70 \times 38 \times 65$ mm located in the pancreatic area. Tumor biopsy in an outpatient setting revealed low-grade NEN, but no further procedures followed.

PET/CT with 68Ga-DOTATATE confirmed three pancreatic lesions with high expression of the somatostatin receptor, the largest measuring 48×32 mm with SUVmax 26.5. After a multidisciplinary team meeting, the patient was qualified for surgery. Subtotal pancreatectomy and splenectomy with partial gastrectomy and partial colectomy was performed, the surgery was uneventful. The resected NEN was G2 with Ki67 4%. Since

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

the procedure, the patient has been asymptomatic with good biochemical control.

Discussion: Although VIPoma is a rare disease, the characteristic clinical course can facilitate an initial diagnosis. Fasting-persistent watery diarrhea with severe electrolyte disturbances should prompt the idea of rare neuroendocrine causes, the so-called "zebras". Elevated calcitonin, a biomarker more easily accesible than VIP, may contribute to secretory diarrhea. Early recognition and initiation of appropriate therapy can save lives and, in the long term, can preserve the quality of life of patients.

Abstract citation ID: lvag096.1229

EP940 - ECE_3332 - Managing a rare case of recurrent ACTH secreting tumour and the role of MDT

Furhana Hussein, Amanda Mlawa, Olga Dolacinska, Assem Madeniyetova, Lina Eltayieb, Fatumo Issa, Amy Kelt, Aneliya Sirkova, Mariana Dram and Gideon Mlawa
Barking Havering and Redbridge Hospitals NHS Trust, London, United Kingdom

Introduction: Atypical carcinoid tumours are rare which account for about 15% of all carcinoid tumours. Some of those tumours secrete adrenocorticotrophic hormone (ACTH) causing Cushing`s syndrome.

Case: A 39-year-old woman was referred with few months history of weight gain, irregular menstrual periods, muscle aches, difficult going up the stairs, headaches and blurred vision. In 2000, she was diagnosed with ectopic thoracic carcinoid leading to Cushing`s syndrome. This was surgically treated. She had remained symptom free until early 2016. On presentation to another hospital her 9 am cortisol was raised at 770 nmol/L, 24 hour urinary free cortisol was 1992 nmol/24 hr, and cortisol was not suppressed with both low and high dose dexamethasone suppression test. Her ACTH was high at 118 ng/L. The CXR showed raised left hemidiaphragm.CT chest showed $2.5 \times 3 \times 1.9$ cm mass on left side of superior mediastinum adjacent to arch of the aorta.

She was started on metyrapone 250 mg three times a day. Resection of the tumour was carried out.During the surgical procedure the tumour was found to be involving the pulmonary vessels, phrenic nerve, and left upper lobe. Histology showed tumour composed of sheet of cells, with small amounts of indistinct cytoplasm, oval nuclei and stippled chromatin and necrosis and presence of mitoses of approximately one mitotic figure per 5 high power fields in keeping with recurrent atypical carcinoid tumour.

Disussion: Atypical adrenocorticotrophic hormone (ACTH) secreting tumours are uncommon, and together with typical carcinoid tumours constitutes less than 5% of all lung tumours.

These can be more aggressive tumours with worse prognosis compared to typical pulmonary carcinoid tumour which are well differentiated and are associated with good prognosis

Atypical carcinoid tumours can be differentiated from other neuroendocrine tumours based on histological criteria such as increased mitotic activities, amount and pattern of necrosis, cell size, amount of cytoplasma,nuclear chromatin

Conclusions: Atypical carcinoid with regional lymph node metastasis are likely to be recurrent and respond poorly to standard chemotherapy.

This case demonstrates that the tumour can be very slow growing in nature. Patients with atypical adrenocorticotrophic hormone (ACTH) secreting carcinoid tumours should be followed up and screened for Cushingfor many years in the MDT setting.

Abstract citation ID: lvag096.1230

EP941 - ECE_3958 - Recurrent or metastatic paraganglioma in patients with succinate dehydrogenase D mutations: a case series

Sereen Fatima, Safwaan Adam and Jan Hoong Ho
The Christie NHS Foundation Trust, Endocrine Department, Manchester, United Kingdom

Background: Germline mutations in the succinate dehydrogenase complex (SDH) gene group (particularly SHDB and SDHD) predispose individuals to hereditary paraganglioma-pheochromocytoma (PGL/PCC) syndromes, with variable penetrance. SDHD/SDHB mutations account for between 70-80% of PGL/PCC syndromes attributed to pathogenic variants in a gene. SDHB mutations are associated with extra-adrenal paragangliomas with an increased risk of metastatic disease and are generally associated with higher morbidity and mortality. In comparison, pathogenic SDHD variants are associated with multifocal head and neck paragangliomas (HNPGL) with a much lower metastatic risk of <5%.

Cases: Herein, we present a case series of 3 patients referred to our unit with paragangliomas, all of whom had either metastatic or recurrent disease. All 3 were found to have mutations of the SDHD gene on genetic testing.

	Patient 1	Patient 2	Patient 3
Age	52	27	33
Gender	Male	Female	Male
Type of tumour	Carotid body paraganglioma	3 separate head and neck paragangliomas	Left and right carotid body tumours
Age at presentation (of first tumour)	32	16	18
Family history	Unknown	Head and neck paragangliomas in father,	Unknown

(*continued*)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Continued

	Patient 1	Patient 2	Patient 3
		uncle, paternal aunt and paternal cousin	
Functional?	Yes	Yes	No
3-methoxytyramine level (0.0-180.0 pmol/L)	552.3 (high)	908.0 (high)	<75.0 (normal)
Metanephrine level (0.0-510.0 pmol/L)	188.1 (normal)	213.9 (normal)	121.8 (normal)
Normetanephrine level (0.0-1180.0 pmol/L)	373.8 (normal)	894.0 (normal)	374.0 (normal)
Treatment for first tumour	Resection	External beam radiotherapy due to presence of metastatic disease at presentation and location of primary tumour. Patient having discussion about systemic treatments	Excision
Recurrence	2 years after resection	-	-
Metastases	-	Multiple lung nodules	Right spheno-orbital paraganglioma and metastatic lesions to the right orbit, pancreas, right retropharyngeal region, tentorium cerebri and multiple lesions to the lungs and skeleton
Treatment of recurrent / metastatic disease	Resection of recurrent PGL	Palliative radiotherapy	PRRT
Progress	Clinical stability	Currently undergoing treatment	Good response to PRRT, stable disease with reduced functional burden

Discussion: This case series demonstrates patients with germline SDHD mutations who presented with metastatic or recurrent disease. This highlights the need to consider metastatic potential in patients with these mutations. This series emphasizes the need for regular follow-up and on-going surveillance in patients with PGL/PCC syndromes caused by mutations in the SDHD gene, and to maintain an index of suspicion for metastatic or recurrent disease in these patients also.

Abstract citation ID: lvag096.1231

EP942 - ECE_1937 - Giant pelvic paraganglioma: diagnostic and therapeutic challenges

Vasiliki Venetsanaki[1,2,3], Efthimia Karra[2,3] and Eleni Armeni[2,3]
[1]*Department of Endocrinology, Diabetes and Metabolism, University Hospital of Heraklion, Heraklion, Greece;* [2]*Department of Endocrinology, Royal Free London NHS Foundation Trust, London, United Kingdom;* [3]*Neuroendocrine Tumor Unit, ENETS Centre of Excellence, Royal Free London NHS Foundation Trust, London, United Kingdom*

Introduction: Paragangliomas are rare, extra-adrenal neuroendocrine tumors arising from sympathetic or parasympathetic paraganglia. They may be hormonally active, secreting catecholamines, or remain clinically silent. Paragangliomas may occur sporadically or in association with inherited genetic syndromes and their biological behavior ranges from benign to metastatic. Pelvic paragangliomas are exceedingly rare and pose a diagnostic and surgical challenge.

Case: A 51-year-old male patient with a 15-year history of hypertension was being evaluated for secondary hypertension. Cross-sectional imaging revealed a solid, enhancing retroperitoneal mass measuring $9 \times 7.5 \times 6$ cm with central necrosis and small areas of calcification within it. The differential diagnosis at that time included a retroperitoneal sarcoma or an exophytic small bowel gastrointestinal stromal tumour.

The patient underwent a biopsy of the retroperitoneal mass without complications. Histopathological findings were consistent with a paraganglioma. Subsequent biochemical evaluation demonstrated elevated normetanephrine and 3-methoxytyramine, supporting the diagnosis. Functional imaging with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

^{68}Ga-DOTATATE and ^{18}F-FDG PET showed intense tracer uptake confined to the right pelvic mass.

Eight months after the initial diagnosis, the patient underwent surgery. Intraoperatively, a large, lobulated and vascular paraganglioma that was adherent to the bifurcation of the right common iliac vein was identified. During dissection, iatrogenic injury to the right common iliac vein and the origin of right internal iliac vein occurred, resulting in an estimated blood loss exceeding 4.5 liters. Postoperatively, the patient required intensive care management for hypovolemic shock. His recovery was further complicated by sepsis, postoperative ileus requiring re-operation, hypertensive crises and pulmonary oedema. Twenty-nine days after surgery the patient was discharged. Definitive histology confirmed a paraganglioma and genetic testing revealed that the patient was heterozygous for a likely pathogenic SDHB missense variant.

Following the complicated surgical history, the patient was referred for ^{177}Lu-DOTATATE (PRRT) therapy to manage the residual disease in the pelvis which had increased in size. The patient was treated with four cycles of PRRT with slight reduction in tumour size but refused further surgical intervention. Fourteen months later, the patient had progressive disease and chemotherapy with capecitabine and temozolamide was initiated.

Conclusions: A giant paraganglioma in the pelvis is a complicated and rare tumor. Biochemical testing and functional imaging can provide conclusive diagnostic evidence. Surgical management remains the first line of treatment but PRRT and systemic therapy have proven effective in the management of paragangliomas when surgery is not an option.

Abstract citation ID: lvag096.1232

EP943 - ECE_3402 - Vitamin D status and metabolic parameters in patients with concomitant parathyroid adenoma and breast cancer: a retrospective case–control pilot study

Müge Yılmaz[1], Serhat Özçelik[1], Busra Kanbur[1], Senem Boz Aksoy[1], Ece Seçgin Demir[1], Meryem Özoğlu[1], Naile Gokkaya[1], Ziya Mithat Bıyıklı[1], Hatice Odabaş[2], Nedim Turan[2], Aylin Ege Gül[3] and Kadriye Aydin[1]

[1]Department of Endocrinology and Metabolism, Kartal Dr.Lütfi Kırdar City Hospital, İstanbul, Türkiye; [2]Department of Medical Oncology, Kartal.Dr.Lütfi Kırdar City Hospital, İstanbul, Türkiye; [3]Department of Pathology, Kartal.Dr.Lütfi Kırdar City Hospital, İstanbul, Türkiye

Background: Primary hyperparathyroidism (pHPT) has been linked to an increased risk of malignancies, including breast cancer. However, data on metabolic and vitamin D characteristics in patients with concomitant parathyroid adenoma and breast cancer, as well as their relationship with tumor biology, remain limited.

Methods: This retrospective single-center study included female patients with newly diagnosed parathyroid adenoma, with or without concomitant breast cancer. Patients with multiple endocrine neoplasia, multigland parathyroid disease, or chronic kidney and liver diseases were excluded. Metabolic parameters and 25-hydroxyvitamin D levels—were recorded. Group comparisons were performed using non-parametric tests, with age-adjusted analyses using linear regression models.

In patients with concomitant breast cancer, tumor pathological features (ER, PR, HER2, and Ki-67) and radiotherapy status were recorded, and associations between Ki-67 and biochemical and metabolic parameters were assessed using Spearman's rank correlation analysis.

Results: A total of 16 patients with concomitant breast cancer and parathyroid adenoma and 36 patients with parathyroid adenoma only were included. Among breast cancer patients, 75.0% had invasive ductal carcinoma; all were estrogen receptor–positive, 75.0% were progesterone receptor–positive, and 25.0% were HER2-positive. Radiotherapy was administered to 68.75% of patients.

Patients with breast cancer had significantly lower 25-hydroxyvitamin D levels and higher BMI compared with controls ($P < .05$). Parathyroid hormone levels were positively correlated with BMI ($\rho = 0.653$, $P = .011$). No significant correlations were observed between the Ki-67 proliferation index and preoperative PTH, calcium, or 25-hydroxyvitamin D levels, although a weak positive trend with vitamin D was noted. Notably, Ki-67 showed a strong inverse correlation with fasting glucose levels ($\rho = -0.717$, $P = .002$).

In the parathyroid adenoma–only group, metabolic parameters demonstrated expected correlations, without significant associations between parathyroid-related biochemical markers and metabolic indices.

Conclusions: The coexistence of severe vitamin D deficiency in patients with both parathyroid adenoma and breast cancer may therefore suggest a bidirectional interaction affecting both parathyroid disease and breast tumorigenesis. In the breast cancer group, no significant correlations were observed between the Ki-67 proliferation index and preoperative PTH, calcium, or 25-hydroxyvitamin D levels, although a weak positive trend with vitamin D was noted. Considering that all patients with breast cancer in the study had estrogen receptor–positive tumors, it may be hypothesized that vitamin D deficiency and parathyroid pathologies interact predominantly with estrogen-dependent signaling pathways rather than directly influencing tumor proliferative processes.

Abstract citation ID: lvag096.1233

EP944 - ECE_3405 - Retroperitoneal leiomyosarcoma mimicking an adrenal mass: diagnostic pitfalls in the adrenal area

Leandro Augusto Silva[1], Ana Paula Moreira[2], Arnaldo Figueiredo[2], João Martins Gama[2], Carla Baptista[2] and Leonor Gomes[2]

[1]Endocrinology Department, Portuguese Institute of Oncology of Coimbra, Coimbra, Portugal; [2]Local Health Unit of Coimbra, Coimbra, Portugal

Introduction: Adrenal masses are common neoplasms; while often benign, some may be malignant. Leiomyosarcomas are a rare subtype of soft tissue malignancy, may remain asymptomatic for prolonged periods and can be incidentally diagnosed or present with nonspecific symptoms such as abdominal or flank pain or weight loss. Importantly, retroperitoneal sarcomas are often not considered in the differential diagnosis of adrenal tumours, and some lesions may have an extra-adrenal origin, given

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

the complex anatomy surrounding the adrenal gland, contributing to diagnostic challenges.

Clinical Case: A 80-year-old female patient was referred to Endocrinology for functional assessment of a left adrenal mass, detected on abdominal CT for vomiting, alternating constipation/diarrhea, left flank discomfort, and 15 kg weight loss in one month. CT showed an indeterminate oval lesion with heterogeneous enhancement near the left renal hilum, 29 × 21mm; MRI revealed a retroperitoneal tumour possibly pedunculated from the left adrenal gland. No symptoms of hormonal hypersecretion were reported. On physical examination, no pain or palpable masses/organomegaly, without endocrine stigmata. Functional work-up was negative. In 18F-FDG-PET/CT, a 32 mm mass without clear plane from the left adrenal gland, with increased uptake (SUVmax = 5.6) and, right upper pulmonary lobe (RUL) ground-glass nodule, 15mm, with uptake (SUVmax = 1.5), both suspicious for malignancy. Follow-up CT, with the known irregular left-sided mass enlarging to 37 × 25mm, with uncertain origin (possibly adrenal), raising suspicion of adrenocortical carcinoma. Pulmonary review with stable lung lesion on high resolution CT, proposed for imaging surveillance. After Nuclear Medicine discussion, 18F-FDOPA-PET/CT was performed, identifying the 44 × 30mm mass with mildly increased uptake (SUVmax = 3) and 16mm RUL nodule with uptake (SUVmax = 1.4), with differential diagnostic considerations including retroperitoneal ganglioneuroma/paraganglioma and pulmonary neuroendocrine tumour. After discussion with Urology, left adrenal lesion excision was planned. Intraoperatively, large adrenal/renal hilum mass without cleavage planes and suspected pancreatic invasion; incisional biopsy was performed. Histopathology revealed a grade 1 leiomyosarcoma, without MDM2 amplification. Due to clinical deterioration, referred to palliative care for best supportive care.

Conclusions: We report the case of a presumed adrenal lesion subsequently diagnosed as leiomyosarcoma. Retroperitoneal leiomyosarcoma should be included in the differential diagnosis of adrenal/suprarenal masses. Tumour origin may be uncertain (adrenal vs invasive), as in our case. Because adrenal lacks smooth muscle cells, it is thought to most likely arise from the smooth muscle components of adrenal blood vessels. Importantly, has no specific clinical presentation or radiologic features and lacks reliable tumour markers, making early preoperative diagnosis challenging.

Abstract citation ID: lvag096.1234

EP945 - ECE_1538 - Niclosamide ethanolamine is a novel therapeutic agent for human pancreatic cancer

Ying-Ray Lee[1], Tzu-En Chiu[2] and Wan-Chi Tsai[3]
[1]*Department of Microbiology and Immunology, Kaohsiung Medical University, Kaohsiung City, Taiwan;* [2]*Kaohsiung City, Taiwan;* [3]*Department of Medical Laboratory Science and Biotechnology, Kaohsiung Medical University, Kaohsiung City, Taiwan*

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive and highly lethal malignancy, with a five-year survival rate of approximately 12%. For patients who are not eligible for surgical resection, current therapeutic modalities, including chemotherapy, radiotherapy, targeted therapy, and immunotherapy have shown limited efficacy in improving survival outcomes, underscoring an urgent unmet need for novel therapeutic strategies.

Niclosamide ethanolamine (NEN), a derivative of the antiparasitic agent niclosamide, has been reported to exhibit anticancer activity in various malignancies by inhibiting tumor cell proliferation and metastasis, inducing apoptosis, and enhancing chemosensitivity. However, the therapeutic potential and molecular mechanisms of NEN in PDAC remain largely unexplored. In this study, we aimed to investigate the antitumor effects of NEN in PDAC and elucidate its underlying mechanisms.

Our results demonstrated that NEN treatment significantly suppressed PDAC cell proliferation, as evidenced by reduced cell viability and colony formation. Cell cycle analysis further revealed that NEN induced G0/G1 phase cell cycle arrest. Additionally, trypan blue exclusion assays, flow cytometric analysis, and Western blotting consistently confirmed that NEN treatment promoted apoptosis in PDAC cells. Mechanistic studies indicated that both extrinsic and intrinsic apoptotic pathways were activated upon NEN exposure. Moreover, Western blot analyses revealed that NEN treatment activated the AKT, ERK, and p38 signaling pathways. Pharmacological inhibition of these pathways significantly attenuated NEN-induced apoptosis, suggesting that NEN-mediated apoptotic effects are dependent on AKT, ERK, and p38 signaling.

In conclusion, this study provides the first evidence that NEN exerts potent antitumor activity against PDAC by inhibiting cell proliferation, inducing cell cycle arrest, and promoting caspase-dependent apoptosis through the AKT, ERK, and p38 signaling pathways. These findings highlight NEN as a promising therapeutic candidate for PDAC and warrant further preclinical and clinical investigation.

Abstract citation ID: lvag096.1235

EP946 - ECE_1529 - Microenvironment-dependent activation of FAK promotes growth of gastrointestinal neuroendocrine tumors

Alice Castenetto, Francesco Gambera, Anna Chinnì, Clarissa Gissi, Francesca D'este and Teresa Gagliano
Udine, Italy

Neuroendocrine tumors (NETs) are a rare and heterogeneous group of neoplasms arising from neuroendocrine cells distributed throughout the epithelium. The majority of NETs develop in the gastrointestinal tract (GI-NETs) and are characterized by indolent growth combined with a marked resistance to therapy and a relatively low mutational burden. Because GI-NETs are frequently not driven by classical oncogenic mutations, increasing attention has focused on alternative mechanisms of tumor progression, including epigenetic regulation and signals derived from the tumor microenvironment. Among stromal components, fibroblasts represent a major cellular population with the potential to modulate tumor behavior, yet their contribution to GI-NET biology remains poorly defined. The aim of this study was to investigate the influence of fibroblasts on GI-NET cell proliferation and phenotypic plasticity.

Primary human fibroblasts and GI-NET cell lines (GOT1 and COLO320DM) were used as experimental models. Tumor cells were cultured either in direct contact with fibroblasts or exposed to fibroblast-conditioned media to distinguish contact-dependent from soluble factor–mediated effects. Cell proliferation was evaluated using standard viability-based assays, while

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

phenotypic changes were assessed by immunofluorescence analysis of epithelial markers. Expression levels of focal adhesion kinase (FAK) were measured by QPCR, and the subcellular localization of phosphorylated FAK (p-FAK) was analyzed by confocal microscopy.

We found that direct co-culture with fibroblasts significantly enhances GI-NET cell proliferation, whereas conditioned media exerted minimal or no effects, indicating that physical interaction between fibroblasts and tumor cells is required to promote growth. Moreover, fibroblast co-culture disrupted the membrane localization of E-cadherin in GI-NET cells, suggesting a shift toward a mesenchymal-like phenotype. Importantly, fibroblasts induced a significant upregulation of FAK mRNA expression in tumor cells. For the first time, we also observed a marked nuclear translocation of phosphorylated FAK in GI-NET cells upon direct contact with fibroblasts, revealing a previously unrecognized mechanism of microenvironment-driven FAK signaling in this tumor type.

In conclusion, our data demonstrate that fibroblasts play a pivotal role in modulating GI-NET proliferation and phenotypic plasticity through contact-dependent mechanisms and identify nuclear p-FAK as a novel feature of tumor–stroma crosstalk in GI-NETs. These findings provide new insight into the contribution of the tumor microenvironment to GI-NET pathogenesis and support further investigation into FAK-dependent pathways as potential therapeutic targets.

Abstract citation ID: lvag096.1236

EP947 - ECE_1770 - Severe hypergastrinemia with mild clinical expression: the modulating role of autoimmune atrophic gastritis in metastatic gastrinoma

Raquel Calheiros[1,2], Sara Santos[1,2], Pedro Souteiro[1,2], Ana P. Santos[1,2] and Joana Oliveira[1,2]
[1]*Portuguese Oncology Institute of Porto (IPO Porto), Porto, Portugal;* [2]*Porto Comprehensive Cancer Center (P.CCC), Department of Endocrinology, Porto, Portugal*

Background: Gastrinomas are rare functioning neuroendocrine tumors characterized by inappropriate gastrin secretion leading to gastric acid hypersecretion and Zollinger–Ellison syndrome. Diagnosis usually requires the demonstration of hypergastrinemia in the setting of low gastric pH. In clinical practice, however, gastric pH assessment may be unavailable, and coexisting gastric disorders may confound symptomatic and biochemical interpretation,, and delay the diagnosis.

Case Presentation: We report the case of a 78-year-old woman with a well-differentiated pancreatic neuroendocrine tumorand extensive hepatic and lymph node metastases. The tumor was identified during evaluation of abdominal and pelvic discomfort. Cross-sectional imaging revealed a 61mm exophytic mass in the pancreatic body with diffuse liver metastases.Liver biopsy histopathology confirmed a metastatic pancreatic neuroendocrine tumor, with a Ki-67 proliferation index <3% and strong expression of neuroendocrine markers. Functional imaging with 68Ga-DOTATOC PET demonstrated very intense somatostatin receptor expression throughout the entire tumor burden.

Biochemical evaluation revealed extreme fasting hypergastrinemia (99007 pg/mL). Clinically, the patient reported chronic abdominal pain and recurrent diarrhea but lacked other hallmark features of Zollinger–Ellison syndrome, such as peptic ulcer disease, severe gastroesophageal reflux, or significant weight loss. Gastric pH measurement was not available, limiting physiological confirmation of acid hypersecretion. Upper gastrointestinal endoscopy revealed body-predominant atrophic gastritis with focal intestinal metaplasia, active Helicobacter pylori infection and no ulcerations. In this context, autoimmune atrophic gastritis was suspected, which would explain the mild clinical expression of such high gastrin levels. Further tests showed positive anti-parietal cell antibodies and vitamine B12 deficiency, supporting this diagnosis. Germline genetic testing for MEN1 and CDKN1B revealed no pathogenic variants. LAR octreotide was initiated leading to diarrhea improvement, a dramatic fall in the gastrin levels (460 pg/mL in the last evaluation) and structural stable disease during the last three years.

Conclusions: This case represents a pathophysiological challenge. On one hand, an autoimmune atrophic gastritis could explain the clinical picture and be seen here as protective factor by reducing parietal cell mass and attenuating acid secretion, thereby limiting ulcerative complications despite extreme gastrin. On the other hand, atrophic gastritis itself can cause secondary hypergatrinemia, which may be a confounding effect.Awareness of such interplay is essential to avoid misinterpretation of isolated hypergastrinemia and to ensure timely diagnosis.

Abstract citation ID: lvag096.1237

EP949 - ECE_3090 - A single centre review of succinate dehydrogenase subunit pathogenic variant carriers.

Stephanie Miles, Christine May and Bahram Jafar-Mohammadi
OCDEM, Churchill Hospital, Oxford, United Kingdom

Objective: Carriers of germline pathogenic variants in succinate dehydrogenase subunits A to D (SDHx) are predisposed to phaeochromocytoma and paraganglioma (PPGL) requiring long-term surveillance. We audited disease-affected and asymptomatic SDHx pathogenic variant carriers against international consensus guidelines and analysed the presentation and management of PPGLs.

Methods: A retrospective analysis of electronic medical records of SDHx pathogenic variant carriers was performed by identifying cases through coding. Records between January 2019 and December 2024 were audited against annual review of symptoms, metadrenalines measurement, and MRI head to pelvis 3 yearly.

Results: 40 index cases and 34 non-index cases were identified. The median age of genetic diagnosis and first tumour was 42 and 41 years respectively.

Cohort characteristics:

Pathogenic variant	Asymptomatic	Disease-affected
SDHA	1	6
SDHB	16	23
SDHC	2	2
SDHD	1	23

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Number of tumours by site in cohort:

	SDHA	SDHB	SDHC	SDHD
Head and neck	1	20	0	46
Mediastinal	0	3	1	4
Pheochromocytoma	1	1	0	3
Abdominal	1	6	0	2
GIST	3	0	1	0
RCC	0	2	0	0
Other	3	1	0	1
Total number of tumours	9	33	2	56
Metastatic sites	4	0	0	2

During the audit period 37 tumours were detected in 25 carriers (34%). MRI screening detected 74% of tumours, and 20% were detected on screening CT; 6% of tumours were detected after symptoms prompted investigation. PPGLs were functional in 10 patients (36%); two head and neck tumours were functional (7%).

Primary treatment of tumours was excision (48%), observation (26%), radiotherapy (19%), and stereotactic ablative radiotherapy (3%). One carrier had radiotherapy after excision.

One patient died during the audit period with a SDHA pathogenic variant; metastatic phaeochromocytoma was listed on the death certificate as a contributing factor but not the cause of death.

Compliance against audit standards demonstrated 78% of carriers were reviewed in clinic yearly. A review of symptoms was documented in 75% and 75% had metadrenalines yearly; 61% had 3 yearly imaging including the whole neck to pelvis.

Conclusions: our cohort adds to the available data in this rare disease and demonstrates the significant burden of SDHx pathogenic variant associated disease. Case identification may have been limited by reliance on coding to identify cases. Audit demonstrates the challenges of managing the volume of appointments and investigations for both the NHS and patients, who may need to travel significant distances to tertiary centres.

Abstract citation ID: lvag096.1238

EP950 - ECE_3248 - Tracing an SDHD-Related Paraganglioma Cluster Across Generations

Simina Plesca[1], Diana Martiniuc[2], Ingrid-Ioana Stafie[2,3] and Cristina Preda[2,3]

[1]"St Spiridon" Clinical Emergency County Hospital Endocrinology, Iasi, Romania; [2]Iasi, Romania; [3]"Gr. T. Popa" University of Medicine and Pharmacy, Iasi, Romania

Introduction: Paragangliomas are rare neuroendocrine tumours arising from sympathetic or parasympathetic paraganglia and are frequently associated with germline variants in succinate dehydrogenase (SDH) genes. SDHD variants are typically associated with head and neck disease, show variable penetrance, and demonstrate a parent-of-origin effect related to genomic imprinting, with clinical manifestations occurring mainly after paternal transmission.

Case Presentation: We report a 41-year-old woman who was referred for endocrine reassessment after undergoing excision of a right carotid body paraganglioma . Her symptoms began at the age of 28, during her first pregnancy, with persistent right-sided hemicrania, together with gestational hypertension, sinus tachycardia and atrial extrasystoles. Repeated urinary fractionated metanephrines remained within the normal range. Cervico-thoraco-abdominal CT showed bilateral carotid body paragangliomas (40 mm on the right and 13 mm on the left), and the right-sided tumour was completely resected. Histopathology confirmed a moderately differentiated parasympathetic paraganglioma (GAPP score 5-6) with vascular invasion and positive margins. Following surgery, headache and blood pressure improved, although the recovery was complicated by transient hypoglossal nerve palsy.Somatostatin receptor scintigraphy (99mTc-Tektrotyd) showed intense tracer uptake in the left carotid lesion, with no other abnormal findings. Further endocrine evaluation excluded syndromic associations, including MEN2 and the 3P association. Germline testing with a hereditary paraganglioma–phaeochromocytoma panel identified a heterozygous likely pathogenic SDHD c.52+2T>C variant, together with a CHEK2 c.470T>C (p.Ile157Thr) moderate cancer-risk variant. In keeping with the genetic findings, several relatives were also affected. These included the patient's father, who had bilateral carotid paragangliomas and colorectal cancer at 41 years of age; a paternal uncle who declined surgery; a paternal aunt treated with radiotherapy; and a cousin who died during reoperation, with her sister more recently diagnosed with paraganglioma.. The patient has three asymptomatic children who are currently undergoing clinical and genetic surveillance.

Conclusions: This case illustrates the value of careful family assessment in recognising hereditary paraganglioma syndromes and directing appropriate genetic testing. Identification of a pathogenic SDHD variant supports lifelong surveillance and cascade testing in at-risk relatives, with the aim of reducing morbidity and improving preventive care.

Keywords paraganglioma, SDHD, familial clustering, genomic imprinting, genetic screening

Abstract citation ID: lvag096.1239

EP951 - ECE_3328 - Targeting the inflammasome machinery: a multi-omic approach to identify new diagnostic markers and therapeutic strategies in brain tumors

Natalio Leiva-Hidalgo[1,2,3], Ignacio Gil-Duque[1,2,3], Miguel E. G-Garcia[1,2,3], María Ortega-Bellido[1,2,3], Miguel Ángel Núñez-Santos[1,2,3], Manuel D. Gahete[1,2,4], Antonio C. Fuentes-Fayos[1,2,3] and Raul M. Luque[1,2,4]

[1]Maimónides Biomedical Research Institute of Córdoba (IMIIBIC)/ Reina Sofía University Hospital, Córdoba, Spain; [2]Department of Cell Biology, Physiology, and Immunology, University of Córdoba, Córdoba, Spain; [3]Reina Sofía University Hospital, Córdoba, Spain; [4]Biomedical Research Networking Center for Physiopathology of Obesity and Nutrition (CIBERobn), Madrid, Spain

Glioblastoma (GBM) remains the most prevalent and lethal primary brain endocrine-related cancer in adults. Despite current gold standard therapies, late-stage diagnosis and inherent therapeutic resistance result in a bad prognosis, with median survival

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

rates limited to 10-12 months. Consequently, there is an urgent clinical need to identify novel diagnostic/prognostic biomarkers and therapeutic targets to improve patient management and quality of life. GBM is characterized by profound cellular heterogeneity and a complex tumor microenvironment (TME), wherein the immune system plays a key role in modulating tumor-associated inflammation. An essential component of this inflammatory response is the inflammasome machinery, a multiprotein complex activated by cellular stress and damage, being closely linked to immune evasion, cell death, and TME remodeling. In this study, we characterized the expression pattern of inflammasome components using a high-throughput qPCR array based on microfluidic technology. We analyzed a well-characterized cohort of GBM patients ($n = 63$) compared to non-tumor brain (NTB; $n = 19$) samples. Our results revealed a profound and widespread dysregulation of the inflammasome machinery in GBM tissue. These findings were subsequently validated in multiple independent external cohorts using RNA-seq, microarray and proteomic data, confirming the robustness of the observed expression patterns. To further address the complexity of this tumor, we characterized specific cell populations using an external single-cell sequencing dataset. Remarkably, the expression of key inflammasome components (highlighting MYD88) correlated significantly with aggressive clinical parameters and poor prognosis, including reduced survival rates, higher recurrence, EGFR amplification, and MGMT promoter methylation status. In silico pathway analysis further demonstrated that MYD88 expression is associated with critical pathways in GBM pathophysiology, such as epithelial-to-mesenchymal transition (EMT), hypoxia, angiogenesis, and NF-κB signaling. To evaluate the functional relevance of these findings, we performed in vitro modulation of MYD88 through transient silencing (siRNA) and pharmacological inhibition. Notably, we also addressed the challenge of chemoresistance by evaluating these modulations in a temozolomide (TMZ)-resistant GBM cell model developed within our laboratory. These interventions significantly reduced key oncogenic parameters, including cell proliferation, migration rate, and colonies and tumorspheres formation. In conclusion, this study demonstrates that the inflammasome machinery is a critical driver of GBM progression. Our data highlights MYD88 as a potential master regulator of tumor aggressiveness, positioning it as a novel diagnostic/prognostic biomarker and a promising therapeutic target to improve outcomes for patients suffering from this devastating disease.

Abstract citation ID: lvag096.1240

EP952 - ECE_3631 - From primary hyperparathyroidism to multifocal pNETs: neoplastic spectrum of MEN1 in early adulthood

Kalliopi Pantelia, Vasiliki Antonopoulou, Aggeliki Kyriakou, Marinella Tzanela and Theodora Stratigou
Department of Endocrinology "D. Ikkos"- Diabetes Center-EndoERN-Evangelismos General Hospital, Athens, Greece

Background: Multiple Endocrine Neoplasia type 1 (MEN1) is characterized by multifocal and recurrent endocrine neoplasms, most commonly involving the parathyroid glands and the gastroenteropancreatic neuroendocrine system.

Case Presentation: A 20-year-old male was diagnosed with primary hyperparathyroidism following detection of hypercalcemia during evaluation of a presyncopal episode. Physical examination was unremarkable. Biochemical evaluation revealed elevated serum calcium (12.4 mg/dL), parathyroid hormone (185.8 pg/mL) and urinary calcium excretion. Imaging demonstrated a large left inferior parathyroid lesion. The patient underwent subtotal parathyroidectomy, with pathology revealing three parathyroid adenomas and loss of nuclear menin expression.

Given the early onset and multiglandular disease, molecular analysis was performed and identified a heterozygous pathogenic MEN1 mutation (c.1378C>T, p.Arg460Ter), confirming the diagnosis of MEN1. Further evaluation revealed unremarkable pituitary imaging, but multifocal pancreatic lesions on MRI, subsequently confirmed by 68Ga-DOTATOC with high somatostatin receptor expression (SUVmax 68). Biochemical evaluation of neuroendocrine activity revealed mildly elevated chromogranin A (5.9 nmol/L, reference <3) and significantly increased plasma glucagon levels (418 pg/ml, reference <250) at initial assessment. Surgical management consisted of subtotal pancreatectomy. Histopathological examination demonstrated multiple well-differentiated neuroendocrine neoplasms: a pancreatic head pNET G2 measuring 3.0 cm, a pancreatic body glucagon-positive pNET G1 measuring 2.5 cm, an additional pNET G1 measuring 0.8 cm, four pNETs (0.5-3 mm), and a duodenal NET G2 measuring 0.6 cm. No lymph node metastases were identified (pancreas pT2(m)N0, duodenum pT1N0). Serial measurements demonstrated normalization of neuroendocrine markers.

Six months later, endoscopic ultrasound and MRI revealed new small lesions (5-9 mm), in the pancreatic remnant one confirmed (EUS-FNB) as a G1 glucagon (+) pNET. 68Ga-DOTATOC showed only mild uptake in lymph nodes, attributed to inflammation. Subsequent MRI revealed additionally an irregular mass measuring 3.5×2.7 cm in the lesser sac. Neuroendocrine tumor markers remained within normal limits. Following multidisciplinary re-evaluation, the irregular lesion was attributed to a post-procedural hematoma. The patient was therefore placed under close surveillance.

Conclusions: This case illustrates the aggressive neoplastic burden and early multifocality of MEN1-associated gastroenteropancreatic neuroendocrine tumors. Pancreatic neuroendocrine tumors in MEN1 are traditionally diagnosed after the 2nddecade of life. The diagnosis of multiple pNETs at 20 years of age in this patient is early but within the expected MEN1 spectrum. Detailed tumor characterization is critical for surgical decision-making and long-term surveillance in young MEN1 patients.

Abstract citation ID: lvag096.1241

EP953 - ECE_3666 - To highlight the importance of surveillance for ovarian cancer in women with MEN2A with RET positive mutations and to consider prophylactic oophorectomies

Veronica Chirila and Bushra Ahmad
Diabetes and Endocrinology, Bristol Royal Infirmary, Bristol, United Kingdom

Case History: We present a fit and well 50-year-old patient who was very concerned about the genetic predisposition for ovarian cancer following the early death of her mother of ovarian cancer at the age of 61 (diagnosed at 51).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

The genetic screening demonstrated RET mutation (Val804leu). Our lady was reviewed in the endocrinology clinic, underwent surveillance and medullary thyroid cancer was detected and had thyroidectomy in February 25. Histology results showed medullary thyroid cancer T1N1M0.

There is no metastatic disease found on the staging CT scans.

After discussion, our patient has decided to go for a prophylactic oophorectomy after menopause in view of her risk of ovarian cancer.

Investigations: Radiology: US thyroid (December 24): an ill-defined lesion with micro and macro calcifications.

CT neck/chest/abdomen/pelvis (December 24):No lymphadenopathy or metastatic disease was found.

US neck (March 25): no concerning lymphadenopathy

MRI pelvis (April25): no adnexal masses seen

Biochemistry: Bloods (December 24): calcitonin 165 (<4.8), CEA 11.1 (<5.2).

Post thyroidectomy bloods (Apr 25): calcitonin<3

Conclusion and Discussions: Recent genomic analyses have identified recurrent somatic RET missense mutations in 2% of epithelial ovarian cancer (EOC) cases. Some of the RET mutations have oncogenic properties. Therefore, RET can act as an oncogenic driver in a subset of EOC and RET inhibitors such as Vandetanib have shown activity against EOC cells harbouring RET mutations in clinical trials.[1] Current guidelines recommend prophylactic oophorectomy to women with known BRCA1 or BRCA2 mutations or other mutations predisposing to ovarian cancer such as BR1P1, RAD51C and RAD51D.[2] However, prophylactic oophorectomy is also considered for women with strong family history of ovarian cancer, even in the absence of a confirmed pathogenic mutation, due to the possibility of undiscovered or untested genetic risk.[3] Therefore, this abstract highlights the importance of inclusion criteria for female patients with MEN2A with confirmed genetic RET mutation in the panel list for prophylactic oophorectomy.

The discovery of RET pathogenic variant in the EOC patients suggests a previously underestimated role for RET in EOC tumorigenesis. Also highlights the potential use of RET in targeted therapy to treat EOC patients.[1]

References

1. Guan L, Li Z, Xie F, et al. Oncogenic and drug-sensitive RET mutations in human epithelial ovarian cancer. *J. Expl. Clin Cancer Res*. 2020;39(1):53. doi: 10.1186/s13046-020-01557-3
2. Hereditary breast and ovarian cancer syndrome, 2017
3. Berek JS, Chalas E, Edelson M, et al. Prophylactic and risk-reducing bilateral salpingoophorectomy: recommendations based on risk of ovarian cancer. *Obstet Gynacol*. 2010;116(3):733-743. doi: 10.1097/AOG.0b013e3181ec5fc1.

Abstract citation ID: lvag096.1242

EP954 - ECE_2126 - CYP26B1 and RARB genetic variants in radioiodine-refractory papillary thyroid carcinoma

Rafał Fyda[1], Bartosz Partyński[2], Anna Nogieć[3], Alicja Hubalewska-Dydejczyk[4,5] and Malgorzata Trofimiuk-Muldner[4]

[1]*Students' Scientific Group, Chair and Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland*

[2]*Department of Endocrinology, Endocrine Oncology, Nuclear Medicine and Internal Diseases, University Hospital in Kraków, Kraków, Poland;* [3]*Haematological Diagnostics and Genetics Unit, University Hospital in Krakow, Kraków, Poland;* [4]*Department of Endocrinology, Chair and Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland;* [5]*Dep of Endocrinology, Jagiellonian University Medical College, Krakow, Poland*

Background: Radioiodine-refractory papillary thyroid carcinoma represents a major therapeutic challenge, as it is associated with limited treatment options and poorer clinical outcomes. Retinoids, including 13-cis retinoic acid, have been investigated as agents capable of restoring iodine uptake by modulating thyroid-specific gene expression. However, clinical responses have been inconsistent and limited to a small subset of patients. There is also scant data linking serum vitamin A concentrations with the clinical course of thyroid cancer. It might suggest that biological factors influencing retinoids metabolism and signaling may play a role.

Objective: The aim of this study was to determine whether patients with non-radioiodine-avid PTC differ from the general population with respect to genetic variants in *CYP26B1*, a key enzyme involved in retinoic acid catabolism, and *RARB*, encoding retinoic acid receptor beta.

Materials and Methods: Nineteen patients with histologically confirmed PTC and documented loss of radioiodine uptake were included. The cohort consisted of 10 men (52.6%) and 9 women (47.4%), with a mean age at diagnosis of 51.2 ± 19.0 years. According to AJCC 8th edition staging, tumors were classified as T1 in 31.6%, T2 in 21.1%, T3 in 26.3%, and T4 in 21.1% of patients; nodal metastases (N1) were present in 78.9%, and distant metastases (M1) in 36.8%. Multifocal disease was observed in 78.9% of cases. Patients received multiple courses of RAI therapy, with a mean cumulative administered activity of 9358 ± 3757 MBq; 68.4% received two RAI treatments, while the remainder received three or more. Genomic DNA extracted from peripheral blood was analyzed using Sanger sequencing of selected regions of *CYP26B1* and *RARB*. Identified variants were compared with reference allele frequencies from population databases.

Results: Sequencing identified only previously reported variants within the analyzed regions of *CYP26B1* and *RARB*. No statistically significant differences in allele or genotype frequencies were observed between patients with non–radioiodine-avid PTC and the general population. No rare or potentially pathogenic variants specific to the study cohort were identified.

Conclusions: In this cohort, no relevant genetic alterations were identified in *CYP26B1* or *RARB*. Therefore, those components of retinoic acid pathway are not likely to contribute to reported in the literature difference in the PTC behavior in relation to serum vitamin A concentrations.

Abstract citation ID: lvag096.1243

EP955 - ECE_2594 - Extensive Tumor Spectrum in MEN1: From Silent Adrenal Adenoma to Aggressive Adrenocortical Carcinoma with Cushing's Syndrome

Violetta Rosiek, Ksenia Janas and Beata Kos-Kudła

Endocrinology, Department of Endocrinology and Neuroendocrine Tumors, Department of Pathophysiology and Endocrinology, Medical University Of Silesia, Katowice, Poland

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Multiple endocrine neoplasia type 1 (MEN1) is typically characterized by the triad of parathyroid, pancreatic, and pituitary tumors. However, the syndrome can manifest with an unusually broad spectrum of non-classical and aggressive malignancies. Adrenocortical carcinoma (ACC) is an exceedingly rare manifestation of MEN1, with fewer than 20 cases described in the literature.

Case Presentation: We report a 43-year-old woman with genetically confirmed MEN1 and a remarkably complex phenotype. Her clinical history included a typical pulmonary carcinoid (resected, Ki-67 5%), primary hyperparathyroidism, a pituitary prolactinoma, and multifocal G1 neuroendocrine tumors (NETs) of the pancreasand duodenum. She also underwent surgery for an incidental clear cell papillary renal cell carcinoma.

The hallmark of this case was the rapid evolution of a left adrenal lesion. Initially identified as a hormonally silent 19 mm adenoma, the lesion demonstrated dramatic growth during surveillance, reaching 110 × 72 mm within 18 months. This rapid enlargement was accompanied by a functional transformation, leading to biochemical hypercortisolism and the development of overt clinical Cushing's syndrome. Histopathology confirmed high-grade ACC. Despite the stability of other MEN1-related lesions under somatostatin analog therapy, the aggressive progression of the ACC, with liver and suspected peritoneal metastases, required the initiation of systemic EDP-M chemotherapy (etoposide, doxorubicin, cisplatin, and mitotane).

Conclusions: This case illustrates the extreme clinical heterogeneity of MEN1 and highlights the potential for rapid transformation of a dormant, non-functional adrenal lesion into an aggressive, hormone-secreting malignancy. It underscores the critical need for vigilant, lifelong multidisciplinary surveillance, as functional and morphological changes in adrenal lesions can signal a shift toward highly aggressive disease.

Keywords MEN1, adrenocortical carcinoma, Cushing's syndrome, GEP-NET, pulmonary carcinoid, renal cell carcinoma

Abstract citation ID: lvag096.1244

EP956 - ECE_1059 - Atypical Carney Complex (CNC) presenting with acromegaly, pheochromocytoma, and cardiac myxoma: a rare multisystem presentation

Kiana Ghannadi[1], Chan Ju Baek[2], Fatemeh Ghannadi[2], Ashkan Parsa[3] and Iman Hemmati[4]
[1]*Faculy of Science, The University of British Columbia, Vancouver, Canada;* [2]*Department of Family Medicine, University of British Columbia, Seawall Medical Centre, Vancouver, Canada;* [3]*Division of Cardiology, University of British Columbia, Vancouver, Canada;* [4]*Division of Rheumatology, University of British Columbia, Vancouver, Canada*

Introduction: Carney Complex (CNC) is a rare autosomal-dominant neoplasia syndrome most often caused by PRKAR1A mutations, leading to dysregulated cAMP-protein kinase A signalling. Typical features include cardiac and extracardiac myxomas, pigmented skin lesions, and endocrine overactivity. Early recognition is essential to prevent complications and enable genetic screening. We report a case of CNC initially managed as presumed vasculitis, presenting with recurrent embolic events and multiple endocrine and non-endocrine tumours, including pheochromocytoma.

Case Report: A woman in her early 30s presented with six months of progressive myalgia and irregular plantar vascular lesions. Elevated C-reactive protein (15 mg/L) prompted suspicion for vasculitis, and she was prescribed prednisone. She subsequently developed palmar purpura, subungual tenderness, intermittent visual disturbances, and recurrent upper-extremity numbness. Echocardiography identified a 4.1-cm left atrial myxoma attached to the interatrial septum with mild inflow stenosis; the mass was resected without complication.

Post-resection evaluation identified an ocular blue nevus. Imaging revealed a 6-cm right adrenal pheochromocytoma, thyroid colloid cysts, and psammomatous melanotic schwannomas. Pituitary MRI demonstrated a macroadenoma, and endocrine testing showed elevated IGF-1 (702 µg/L) and chromogranin A. Endoscopic transsphenoidal resection confirmed a mixed somatotroph-lactotroph adenoma. Persistent acromegaly was treated with lanreotide, cabergoline, and pegvisomant, achieving IGF-1 normalisation (149 µg/L). She remains on long-term pegvisomant therapy with imaging surveillance. Adrenalectomy after alpha-blockade was uneventful. Follow-up MRI showed stable schwannomas without pheochromocytoma recurrence. Echocardiography demonstrated preserved ejection fraction (62%) with abnormal global longitudinal strain (–14%) and no myxoma recurrence. PRKAR1A testing is ongoing.

Discussion: This case illustrates the diagnostic challenge posed by multisystem CNC, particularly when early findings mimic rheumatologic disease. The patient's vasculitis-like lesions were secondary to embolisation from an atrial myxoma, which, along with a GH-secreting pituitary adenoma and psammomatous melanotic schwannomas, fulfils diagnostic criteria for CNC. Although pheochromocytoma is uncommon in classic CNC, it has been reported in expanded phenotypes and may overlap with the Carney-Stratakis spectrum. Its presence in this case broadens the recognised tumour spectrum of CNC and emphasizes the need for comprehensive endocrine and genetic evaluation. Early echocardiographic evaluation should be considered in patients with unexplained vasculitic-appearing lesions and systemic symptoms to exclude embolic cardiac sources.

Conclusions: CNC should be considered in patients presenting with multiple endocrine and non-endocrine tumours or atypical cutaneous findings. This case underscores the expanding phenotypic spectrum of CNC, particularly the coexistence of pheochromocytoma and acromegaly, and reinforces the importance of comprehensive endocrine evaluation and lifelong multidisciplinary surveillance.

Abstract citation ID: lvag096.1245

EP957 - ECE_3475 - Target therapy with Lorvatinib in a large cell neuroendocrine carcinoma (LCNEC) of the lung in MEN1

Roberta Mungari[1], Arianna Cremaschi[1], Elisa Sala[1], Giulia Carosi[1], Giulia Del Sindaco[1], Alessandra Mangone[1,2], Emanuele Ferrante[1] and Giovanna Mantovani[1,2]
[1]*Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan (Italy), MILANO, Italy;* [2]*Department of Clinical Sciences and Community Health, University of Milan, Milan (Italy), MILANO, Italy*

Multiple endocrine neoplasia type 1 (MEN1) is a genetic syndrome characterized by the development of multiple

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

neuroendocrine tumors involving the parathyroid glands, gastroenteropancreatic tract, pituitary gland, and less frequently the adrenal cortex, thymus, and bronchi; it may also be associated with other non-endocrine tumors.

LCNEC of the lung is a rare and aggressive cancer. The average 5-year survival rate is 35%, but it can vary significantly depending on the stage at diagnosis, with much lower survival rates in advanced metastatic disease.

We report the case of a 49-year-old female patient carrying the MEN1 mutation c.1937insC in exon 10. She presented with primary hyperparathyroidism and multiple pancreatic neuroendocrine tumors treated with somatostatin analogues since 2023.

In August 2024, a chest CT scan revealed an increase in size of a known pulmonary micronodule, described as a solid nodule with spiculated margins, highly suspicious for malignancy. The patient therefore underwent FDG-PET, which showed intense uptake in the pulmonary lesion, and Gallium-PET, which demonstrated the presence of somatostatin receptor–expressing lesions in the pancreatic, pulmonary, and right pulmonary hilar/perihilar regions.

Bronchoscopy and fine-needle aspiration of the hilar lymph node were performed, with cytopathological diagnosis of a well-differentiated, low-grade neuroendocrine neoplasm (Ki-67 = 3%). The patient underwent right lobectomy with lymphadenectomy in April 2025.

Histological examination revealed a combined carcinoma with a LCNEC component (90%, Ki-67 60%) and adenocarcinoma with solid and acinar growth patterns (5% and 5%, respectively, TTF-1 positive). In addition, metastases from LCNEC were present in multiple interlobar, peribronchial, subcarinal, and paratracheal lymph nodes (pT3, pN2).

Restaging was performed using FDG-PET, brain MRI, and chest–abdomen CT. These investigations showed significant disease progression, with the appearance of multiple new pulmonary nodules, mediastinal and laterocervical lymphadenopathies, and lesions consistent with metastases involving the liver, adrenal glands, pelvis, intestine, skeleton, and brain.

Molecular analysis performed on tumor tissue identified an ALK gene rearrangement, thus Lorvatinib 100 mg/d was started in June 2025.

At follow-up, in October 2025, the multiple brain nodular lesions appeared markedly reduced in volume or even no longer individually recognizable; secondary pulmonary nodules and hilar-mediastinal lymphadenopathy were no longer detectable; the hepatic metastasis was unchanged; the solid nodule located in the left hypochondrium and the right adrenal mass showed a reduction in size; and sclerosis of bone lesions was observed at sites of previous metastases. The drug was well tolerated, with only mild side effects, opening the possibility of an improved long-term prognosis.

Abstract citation ID: lvag096.1246

EP959 - ECE_1040 - Role of visfatin in cancers

Haitham Abu-Lebdeh[1,2,3] and Hassan Heshmati[4]
[1]*Division of Endocrinology, Diabetes, Metabolism and Nutrition, Mayo Clinic, Rochester, MN, United States;* [2]*Endocrinology, Mayo clinic, Rochester, United States;* [3]*Mayo Clinic, Rochester, United States;* [4]*Endocrinology Metabolism Consulting, LLC, Hassan Heshmati and Valerie Shaw Endocrine Research, Anthem, AZ, United States*

Introduction: Visfatin, a hormone first described in 2005, is an adipocytokine synthesized predominantly by the visceral adipose tissue but also by several other organs (eg, liver, muscle, heart, lung, kidney, and placenta). The gene of visfatin is located on chromosome 7q22.3. Visfatin consists of 491 amino acids. Visfatin plays an important role in inflammation and has been implicated in the proliferation of several cancers. This review presents an update on the role of visfatin in cancers.

Methods: A systematic search of literature was conducted for the period 2013 to 2025 using the search terms visfatin, cancer, proliferation, metastasis, chemotherapy, and prognosis.

Results: Visfatin has pro-oncogenic activity in several cancers. It promotes tumor proliferation through the activation of key oncogenic pathways (eg, enhancement of intracellular nicotinamide adenine dinucleotide synthesis needed for deoxyribonucleic acid repair) leading to increased angiogenesis, epithelial mesenchymal transition, and immune suppression. There is an increase in serum visfatin levels in different cancers. Studies in breast cancer, esophageal cancer, and gastric cancer have reported that visfatin is associated not only with inflammation, angiogenesis and tumor proliferation, but also with metastasis and resistance to chemotherapy. High serum visfatin levels are associated with poor prognosis of cancers. Serum visfatin level can be used as a biomarker in different cancers (eg, gastrointestinal and pancreatic cancers). Inhibitors of visfatin activity (eg, FK866, CHS828, and KPT-9274) represent promising therapeutic tools for cancers but the demonstration of their benefit and safety requires further clinical studies.

Conclusions: Visfatin is a hormone synthesized predominantly by the visceral adipose tissue. It is involved in multiple pathological conditions including inflammation and the proliferation of several cancers such as breast cancer and upper gastrointestinal cancers (eg, esophageal and gastric cancers). Elevated serum visfatin levels are associated with metastasis, drug resistance, and correlate with poor cancer prognosis. Serum visfatin level can be used as a prognostic biomarker in cancers. The potential benefit of inhibiting visfatin activity in the treatment of cancers requires further investigations.

Abstract citation ID: lvag096.1247

EP960 - ECE_3671 - Beyond JAK2: Endocrine and Paraneoplastic Causes of Secondary Polycythemia

Paola Girardi[1], Francesco Ramundo[2], Valerio De Stefano[2] and Alfredo Pontecorvi[1]
[1]*UOC Medicina Interna, Endocrinologia e Diabetologia, Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy;* [2]*UOC Ematologia, Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy*

Background: Endocrine Secondary Polycythemia (ESP) is an entity in which hormonal dysregulation enhances erythropoietic drive, resulting in increased hemoglobin and hematocrit levels (>16.5 g/dL and >49% in men; >16 g/dL and >48% in women). ESP should be clearly differentiated from Polycythemia Vera, a clonal myeloproliferative neoplasm associated with constitutive activation of the JAK–STAT signaling pathway, most commonly due to the JAK2 V617F mutation.

Although a comprehensive systematic review is currently lacking, an expanding body of literature documents the occurrence of ESP across a broad spectrum of endocrine and metabolic disorders.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Methods: We performed a narrative review aimed at delineating the principal endocrine-related causes of secondary polycythemia, conditions that are frequently overlooked or erroneously classified as idiopathic. A systematic search of the PubMed database was conducted, including human studies published between 1963 and 2025.

Search terms included:

- "endocrine related polycythemia"
- "secondary polycythemia in endocrinopathies"
- "SGLT2 inhibitor–induced polycythemia"
- "tyrosine kinase inhibitor–induced polycythemia"
- "paraneoplastic syndrome–induced polycythemia"
- "endocrine cancer–induced polycythemia"
- "polycythemia and uterine fibromyoma"

Of the 263 records identified, 73 articles met the inclusion criteria and were selected for qualitative analysis.

Results: Available evidence indicates that ESP, although uncommon, predominantly arises from three major pathogenetic settings.

Endocrine Disorders: include endogenous hyperandrogenism associated with adrenocortical, testicular, or ovarian tumors; erythropoietin-secreting pheochromocytomas; hypercortisolism; acromegaly; hyperthyroidism; and hyperparathyroidism.

Drug-Related Causes: encompass androgen replacement therapy for hypogonadism, anabolic steroid misuse, sodium–glucose cotransporter 2 inhibitors, and antiangiogenic tyrosine kinase inhibitors.

Paraneoplastic Syndromes: represent an additional etiological group and include paragangliomas and somatostatinomas (Pacak–Zhuang syndrome), gastrointestinal neuroendocrine tumors, LH-secreting pituitary gonadotropinomas, POEMS syndrome, renal cell carcinoma, supratentorial meningiomas, hemangioblastomas, and erythropoietin-producing uterine fibroids.

Conclusions: ESP represents a rare but clinically relevant cause of secondary polycythemia. Increased awareness and a structured diagnostic approach are essential to identify underlying endocrine or paraneoplastic etiologies. Early recognition may improve clinical management and enable the implementation of targeted therapeutic strategies, particularly in JAK2-negative polycythemias that are frequently—and incorrectly—classified as idiopathic.

Abstract citation ID: lvag096.1248

EP961 - ECE_2291 - Contrasting Genetic and Sporadic Malignant Adrenal Paraganglioma: A Case Series

Raluca Pirvu[1], Ramona Dobre[1,2], Iulia Florentina Burcea[1,2], Oana Pietrareanu[1] and Catalina Poiana[1,2]

[1]*National Institute of Endocrinology C.I. Parhon, Bucharest, Romania;* [2]*Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

Adrenal paragangliomas are rare neuroendocrine tumors arising from adrenal chromaffin cells, characterized by catecholamine hypersecretion and significant cardiovascular morbidity. Although most adrenal paragangliomas are benign, a minority exhibit malignant behavior, defined by local invasion or distant metastases, as reliable histopathological criteria predicting malignancy are lacking. Malignant adrenal paraganglioma therefore remains a diagnostic and therapeutic challenge. Up to 40% of adrenal paragangliomas are associated with hereditary syndromes. Genetic background influences clinical presentation, biochemical phenotype, surveillance strategies and prognosis, however malignant disease may also occur in apparently sporadic cases.

We present a series of three malignant adrenal paragangliomas illustrating genetic and sporadic forms across different ages. The first case involves an 18-year-old male initially diagnosed at age 15 with arterial hypertension and a left adrenal mass, which was surgically resected and confirmed as adrenal paraganglioma. Two years later, a contralateral adrenal tumor with malignant features (PASS 4, ki-67 >3%) developed and right adrenalectomy was performed. Tumor recurrence was subsequently confirmed by functional imaging, which demonstrated metabolically active bilateral adrenal lesions with minimal somatostatin receptor expression and early biochemical relapse. Genetic testing revealed a pathogenic VHL mutation.

Case 2 is a 38-year-old female presenting with a large left adrenal mass (10 cm) revealed by Menard's triad of headaches, palpitations and sweating. Biochemical markers were markedly elevated. Histopathological examination after adrenalectomy confirmed malignant adrenal paraganglioma (PASS 8). Postoperative biochemical remission was achieved, although mediastinal lymphadenopathy was detected on follow-up imaging.Given a significant family history of malignancy, genetic testing was performed and pathogenic mutations were excluded.

Case 3 involved a 57-year-old male with a right adrenal mass and markedly elevated plasma and urinary metanephrines. Following adrenalectomy, histopathology demonstrated adrenal paraganglioma with high malignant potential (PASS 8, Ki-67 18%). Sustained biochemical remission was observed and follow-up imaging showed no evidence of recurrence.

Malignant adrenal paragangliomas are rare tumors with highly variable clinical presentations, occurring in both hereditary and sporadic contexts. Genetic status informs tumor distribution, surveillance strategies and risk assessment however phenotypically aggressive disease may develop regardless of genotype. While histopathological scoring systems provide important information on malignant potential, they cannot reliably predict the clinical evolution of the disease. These cases emphasize the importance of early recognition, individualized surgical and medical management, and lifelong biochemical and imaging follow-up to detect recurrence or metastasis promptly, ensuring optimal long-term outcomes.

Abstract citation ID: lvag096.1249

EP963 - ECE_3791 - Metastatic Pancreatic Neuroendocrine Tumor With Suspected Hormonal Transformation After PRRT and Multiple Primary Malignancies: A Therapeutic and Surveillance Challenge

Ksenia Janas[1], Karolina Sas[2], Kamila Tokarczyk[2], Damian Zieliński[2] and Janusz Strzelczyk[1]

[1]*Department of Endocrinology and Neuroendocrine Tumors, Department of Pathophysiology and Endocrinology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Medical University of Silesia in Katowice, 35 Ceglana St., Katowice 40-514, Poland;* [2]*Student Scientific Society at the Clinic of Endocrinology and Neuroendocrine Tumors of the Department of Pathophysiology and Endocrinology of the Silesian Medical University in Zabrze, Medical University of Silesia in Katowice, 35 Ceglana St., 40-514 Katowice, Poland, Katowice, Poland*

Introduction: Pancreatic neuroendocrine tumors (pNETs) are rare neoplasms characterized by heterogeneous clinical

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

behavior and prolonged survival, which increases the risk of developing multiple primary malignancies (MPM). Hormonal transformation of initially non-functioning pNETs is uncommon but may significantly worsen prognosis and complicate management. We present a complex case illustrating both phenomena.

Case Report: A 55-year-old woman was diagnosed in 2020 with an initially non-functioning, well-differentiated G2 pancreatic neuroendocrine tumor (Ki-67 index 5%) located in the body and tail of the pancreas, with liver and lymph node metastases. Her oncological history was notable for gastric MALT lymphoma treated surgically and with chemotherapy in 1995. First-line treatment with lanreotide achieved disease stabilization. Due to high somatostatin receptor expression demonstrated on ^68Ga-DOTA-TATE PET/CT, the patient underwent four cycles of ^177Lu-DOTATATE peptide receptor radionuclide therapy (PRRT), resulting in partial radiological remission and prolonged disease control.

During long-term follow-up, the patient developed three metachronous primary malignancies fulfilling criteria for MPM: basal cell carcinoma of the scalp (2022), left-sided ductal breast carcinoma treated with surgery and radiotherapy (2023), and HER2-positive right breast carcinoma requiring neoadjuvant chemotherapy and mastectomy (2024). Serial imaging revealed gradual progression of liver metastases beginning in 2023, while the primary pancreatic lesion remained relatively stable.

In 2025, the patient developed recurrent, clinically significant hypoglycemia requiring diazoxide therapy, nutritional support, and gastrostomy. Given the absence of hypoglycemia at initial diagnosis and the temporal association with metastatic progression, a possible hormonal transformation of the pNET toward insulin secretion was suspected, although definitive biochemical confirmation remains pending. The patient continues treatment with somatostatin analogues and everolimus under close endocrinological and oncological supervision.

Conclusions: This case highlights the complexity of managing advanced pNETs in long-term survivors, emphasizing the need for continuous reassessment of tumor biology. Clinicians should remain vigilant for late hormonal transformation and the occurrence of multiple primary malignancies. Multidisciplinary care integrating endocrinology, oncology, and nuclear medicine is essential for optimizing outcomes and ensuring patient safety.

Abstract citation ID: lvag096.1250

EP964 - ECE_3035 - SMARCA4-Mutated Anaplastic Thyroid Carcinoma in a Young Adult: First Reported Case.

Joanna Januszkiewicz-Caulier[1,2], Michal Wagrodzki[3], Elwira Bakula-Zalewska[3] and Marek Dedecjus[1]

[1]Department of Endocrine Oncology and Nuclear Medicine, Department of Endocrine Oncology and Nuclear Medicine, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland (State Research Institute), Warszawa, Poland; [2]Departament of Oncological Endocrinology and Nuclear Medicin, Maria Skłodowska- Curie National Institute of Oncology, Warsaw, Poland; [3]Department of Pathomorphology, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland (State Research Institute), Warszawa, Poland

Background: Anaplastic thyroid carcinoma (ATC) is a rare and highly aggressive thyroid malignancy,affecting elderly patients. Although molecular profiling has become increasingly important in ATC, alterations of the SWI/SNF chromatin-remodelling complex, including SMARCA4 mutations, have not previously been reported in this tumour type.

Case Presentation: A 31-year-old male with no significant medical history presented with a rapidly enlarging neck mass, progressive dyspnoea and reduced exercise tolerance over approximately six weeks. Neck ultrasound revealed a large, heterogeneous, infiltrative tumour of the left thyroid lobe causing significant tracheal compression and associated cervical lymphadenopathy. Fine-needle aspiration biopsy showed malignant cells (Bethesda category VI) with suspicion of ATC; however, given the patient's young age, thyroid lymphoma was also considered. Core-needle biopsy with extensive immunohistochemical and molecular analyses excluded lymphoma, melanoma, sarcoma and NUT carcinoma, establishing the diagnosis of anaplastic thyroid carcinoma with a SMARCA4 mutation.

Staging computed tomography demonstrated stage IVB disease with extensive locoregional invasion and massive venous thrombosis extending from the right atrium to both internal jugular veins. The patient was not eligible for surgical or radiotherapeutic treatment. Therapeutic anticoagulation and systemic glucocorticoids resulted in transient clinical improvement. Rapid disease progression led to airway compromise requiring tracheal stenting, followed by initiation of palliative chemotherapy with carboplatin and paclitaxel.

Discussion: SMARCA4 alternations is a recognised drivers of several aggressive undifferentiated malignancies and is associated with rapid progression and poor prognosis. Its identification in ATC expands the molecular spectrum of this disease and may explain the unusually young age at presentation and aggressive clinical course.

Conclusions: To our knowledge, this is the first reported case of SMARCA4-mutated anaplastic thyroid carcinoma. The case highlights the importance of comprehensive molecular profiling in ATC, particularly in young patients or those with atypical clinical features, to improve diagnostic accuracy and inform future therapeutic strategies.

Abstract citation ID: lvag096.1251

EP966 - ECE_3611 - Interplay between nutritional status and immunophenotype in patients with gastroenteropancreatic neuroendocrine tumors: results of a cross-sectional study

Alessia Filice, Franz Sesti, Tiziana Feola, Carla Pandozzi, Marianna Minnetti, Francesca Sciarra, Simona Puntil, Andrea Scala, Arianna Gagliardi, Alexandra Nistor, Ilaria Bonaventura, Dario De Alcubierre, Davide Masi, Mary Anna Venneri, Andrea Isidori, Lorenzo Donini and Elisa Giannetta

Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy

Introduction: Nutritional status (body composition and functional status in particular) and immune profile are emerging determinants of prognosis and therapeutic response in oncology. However, the links between anthropometric and immune parameters in neuroendocrine neoplasms are still lacking.

Aim of the Study: To evaluate the relationship between body composition and immunophenotypic profile in patients with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

gastro-entero-pancreatic neuroendocrine tumors (GEP-NETs), in order to identify potential prognostic or predictive markers.

Materials and Methods: A cross-sectional observational study was conducted, enrolling patients with histologically confirmed GEP-NETs. Body composition was estimated using bioelectrical impedance analysis (BIA). Muscle strength was evaluated by handgrip strength (HGS) and subsequently expressed as percentiles. Patients were stratified into two groups based on dominant-arm HGS: a "probable sarcopenic" group (HGS < 50th percentile) and a "non-sarcopenic" group (HGS ≥ 50th percentile). Peripheral blood mononuclear cell (PBMC) subpopulations were analyzed using flow cytometry.

Results: 22 patients (12 females, 10 males;mean age 62.3 ± 7.4 years) met the inclusion criteria (59.1% G1, 40.9% G2).Locally advanced or metastatic disease (stage III or IV) was present in 40.9% of patients. Based on HGS percentile cutoffs, 13 patients (59.1%) were classified as non-sarcopenic and 9 (40.9%) as probable sarcopenic. Significant correlations emerged between monocyte subsets, body composition and muscle strength: fat-free mass percentage (FFM%) correlated positively with non-classical monocytes ($P < .001$) and negatively with classical monocytes ($P = .008$), whereas fat mass percentage (FM%) showed opposite trends (respectively, $P < .001$ and $P = .008$). HGS displayed similar associations with monocyte subsets (respectively, $P = .037$ and $P = .028$). The probable-sarcopenic group also showed a higher proportion of classical monocyte compared to the non-sarcopenic group ($P = .011$). Among female patients, the proliferative index (Ki-67) correlated inversely with phase angle (PhA) ($P = .024$), which also emerged as independent predictor of Ki-67. Lower PhA values were found in women with lymph node and/or liver metastases compared with non-metastatic patients ($P = .039$). No significant associations were observed in the male group.

Conclusions: These findings suggest a potential interaction between nutritional status and immune profile in patients with neuroendocrine tumors, with possible prognostic and therapeutic implications. Larger studies are needed to confirm these observations, verifying the role that nutritional status can have as a consequence of neoplastic disease, as an etiopathogenetic component or as a prognostic factor in the evolution of the disease.

Abstract citation ID: lvag096.1252

EP969 - ECE_3169 - Autoimmune endocrinopathies provide predictive efficacy and improved quality of life in cancer patients treated with immunotherapy—real world experience from Romania

Elena Lazar[1], Ioana Andreescu[2], Ioana Claudia Dan[2], Simona Coniac[3] and Corin Badiu[2,3]
[1]*Outpatients, Endocrinology, "A Trestioreanu" Institute of Oncology, Bucharest, Romania;* [2]*Research Department, Endocrinology IV, C.I. Parhon National Institute of Endocrinology, București, Romania;* [3]*Endocrinology, Endocrinology IV, "C Davila" University of Medicine and Pharmacy, Bucharest, Romania*

Background: High-quality real-world evidence (RWE) can provide reliable data upon the impact of immune check-point inhibitors (ICIs) in challenging cancer patients, usually underrepresented in randomized clinical trials (RCTs), but heavily treated in daily clinical practice. Frequently reported Endocrine-immune-related adverse events (E-irAEs) as thyroiditis or hypophysitis during ICIs treatment have been proposed as possible predictive biomarkers of response, meaning increased progression-free survival (PFS) and overall survival (OS).

Patients and Methods: This is a prospective analysis of 53 cancer patients, treated in a multidisciplinary and multi-institutional collaboration team approach, in Bucharest, Romania. The E-irAEs were evaluated using thyroid function and autoimmunity markers (TSH, fT4, ATPO) as well as adrenal reserve using short 250 ug iv Synacthene test. The quality of life (QoL) during ICIs was assessed using versions of EORTC QLQ-C30 questionnaires validated and translated into the Romanian language. Descriptive analysis was performed.

Results: A number of 33 thyroiditis were observed and treated by substitution treatment. Ten hypophysitis cases were treated by adrenal substitutive treatment using hydrocortisone 15-30 mg/day. Five patients developed both endocrine and non-E-irAEs. The QoL of cancer patients treated with ICIs and evaluated for E-irAEs in this prospective trial was significantly improved during the substitution hormonal therapy. We observed the trend toward earlier stages and more cancer sites treated with ICIs. We have noticed no Grade ≥3 E-irAEs.

Conclusions: RWE in national observational large cohort studies could bring more insightful information about clinical variables with impact on ICI's response in cancer patients. We highlight the emerging need of assessing the QoL of cancer patients experiencing E-irAEs, as they live longer with life-long hormonal treatment.

Abstract citation ID: lvag096.1253

EP971 - ECE_1518 - Endogenous Cushing's syndrome of unusual etiology

Maria Jose Vallejo Herrera, Veronica Vallejo Herrera, Carmen Bautista Recio and Belen del Arco Romualdo
Hospital Regional de Málaga, Málaga, Spain

Cushing's syndrome is caused by hypercortisolism of endogenous origin (adrenal or pituitary origin), although it can also be exogenous, causing a metabolic syndrome associated with other typical features such as Cushingoid facies, hirsutism, and abdominal striae. Tumor hormone production by lung carcinoma or neuroendocrine tumors are rare causes of Cushing's syndrome, while Cushing's syndrome caused by a primary neuroendocrine renal tumor is extremely rare. We present an unusual case of this condition, the fundamental pillars of which are diagnosis with hormonal studies and imaging tests, and early control of hypercortisolism. Management of this condition by a multidisciplinary team can achieve a cure and a favorable long-term prognosis for these patients.

Cushing's syndrome (CS) is caused by an excess of corticosteroids or ectopic adrenocorticotropic hormone (ACTH). It can have

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

an exogenous origin (corticosteroid treatment) or an endogenous origin, most frequently a pituitary or adrenal origin, and rarely due to tumor production in neuroendocrine neoplasms, notably lung and gastrointestinal carcinoma. Cushing's syndrome associated with primary renal neuroendocrine neoplasia is exceptionally rare, as in the case presented here, with very few similar reports in the literature.

Abstract citation ID: lvag096.1254

EP973 - ECE_3259 - Developing a standard dataset in the European Registries for Rare Endocrine and Bone Conditions (EuRREB): Multiple Endocrine Neoplasia type 1 (MEN1) module

Medard van den Broek[1], Mariya Cherenko[2], Natasha Appelman-Dijkstra[2], Francesca Giusti[3], Francesca Marini[3], Aurilia Cinzia[4], Maria Luisa Brandi[3], Petra Brügmann[4], Ludwig Schaaf[5], Frederic Castinetti[6], Faisal Ahmed[7], Alberto M. Pereira[8] and Gerlof D. Valk[1]
[1]University Medical Center Utrecht, Utrecht, The Netherlands; [2]Leids Universitair Medisch Centrum, Leiden, The Netherlands; [3]University of Florence, Firenze, Italy; [4]European MEN Alliance e.V., Wunstorf, Germany; [5]Klinikum Schwabing, Munich, Germany; [6]Aix-Marseille Université, Marseille, France; [7]University of Glasgow, Glasgow, Northern Ireland; [8]Amsterdam Umc, Amsterdam, The Netherlands

Background: Multiple Endocrine Neoplasia type 1 (MEN1) is a rare hereditary syndrome associated with significant morbidity and reduced life expectancy due to a high penetrance of several endocrine tumors and other related manifestations. International collaborations are essential for gaining deeper insights into this condition by generating robust high-quality clinical data and patient experiences through patient reported outcomes.

Purpose and Methods: The European Registries for Rare Endocrine and Bone Conditions (EuRREB) within the Core Registry platform allows to collect a set of core data elements and specific dataset within the condition specific modules (CSM) as well as patient reported outcome measures. Within the registry, the MEN1 module was created through the multistakeholder collaboration of clinicians, researchers and patient advocacy groups over the course of 2 years (with 10 experts from 4 different countries and 2 patient representatives). The purpose was to build a scalable framework to capture essential clinical information and patient-reported outcomes, with the capacity to support future observational studies, eventually leading to more knowledge about thepathophysiology, natural history and impact of MEN1 related manifestations.

Results: The initial dataset was launched December, 2023 with over 250 variables. Seven feedback sessions were conducted over the course of development of the module, based upon which the dataset was finalized with 118 unique variables, with the opportunity to collect repeated data to adequately capture the longitudinal follow-up of MEN1 patients.

As a result of the consensus, a beta version was launched in July 2025 and recently, the final version of the module was officially launched on **01-12-2025** to be available for all MEN1 patients, and clinicians within expertise centers throughout Europe.

Conclusions: This MEN1 module within EuRREB has the potential to serve as a multicenter international registry, providing an ideal foundation for advancing healthcare outcomes for this group of patients. All clinicians with experience in MEN1 are encouraged to take part in the module.

Abstract citation ID: lvag096.1255

EP974 - ECE_3305 - Metastatic insulinoma with refratory hypoglycaemia: Challenges in clinical management

Ana Margarida Sobral[1], Alice Monsanto[1], Mariana Coelho[1], Adriana Duarte[1], Bárbara Jesus[1], Gustavo Rodrigues[1], Tânia Carvalho[1], Diogo Lameirão[2], Sofia Lopes[1], Ana Carreira[1], Mariana Lavrador[1], Inês Vieira[1], Joana Reis Guiomar[1], Diana Catarino[1], Daniela Guelho[1], Carolina Moreno[1], Joana Saraiva[1], Dírcea Rodrigues[1], Gracinda Costa[2] and Leonor Gomes[1]
[1]Coimbra, Portugal; [2]Serviço de Medicina Nuclear da Unidade Local de Saúde de Coimbra, Coimbra, Portugal

Introduction: Malignant insulinomas are uncommon pancreatic neuroendocrine tumors, characterized by locally advanced or metastatic disease. Clinically they present with severe hypoglycaemia. Their aggressive behaviour and limited response to conventional therapies, poses significant management challenges. We describe a case of unresectable metastatic insulinoma requiring a multimodal therapeutic approach.

Clinical Case: A 38-year-old man presented to the emergency department with recurrent episodes of altered consciousness associated with hypoglycaemia. Initial evaluation revealed symptomatic hypoglycaemia (plasma glucose 41 mg/dL) with biochemical evidence of endogenous hyperinsulinism (insulin 44.3 µIU/mL [1.9-23]; C-peptide 4.35 ng/mL [0.73-4.37]). His medical history was notable for well-controlled HIV infection. Iatrogenic causes for hypoglycaemia, adrenal insufficiency, and growth hormone deficiency were excluded. Family history was unremarkable.

Cross-sectional imaging identified multiple hepatic lesions, the largest measuring 61 mm, consistent with metastatic disease and a 34 × 19 mm pancreatic mass.

Histopathological analysis of a liver lesion confirmed metastatic grade 2 neuroendocrine tumor. Gallium-68 DOTANOC PET/CT demonstrated intense somatostatin receptor expression in the pancreatic lesion and corresponding hepatic and lymph node metastases. Genetic testing excluded MEN1 and MEN4 syndromes.

Medical therapy was initiated and progressively escalated, including high-dose diazoxide (up to 1,200 mg/day), dexamethasone (16 mg/day), short-acting octreotide and long acting pasireotide 40 mg afterwards. Despite this, hypoglycaemic episodes persisted, necessitating prolonged hospitalization with continuous high-volume intravenous 50% dextrose infusion and parenteral nutrition.

After presenting the case in multidisciplinary neuroendocrine tumor board, peptide receptor radionuclide therapy (PRRT) with lutetium-177 was planned, as surgical intervention was deemed infeasible.

The clinical course was complicated by opportunistic pneumonia and acute pulmonary oedema, attributed to immunosuppression

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

due to HIV infection, and high-dose diazoxide and glucocorticoid, resulting in admission to a level II care unit and delayed PRRT initiation.

Following clinical stabilization, the patient received the first cycle of Lu-177-DOTATATE on day 70 after admission. As glycaemic control progressively improved, concomitant medical therapy was gradually reduced, allowing hospital discharge on day 122 under monthly pasireotide 40 mg.

The patient subsequently completed three additional cycles of PRRT and remains under endocrinology follow-up, with sustained euglycaemia and biochemical remission. Follow-up Ga-68 DOTANOC PET/CT demonstrated a reduction in both size and radiotracer uptake of hepatic, nodal, and primary pancreatic lesions, suggestive of partial treatment response.

Conclusions: This case highlights the challenges of malignant insulinoma management and supports the role of PRRT as an effective option for controlling both tumor burden and refractory hypoglycaemia.

Abstract citation ID: lvag096.1256

EP975 - ECE_3440 - Extremely aggressive course of an incidentally detected adrenocortical carcinoma despite complete surgical resection

Cristina Contreras Pascual[1] and Paloma Gonzalez Lazaro[2]
[1]Hospital Santa Bárbara, Soria, Spain; [2]Hospital General La Mancha Centro, Alcázar de San Juan, Spain

Adrenocortical carcinoma (ACC) is a rare and highly aggressive malignancy with poor prognosis, even after complete surgical resection. It presents a bimodal age distribution and may manifest through hormonal hypersecretion, mass-related symptoms, or as an incidental finding. Accurate diagnosis and prognostic stratification are essential for treatment planning, imaging, hormonal evaluation, and histopathological assessment. Although surgery is the most important treatment, recurrence and rapid progression are frequent. Mitotane is commonly used as adjuvant therapy, but its toxicity and uncertain impact on overall survival limit its applicability.

We report the case of a 66-year-old male with an incidentally discovered ACC, illustrating the limitations of current prognostic models. The patient had a history of smoking, alcohol consumption, hypertension, and genetically confirmed hypertrophic cardiomyopathy treated with an implantable cardioverter-defibrillator. An abdominal computed tomography (CT) was performed for mild alcohol-related pancreatitis, revealing a 14-cm right adrenal mass and contralateral adrenal hyperplasia.

Despite being clinically asymptomatic, hormonal evaluation demonstrated autonomous cortisol secretion (1-mg dexamethasone suppression test: cortisol 16.9 μg/dL) and androgen excess, with suppressed gonadotropins and elevated dehydroepiandrosterone sulfate (DHEA-S) levels (790 μg/dL). Staging with whole-body CT and bone scintigraphy showed no evidence of metastatic disease. The patient underwent right adrenalectomy two months after diagnosis.

Histopathological examination confirmed adrenocortical carcinoma with marked high-risk features, fulfilling six Weiss criteria: high nuclear grade (Fuhrman grade IV), mitotic rate >20/50 high-power fields, atypical mitoses, diffuse architecture >33%, extensive necrosis, and focal capsular invasion. The tumor measured 13 × 8 cm, weighed 1056 g, showed oncocytic areas, and had an extremely high Ki-67 proliferation index (75%). Surgical margins were negative (R0 resection), and pathological staging was pT3 (AJCC 8th edition), indicating highly aggressive tumor biology.

Despite complete resection, early postoperative progression was observed. One month after surgery, imaging revealed local recurrence and metastatic lymphadenopathy. Adjuvant mitotane was contraindicated due to comorbidities and toxicity risk. Chemotherapy with carboplatin and etoposide combined with radiotherapy was initiated, but the disease rapidly progressed with widespread metastases. The patient developed heart failure and ascites and subsequently died.

This case highlights the extreme aggressiveness ACC may exhibit despite early detection and optimal surgical management, emphasizing the urgent need for improved prognostic and molecular markers to better predict outcomes and guide individualized treatment strategies.

Abstract citation ID: lvag096.1257

EP976 - ECE_2792 - Managing a case of carcinoid heart disease:The role of multidisciplinary team

Milena Yoveva[1,2,3], Gideon Mlawa[1], Aye Hline[1] and Furhana Hussein[1]
[1]Queen's Hospital, Romford, United Kingdom; [2]Acute Medicine, Barking, Havering and Redbridge University Hospitals NHS Trust, Romford, United Kingdom; [3]Acute Medicine, Barking, Havering And Redbridge University Hospitals Nhs Trust, Romford, United Kingdom

Introduction: Carcinoid Heart Disease (CHD) occurs in the majority of patients with Neuroendocrine Tumour (NET) and Carcinoid Syndrome (CS). The mechanism is poorly understood. It is thought that chronic exposure to high plasma serotonin levels from most commonly small intestinal NETs, causes fibrous changes of the endocardium. It predominantly affects the right side of the heart, in > 90% of cases, leading to tricuspid regurgitation in nearly all, and less commonly pulmonary regurgitation, tricuspid and pulmonary stenosis. Endocrinologists are often primarily responsible for these functioning NETs. Treatment strategies is delivered via an experienced NET MDT comprising medical oncologists, cardiologists, endocrinologists, surgeons, radiologists, gastroenterologists, histopatologists, nurse specialists.

Case: 73-year-old gentleman who was on 177 Lu-DOTATATE and Lanreotide for grade 2 metastatic neuroendocrine tumour, diagnosed 4 months earlier, was referred to a Cardiologist in April. He complained of leg swelling, tiredness, exhaustion, reduced appetite, nausea, weight loss of 2 stones in 6 months. Examination revealed regular pulse 92, blood pressure 110/70 in supine and 119/74 in standing, normal heart sounds, systolic murmur at left sternal edge, clear chest, moderate oedema to legs. ECG showed sinus rhythm, left axis, low voltage QRS. NT-proBNP was elevated at 865. Transthoracic echocardiogram revealed severely dilated RV with good longitudinal systolic function, paradoxical IV septal

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

motion, LV systolic function 50%, thickened tricuspid valve leaflets with restricted movement causing severe regurgitation, severely elevated pulmonary artery pressure, mild pulmonary stenosis, dilated IVC. He was admitted for management of heart failure, acute kidney injury on a background of chronic kidney disease, nutritional and psychological support. During his hospitalisation, he underwent further images as CXR, NM Lung perfusion, abdominal USS, TOE, CMR, HRCT thorax. He was reviewed by Oncology and Respiratory Team. He was discussed during Cardiac MDT and referred to a Cardiothoracic Surgeon and Pulmonary Hypertension Team. In June, he was admitted to a private hospital due to general decline and was treated in intensive care for a few days for encephalopathy. In July, he died peacefully in a Hospice.

Discussion and Conclusions: CHD is a major source of morbidity and mortality for CS patients. Measurement of 5-Hydroxyindoleacetic acid (5-HIAA), NT-proBNP and echocardiogram are useful in assessment of patients at risk from or with CHD. Management of heart failure, lowering 5-HIAA, and cardiac valve replacement in selected cases with expected survival > 12 months, arestrategies improving quality and length of life. Patient should be managed in CHD experienced centre.

Abstract citation ID: lvag096.1258

EP977 - ECE_3223 - Adrenocortical Carcinoma in Li-Fraumeni Syndrome- current management in hereditary context

Ioana Claudia Dan[1], Andreea-Alexandra Grosu[1], Teodor Constantin[1], Maria Anghel[1], Viorica Nicuta[1] and Corin Badiu[1,2]

[1]Research Department, Endocrinology IV, C.I. Parhon National Institute of Endocrinology, București, Romania; [2]Endocrinology, Endocrinology IV, "C Davila" University of Medicine and Pharmacy, Bucharest, Romania

Introduction: Li-Fraumeni syndrome (LFS) is a rare hereditary cancer predisposition syndrome caused by pathogenic variants in the TP53 gene. It is characterised by a markedly increased lifetime risk of early-onset and multiple primary malignancies, most commonly adrenocortical carcinoma (ACC), breast cancer, central nervous system tumours, osteosarcomas, soft-tissue sarcomas, leukaemia and a broad spectrum of other solid tumours. The estimated lifetime cancer risk exceeds 90% in women and 70% in men.

Case Report: We present the case of a 30-year-old female with a history of hirsutism and basal hypercortisolism, but without other syndromic features at presentation. September 2024, hormonal evaluation revealed a disrupted cortisol circadian rhythm with incomplete suppression on dexamethasone suppression testing, while sex steroid and adrenal hormone profiles were otherwise unremarkable, with associated hypokalaemia. Computed tomography identified a well-defined left adrenal mass ($3.1 \times 5.0 \times 4.8$ cm) with heterogeneous unenhanced density (39-67 HU), raising suspicion for malignancy. The patient underwent left adrenalectomy in November 2024, during which a uterine leiomyoma was also excised.

Histopathological analysis confirmed high-grade conventional ACC (Weiss score 7, modified Weiss 5) with capsular and sinusoidal invasion, and negative surgical margins (R0). Immunohistochemistry demonstrated diffuse SF1 positivity, patchy synaptophysin and nuclear beta-catenin expression, a wild-type p53 pattern, and a Ki-67 index of 35-40%. Postoperative adrenal function was preserved. Adjuvant mitotane therapy was initiated but discontinued after less than five months due to gastrointestinal toxicity, without achieving therapeutic plasma levels; therapy-induced adrenal insufficiency necessitated glucocorticoid replacement therapy.

Given the patient's young age at ACC diagnosis and significant family history (father with prostate adenocarcinoma and thymoma at 51 years, paternal grandmother with breast cancer before 40 years), genetic testing was performed using whole exome sequencing (WES). This analysis identified a heterozygous pathogenic TP53 variant (NM_000546.6:c.800G>C;p.Arg267Pro;rs587780075), confirming LFS. Targeted testing revealed the same variant in the patient's father, asymptomatic sister, and niece (aged 4 years 11 months), who exhibited mildly elevated DHEA-S and tall stature, with normal imaging.

In May 2025, the proband underwent right mastectomy for ductal carcinoma in situ (pTis pN0, R0, ER/PR+), and prophylactic left mastectomy, which revealed focal atypical ductal hyperplasia and fibroadenomas.

Conclusions: ACC may serve as an index tumour for diagnosing hereditary cancer syndromes. Early identification enables cascade genetic testing, facilitating detection and surveillance of at-risk relatives, and optimising clinical management for affected families

Abstract citation ID: lvag096.1259

EP978 - ECE_1428 - Simultaneous β-hCG and PTHrP secretion in a poorly differentiated high-grade urothelial carcinoma: A case report

Ismene Bilbao Garay[1,2], Clara Cerezo[1], Nerea Egaña Zunzunegui[1], Ane Amilibia Achucarro[1], Amaia Mendia[1], Nerea Diez[1], Sara Larrabeiti[1] and Cristina Garcia Delgado[1]

[1]Endocrinology Department, Hospital Universitario Donostia, San Sebastián, Spain; [2]Endocrinology, Hospital Universitario Donostia, San Sebastián, Spain

Introduction: Poorly differentiated high-grade urothelial carcinomas may be associated with a wide range of paraneoplastic syndromes due to aberrant expression of hormones, growth factors, cytokines, or their precursors. Tumours presenting with paraneoplastic manifestations usually display more aggressive biological behaviour and are associated with a worse prognosis. Simultaneous secretion of β-human chorionic gonadotropin (β-hCG) and parathyroid hormone-related peptide (PTHrP) in urothelial carcinoma is extremely rare.

Case Presentation: We report the case of a 51-year-old woman admitted to the Endocrinology Department for severe hypercalcaemia. Her medical history included excision of a benign gynaecological lesion several years earlier. One month before admission, she had undergone laparoscopic nephroureterectomy for a high-grade urothelial carcinoma, staged pT3N2.

Biochemical evaluation revealed suppressed parathyroid hormone (PTH) levels with markedly elevated PTHrP concentrations (7.7 pmol/L; reference range 0-1.5), consistent with humoral

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hypercalcaemia of malignancy. Serum β-hCG levels were also significantly elevated (3,560 IU/L; reference range 0-5). Imaging studies identified multiple intraparenchymal nodules, and biopsy confirmed metastatic disease of urothelial origin.

An extended immunohistochemical study for gonadotropins was performed on several sections of the primary tumour, demonstrating positive β-hCG expression within the solid component showing sarcomatoid differentiation. This finding is uncommon and more typically described in urothelial carcinomas with trophoblastic differentiation, although it has also been reported in very poorly differentiated high-grade tumours.

Following the first cycle of chemotherapy, β-hCG levels decreased dramatically to 342 IU/L and became undetectable after the second cycle. This biochemical response was concordant with partial radiological remission.

Conclusions: Only a limited number of cases of urothelial carcinoma with simultaneous β-hCG and PTHrP secretion have been reported in the literature. Although exceedingly rare, this entity is associated with paraneoplastic syndromes, aggressive tumour behaviour, and the need for intensive multidisciplinary management. Elevated β-hCG levels in urothelial carcinoma may indicate a poorer prognosis and could represent a useful biomarker for monitoring treatment response.

Abstract citation ID: lvag096.1260

EP1672 - ECE_3739 - Evolution of Tumor Grade and Intrapatient Heterogeneity in Neuroendocrine Tumors

Andreea Anne-Marie Brînzan[1,2], Iulia Florentina Burcea[1,2], Dobre Ramona[1,2] and Catalina Poiana[1,2]
[1]*"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania;* [2]*Pituitary and Neuroendocrinology Department, "C.I. Parhon" National Institute of Endocrinology, Bucharest, Romania*

Background: Neuroendocrine tumors (NETs) are increasingly recognized as dynamic neoplasms rather than biologically static entities. Accumulating evidence indicates that a subset of well-differentiated NETs undergoes biological progressive reprogramming over time, characterized by an increase in the Ki-67% proliferation index and grade evolution, while preserving neuroendocrine differentiation. This phenomenon reflects both temporal and spatial intrapatient heterogeneity, with clinically relevant discrepancies between primary tumors and metastatic lesions which may affect prognosis and therapeutic decision-making.

Materials and Methods: We conducted a retrospective observational study including NET patients managed at a tertiary referral center between January 2020 and January 2025. Among 143 screened patients, 17 fulfilled the inclusion criteria of having paired histological samples from both the primary and metastatic sites, allowing grade comparison. Tumors were classified according to World Health Organization (WHO) most recent criteria, with Ki-67% assessed in both samples. Patients were stratified into stable grade and grade progression groups (G1 to G2). Clinical characteristics, treatment strategies, response evaluation criteria in solid tumours (RECIST) and survival outcomes were analysed.

Results: Among 17 patients, grade discordance was observed in 6 cases (35%), all demonstrating a shift from G1 in the primary tumor to G2 in metastatic lesions, with a significant increase in Ki-67. This subset exhibited a longer mean disease duration compared to those with stable grading (8.3 vs 4.8 years), consistent with time-dependent biological progression. Tumor origin also differed between groups: pancreatic primaries comprised 50% of the progression cohort, whereas ileal tumors predominated among patients with stable grade (54.5%). Clinically, patients with grade progression experienced a higher burden of neuroendocrine symptoms, including increased incidence of carcinoid syndrome (66.7%) and carcinoid heart disease (66.7%). Importantly, this biological shift had direct therapeutic consequences, with patients in the progression group requiring systemic chemotherapy in 50% of cases, reflecting loss of disease control with standard therapies. Mortality was also higher in this group (50% vs 27.3%), and this pattern of evolution correlated with shorter overall survival, despite aggressive management.

Conclusions: Intrapatient heterogeneity and tumor grade evolution represent critical determinants of NET behaviour and prognosis, often leading to more aggressive disease over time. Our findings emphasize the importance of reevaluating tumor biology during disease evolution, rather than relying solely on the grade of the primary lesion; targeted reassessment of metastatic site, guided by clinical indicators and advanced functional imaging, is essential to ensure accurate characterization and optimal therapy selection.

Abstract citation ID: lvag096.1261

EP983 - ECE_2480 - Outdoor Light at Night and the Progression of Cardiovascular-Kidney-Metabolic Syndrome

Shaoqing Wei[1,2], Fulin Wang[3,4], Wanzhou Wang[3,4], Chao Yang[1], Feifei Zhang[5] and Luxia Zhang[1,2,4]
[1]*Renal Division, Department of Medicine, Peking University First Hospital, Beijing, China;* [2]*Peking University, Beijing, China;* [3]*Peking University, National Institute of Health Data Science, Beijing, China;* [4]*Peking University Health Science Center, Institute of Medical Technology, Beijing, China;* [5]*Center for Digital Health and Artificial Intelligence, Peking University First Hospital, Beijing, China*

Introduction: Cardiovascular-kidney-metabolic (CKM) syndrome is a dynamic and progressive condition characterized by continuous transitions among metabolic dysregulation, chronic kidney disease, and cardiovascular dysfunction, and it imposes a substantial global disease burden. Outdoor light at night (LAN), an emerging environmental exposure, has been associated with circadian disruption and adverse cardiometabolic outcomes. However, evidence regarding the association between LAN exposure and longitudinal CKM progression across different stages remains limited. This study aimed to examine the association between LAN exposure and CKM progression.

Methods: Participants with Stage 1 CKM at baseline were included from the UK Biobank. LAN exposure was assessed using satellite-derived residential data and analyzed per interquartile range (IQR) increase. CKM stages including Stage 1, Stage 2,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Stage 4, and death were defined using biochemical measurements and International Classification of Diseases (ICD)-10 codes. A multi-state model was applied to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between LAN exposure and CKM progression across different transitions. Model 1 was adjusted for age and sex; Model 2 was further adjusted for smoking status, alcohol status, urbanicity, household income, and educational qualification.

Results: A total of 82,712 participants were included in the study. Higher LAN exposure was associated with increased risks of CKM progression across several key transitions. Higher LAN exposure per IQR increase was associated with an elevated risk of CKM progression from Stage 1 to Stage 2 (HR: 1.045, 95% CI 1.024-1.066) and from Stage 2 to Stage 4 (HR: 1.058, 95% CI 1.001-1.119), as well as a higher mortality risk among individuals with advanced CKM, particularly for the transition from Stage 4 to death (HR: 1.097, 95% CI 1.026-1.174]). Associations between LAN exposure and other transitions were not statistically significant.

Conclusions: Our findings indicate that higher LAN exposure is associated with the progression of CKM syndrome, particularly for transitions involving metabolic deterioration and late-stage mortality. These results highlight LAN as a potentially modifiable environmental risk factor in the CKM trajectory and underscore the importance of considering environmental factors when developing strategies for early risk stratification and prevention of CKM progression.

Keywords outdoor light at night, cardiovascular-kidney-metabolic syndrome, disease progression, multi-state model, environmental exposure

Abstract citation ID: lvag096.1262

EP984 - ECE_3258 - Differential sensitivity of endocrine and non-endocrine tissues to cadmium-induced lipid peroxidation and the protective role of melatonin.

Aleksandra Gładysz[1], Jan Stępniak[1] and Małgorzata Karbownik-Lewińska[1,2]
[1]*Department of Endocrinology and Metabolic Diseases, Medical University of Lodz, Lodz, Poland;* [2]*Polish Moter's Memorial Hospital—Research Institute, Łódź, Poland*

Objectives: Exposure to a heavy metal, specifically cadmium (Cd), a recognized IARC carcinogen, poses a significant public health risk due to its ability to induce oxidative stress, inflammation, and endocrine disruption. This study investigated the protective potential of melatonin against Cd-induced oxidative damage to membrane lipids (lipid peroxidation, LPO) in porcine tissue homogenates. To evaluate tissue-specific susceptibility and antioxidant efficacy, the study compared two endocrine tissues (the thyroid and the ovary) with two non-endocrine tissues (the liver and the kidney).

Methods: Porcine tissue homogenates were incubated in the presence of tested Cd compound, ie cadmium chloride ($CdCl_2$, 2.5-1000 μM), with or without melatonin (0.1-5.0 μM). The malondialdehyde + 4-hydroxyalkenals (MDA + 4-HDA) level (LPO index) was measured spectrophotometrically.

Results: Cadmium treatment significantly increased LPO in the kidney (25-1000 μM) and in the liver (2.5-1000 μM), whereas no increase was observed in the thyroid and in the ovary. Melatonin exhibited tissue-specific protective effects, namely protection in the kidney was limited to higher melatonin concentrations (2.5-5.0 μM) against damage induced by 100-1000 μM Cd, while liver damage was mitigated by melatonin doses as low as 0.1 μM across the 250-1000 μM cadmium range. In the ovary, Cd (1000 μM) unexpectedly reduced basal LPO level, an effect further enhanced by 5.0 μM Mel.

Conclusions: This study demonstrates that cadmium-induced oxidative damage is highly tissue-specific, with the liver and the kidney exhibiting the highest sensitivity to lipid peroxidation. This vulnerability is likely due to specificity of these organs serving as the primary sites for cadmium accumulation and detoxifying properties of the liver and the kidney, such as for example the synthesis of metal-binding proteins like metallothionein. Melatonin serves as an effective antioxidant against cadmium toxicity, though its protective efficacy varies significantly across different organs. The liver exhibited the most consistent response to melatonin across a wide range of concentrations, potentially due to its high metabolic turnover and the hormone's synergy with hepatic antioxidant enzymes. In contrast, the kidney required significantly higher doses of melatonin to achieve protective effects. Interestingly, the thyroid's resistance to cadmium-induced LPO suggests that its high physiological oxidative activity (indispensable for hormone synthesis) paradoxically makes the organ less vulnerable to further pro-oxidative factors. Overall, these findings suggest that cadmium toxicity occurs via, among others, a mechanism of lipid peroxidation. Additionally, they support the potential of melatonin as a preventive agent against heavy metal-induced oxidative stress, particularly in non-endocrine organs.

Abstract citation ID: lvag096.1263

EP985 - ECE_2290 - Investigation of the effects of sweeteners on AVP and OT secretion

Krisztian Sepp[1], Anna Laszlo[2], Marianna Radács[3], Peter Kiss[3], Márta Gálfi[3] and Zsolt Molnár[3]
[1]*Metabolic and Endocrine Center, Department of Internal Medicine, University of Szeged, Szeged, Hungary;* [2]*Department of Applied Statistics, Hungarian University of Agriculture and Life Sciences, Institute of Mathematics and Natural Sciences, Gödöllő, Hungary;* [3]*Institute of Applied Health Sciences and Environmental Education, Department of Environmental Biology and Education, Juhász Gyula Faculty of Education, University of Szeged, Szeged, Hungary*

The material and energy processes of homeostasis are determined, among other things, by glucose metabolism in vertebrates. The neuroendocrine system plays a dominant role in this cascade processes that maintain sugar metabolism. However, the use of sweeteners modifies the synthesis results of the mechanism networks mentioned above, which can even generate endocrine disrupting (ED) effects. The aim of our work is to study the effects of sugar substitute compounds on hormone release in the presence of arginine vasopressin (AVP) and oxytocin (OT) bases and histamine (HIS).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

In vivo experiments were conducted on Wistar rats (♂; bw: 80-100 g) with sweeteners [aspartame (40.0 mg/kg bw), saccharin (0.2 mg/kg bw), xylitol (40.0 mg/kg bw), stevia (40.0 mg/kg bw), glucose (40.0 mg/kg bw), K-acesulfame (40.0 mg/kg bw), and erythritol (0.05 g/500 cm^3)] via a gastric tube for 16 weeks. The untreated group served as the control. After exposure, the neurohypophyses of the rats were dissociated enzymatically (trypsin [0.2 mg/ml], DNAase I and II [10 µg/ml], Dispase [1 mg/ml]), and mechanical (Nylon-Blutex 80 µm = Ø] dissociation, monolayer primary cell cultures (NH) were prepared (n = 3 in each series of experiments) in 24-well Costar culture dishes (with 3 technical replicates). The AVP and OT hormone secretion functions of confluent NH cultures were checked as an *in vitro* model with non-specific (+30 mM [K^+]) and specific (+10^{-6} M [5-HT]) activation. Baseline and then HIS-receptor-activated AVP and OT release were followed in the presence of 10^{-6} M HIS *in vitro* over 120 min. Secreted AVP was determined by RIA, and OT was determined using ELISA, which was expressed relative to the protein content of NH cultures detected using the modified Lowry method. The results were analysed using a two-way ANOVA test. The results showed that *in vivo* sugar substitute treatments modified the basal AVP and OT secretion. Furthermore, they also altered the AVP and OT release functions measurable in the presence of HIS in the sugar substitute compounds. Based on our results, we can attribute a possible ED effect to the sweeteners studied.

Abstract citation ID: lvag096.1264

EP986 - ECE_2656 - Beyond the tumour: endocrine toxicities of hormonal and targeted anti-cancer therapies

David Lopez-Lazaro, Muhammad Sohail Akhtar, Shebina Liz Mathews and Cornelius Fernandez James
Diabetes & Endocrine, Pilgrim Hospital Boston (United Lincolnshire Hospitals NHS Trust), Boston, United Kingdom

Introduction: Endocrinopathies are common with immune checkpoint inhibitors but relatively rare with other systemic anti-cancer treatments. Here, we will discuss a few endocrinopathies.

Case Presentation: A 64-year-old gentleman with metastatic prostate cancer presented with headaches, dizziness and hypotension. He had been on Abiraterone with prednisolone for 4 years, the latter inadvertently discontinued. Labs showed euvolemic hyponatremia. Morning cortisol 87. Post synacthen cortisol 296. He was managed as adrenal crisis and stabilised.

A 83-year-old gentleman with post-thyroidectomy hypothyroidism, receiving LHRH analogues and Apalutamide for metastatic hormone-sensitive prostate cancer, presented with worsening hypothyroidism, requiring doubling of Levothyroxine dose. Upon discontinuation of Apalutamide due to newly developed lung cancer, he developed symptomatic iatrogenic hyperthyroidism, requiring a decrease in Levothyroxine dose to baseline.

A 73-year-old woman with a background of recurrent metastatic breast cancer on Alpelisib presented with recurrent vomiting. Bloods showed pH 7.28, Ketones 4.5 and glucose of 18.8-DKA secondary to Alpelisib. She was discharged and started on a BD Insulin regimen.

Discussion: Case 1: Abiraterone selectively inhibits CYP17A1, leading to suppression of androgen and cortisol. It is used in castration-resistant metastatic prostate cancer, always with prednisolone to suppress ACTH and mineralocorticoid excess. Abiraterone could cause secondary adrenal insufficiency when prednisolone is inadequate or interrupted. Recognition and glucocorticoid replacement, often at stress doses, are essential to prevent deterioration.

Case 2: Apalutamide and Enzalutamide, selective androgen receptor blockers used in prostate cancer, are known to cause hypothyroidism. Mechanisms include enhanced biliary excretion (increased hepatic UDP-glucuronosyl-transferase) and decreased gastrointestinal absorption (unknown mechanism) of levothyroxine. Apalutamide discontinuation can result in hyperthyroidism, unless levothyroxine doses are promptly adjusted

Awareness of this reversible drug effect is essential to ensure timely dose modification

Case 3: Alpelisib and capivasertib inhibit the PI3K/AKT pathway, disrupt insulin signalling, and reduce GLUT4-mediated glucose uptake, causing hyperglycemia and DKA. When these agents are discontinued, insulin sensitivity improves, lowering glucose levels, requiring prompt insulin dose reduction.

Conclusions: An increased awareness of anti-cancer agent associated endocrinopathies will empower endocrinologists to manage these conditions. Key learning points: Abiraterone, used in castration resistant prostate cancer should always be prescribed with prednisolone to prevent secondary adrenal insufficiency and mineralocorticoid excess. Apalutamide can cause reversible hypothyroidism, especially in those with pre-existing hypothyroidism, and TFT monitoring is vital. Alpelisib causes insulin resistance, therefore regular glucose monitoring must be performed to titrate insulin, especially in pre-existing diabetes.

Abstract citation ID: lvag096.1265

EP987 - ECE_1253 - Risk factors and reversibility of endocrine complications in children and adolescents with chronic iron deficiency anemia

Fawziya Alyafei, Ashraf Soliman, Nada Alaaraj, Noora Alhemaidi, Noor Hamed, Shayma Ahmed and Ahmed Elawwa
Hamad Medical Center, Pediatric Endocrinology, Doha, Qatar

Background: Iron deficiency anemia (IDA) remains the most prevalent micronutrient deficiency worldwide, particularly affecting children and adolescents in low- and middle-income settings. While the hematological manifestations of IDA are well recognized, emerging evidence highlights its broader impact on endocrine development, including growth retardation, pubertal delay, and neuroendocrine dysfunction. The pathogenesis of these endocrine sequelae involves impaired cellular oxygenation, mitochondrial dysfunction, and hormonal axis disruption. Understanding the reversibility of these effects following iron repletion and identifying modulating factors such as nutrition, pubertal stage, environment, and genetics is essential for effective prevention and intervention.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Objective: To review the literature from the past 25 years evaluating the endocrine consequences of chronic iron deficiency anemia in children and adolescents, quantify the impact of key risk factors, and examine the reversibility of endocrine dysfunction following treatment.

Methods: A systematic review of studies from 1999 to 2024 was performed using PubMed, Scopus, and relevant pediatric and endocrine databases. Inclusion criteria were studies assessing endocrine outcomes (eg, growth, puberty, thyroid, adrenal, GH-IGF axis) in patients aged 0-18 years with diagnosed IDA. Extracted data included sample size, age, iron status, endocrine abnormalities, treatment modalities, and recovery patterns. Real-world impact estimates were synthesized based on prevalence and odds ratios.

Results: Six principal risk factors were identified as major contributors to endocrine complications in pediatric IDA, with the following estimated impact based on pooled evidence:

- **Chronic iron deficiency (50%)**: associated with growth retardation, short stature, and pubertal delay.
- **Delayed treatment initiation (40%)**: linked to irreversible neurodevelopmental deficits and suboptimal catch-up growth.
- **Nutritional deficiencies (35%)**: particularly vitamin D and zinc deficiency, exacerbating skeletal and hormonal issues.
- **Delayed puberty (30%)**: both a consequence and a compounding factor of IDA-related endocrine disruption.
- **Environmental stressors (25%)**: such as food insecurity and high-altitude living, which increase metabolic strain.
- **Genetic susceptibility (20%)**: Polymorphisms in iron metabolism or hormone regulation genes may predispose individuals to endocrine vulnerability.

The reversibility of endocrine dysfunction was variable. While growth velocity often improved with iron repletion, pubertal normalization and cognitive gains were less consistent, especially in cases with prolonged deficiency. Early diagnosis and comprehensive nutritional and hormonal monitoring were key to better outcomes.

Conclusions: Endocrine complications in pediatric IDA are multifactorial and partially reversible. Prompt intervention, nutritional support, and individualized care plans considering pubertal status, environmental context, and genetic background are critical to mitigate long-term endocrine sequelae.

Abstract citation ID: lvag096.1266

EP1674 - ECE_1157 - Metabolic effects of sucralose below the acceptable daily intake: pooled evidence from 14 randomised trials

Leen Zayer[1], Zarish Hussain[1], Sharon Shiju[1], Bindhu Nair[1], Naji Alamuddin[1], Christopher Corpe[2] and Nitya Kumar[1]
[1]*Muharraq, Bahrain;* [2]*Kings College London, London, United Kingdom*

Background: The non-nutritive sweetener, Sucralose, is widely used in sugar-reduction strategies but may not be metabolically inert.

Objective: To assess the association of sucralose with insulin resistance (HOMA-IR), insulin sensitivity (Matsuda index), and OGTT-stimulated insulin response (tAUC120), and to examine dose and exposure duration effects.

Data Sources: Embase, Cochrane, and Scopus (final update March 14, 2025), plus trial registries and reference lists.

Study Selection: Randomized human trials reporting pre/post data for ≥1 prespecified metabolic outcome with sucralose exposure.

Data Extraction, Synthesis and Appraisal: Dual independent extraction; random-effects meta-analysis with Hartung-Knapp adjustments; meta-regression for association with dose and duration; RoB2, funnel plots and Egger tests for bias assessment; GRADE assessment for certainty of evidence.

Results: Fourteen trials ($n = 754$) were included ($n = 383$ for insulin response; $n = 300$ for HOMA-IR; $n = 215$ for Matsuda). Sucralose was associated with reduced insulin sensitivity (Matsuda pooled mean difference = 0.52, 95% CI 0.08 to 0.95; $I^2 = 0\%$) and increased insulin resistance (HOMA-IR mean difference = -0.42, CI −0.70 to −0.14; $I^2 = 78.5\%$). Overall effects on insulin $tAUC_{120}$ were imprecise, but longer exposure (≥30 days) was significantly associated with higher OGTT insulin response ($tAUC_{120}$ MD = −1632; 95% CI −2807 to −458; $I^2 = 0\%$); meta-regression supported a duration–effect relationship. No dose–response gradient was detected; small-study and sensitivity analyses did not materially change conclusions

Conclusions and Implications: In non-diabetic adults, sucralose exposure increases fasting insulin resistance, reduces insulin sensitivity, and—after ≥30 days—raises OGTT insulin response. Effects occurred at typical-use, sub-ADI exposures, indicating metabolic activity below toxicology-based thresholds. Clinical counselling and clearer labelling (mg per serving/container) may be warranted; diabetes-specific, ≥12-week RCTs with weight-normalised dosing are needed

Abstract citation ID: lvag096.1267

EP989 - ECE_3962 - Slipped capital femoral epiphysis following growth hormone replacement in a child with Panhypopituitarism secondary to Craniopharyngioma: A Case Report

Francisca Leitão H.[1], Beatriz Tavares Da Silva[2], Alice Monsanto[3], Leandro Kasuki[4], Elisa Lamback[4], Christhiane Fialho[4], Luiz Eduardo Wildemberg[4] and Mônica Gadelha[4]
[1]*Unidade Local de Saúde de Almada-Seixal, Almada, Portugal;* [2]*Centro Hospitalar Universitário Santo António, Porto, Portugal;* [3]*Unidade Local de Saúde de Coimbra, Coimbra, Portugal;* [4]*Neuroendocrinology, Instituto Estadual do Cérebro Paulo Niemeyer, Rio de Janeiro, Brazil*

Introduction: Recombinant human growth hormone (GH) is widely prescribed in children and adolescents with GH deficiency or short stature secondary to chronic medical conditions. Although GH therapy is generally considered safe, several

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

uncommon adverse effects have been reported, including increased intracranial pressure, glucose metabolism alterations, hypothyroidism, and musculoskeletal complications. Among these, slipped capital femoral epiphysis (SCFE) is a rare but potentially severe condition, typically occurring within the first months of treatment, particularly during periods of accelerated linear growth. Patients with underlying endocrine disorders and obesity appear to be at increased risk.

Case Report: We report the case of a 13-year-old boy with panhypopituitarism secondary to an adamantinomatous craniopharyngioma. The patient initially presented with progressive visual impairment, headaches, marked short stature, delayed puberty, and obesity. He underwent subtotal surgical resection of the tumor followed by adjuvant fractionated radiotherapy, with persistent gonadotropic, thyrotropic, and somatotropic deficiencies.

At 14 years and 7 months of age, recombinant human GH therapy was initiated after confirmation of GH deficiency. At treatment onset, the patient had a height below the 3rd percentile, delayed bone age, and obesity. Two months after GH initiation, during a period of rapid linear growth, he developed progressive right hip pain radiating to the thigh and knee, accompanied by gait disturbance. Symptoms later became bilateral and persistent.

Given the temporal association with GH therapy and the emergence of musculoskeletal symptoms, SCFE was suspected, and GH treatment was immediately discontinued. Imaging studies, including computed tomography and magnetic resonance imaging, demonstrated bilateral physeal widening and early posterior epiphyseal displacement, consistent with bilateral SCFE. The patient subsequently underwent bilateral *in-situ* percutaneous screw fixation with satisfactory stabilization.

Conclusions: This case illustrates SCFE as a rare but clinically significant complication of GH therapy, particularly in patients with multiple predisposing factors such as panhypopituitarism, obesity, delayed puberty, and rapid growth velocity. Early clinical manifestations may be subtle and nonspecific, leading to delayed diagnosis and increased risk of long-term complications. Clinicians should maintain a high index of suspicion for SCFE in children receiving GH therapy who present with hip, thigh, or knee pain, especially during the early phases of treatment. Prompt imaging evaluation, orthopedic referral, and temporary suspension of GH therapy are essential to prevent irreversible morbidity. This case underscores the importance of close multidisciplinary monitoring in pediatric patients undergoing GH replacement therapy.

Abstract citation ID: lvag096.1268

EP990 - ECE_1126 - Severe hyponatreamia revealing suspected autoimmune polyglandular syndrome type 2 in a patient labelled as panhypopituitarism: A diagnostic challenge

Paolo Augusto Romero Merino[1], Raysha Shirley Silva Jordan[2] and Luz Marina Medina Puma[3]
[1]*Hospital Clinico Universitario of Valladolid, Valladolid, Spain;*
[2]*Universidad Nacional de San Antonio Abad del Cusco, Cusco, Peru;*
[3]*Hospital Nacional Sergio E.Bernales, Lima, Peru*

Background: Hyponatraemia is a common but potentially life-threatening presentation of adrenal insufficiency. In patients previously diagnosed with panhypopituitarism, adrenal crisis is often attributed to secondary adrenal insufficiency. However, discordant biochemical findings should prompt reassessment of the underlying endocrine diagnosis and consideration of autoimmune polyglandular syndromes.

Case Presentation: A 63-year-old woman with a long-standing diagnosis of panhypopituitarism (reported as probable Sheehan syndrome) on chronic levothyroxine and glucocorticoid replacement (with documented treatment interruption) and a previous diagnosis of type 2 diabetes mellitus was admitted with a progressive 1-2-month history of anorexia, functional decline, intermittent confusion, and hypoxaemia in the context of community-acquired pneumonia. Past history included an ischaemic stroke with left hemiparesis and severe frailty with immobility-related complications. Initial evaluation showed hypoxaemia (SpO_2 88% on room air), acute kidney injury on chronic kidney disease, malnutrition, and pressure ulcers.

Results: Arterial blood gas revealed severe hyponatraemia (Na^+ 115.9 mmol/L) with alkalemia (pH 7.537) and hypocapnia (pCO_2 25.3 mmHg). Morning serum cortisol was profoundly low (0.05 µg/dL; reference 6.2-19.4) with markedly elevated ACTH (663 pg/mL; reference 7.2-63.3), confirming adrenal crisis and suggesting a primary component of adrenal failure despite the previous label of panhypopituitarism. Thyroid function tests showed free T4 1.00 ng/dL (reference 0.72-1.56), free T3 2.45 pg/mL (reference 2.42-3.98), and elevated TSH 10.7 µIU/mL (reference 0.27-4.2), which was inconsistent with isolated central hypothyroidism. Vitamin D insufficiency (25-hydroxyvitamin D 19.5 ng/mL) and hypocalcaemia (total calcium 7.83 mg/dL) were also documented. The patient was treated with intravenous hydrocortisone, supportive care, antibiotics, and correction of electrolyte abnormalities, with subsequent improvement in serum sodium and clinical status.

Conclusions: This case highlights that, even in patients labelled as panhypopituitarism, adrenal crisis may present with biochemical patterns inconsistent with secondary adrenal insufficiency. Markedly elevated ACTH with very low cortisol should prompt reassessment of adrenal axis aetiology and avoid diagnostic anchoring. The combination of primary adrenal insufficiency, hypothyroidism and diabetes raised suspicion of autoimmune polyglandular syndrome type 2. Although the patient carried a previous diagnosis of type 2 diabetes mellitus, latent autoimmune diabetes in adults (LADA) could not be excluded in the absence of pancreatic autoantibody testing. Autoimmune screening (21-hydroxylase antibodies, thyroid antibodies and diabetes-related antibodies) should be considered when APS-2 is suspected.

Keywords adrenal crisis, hyponatraemia, autoimmune polyglandular syndrome, APS-2, Addison's disease, hypothyroidism, LADA

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1269

EP991 - ECE_1551 - Reduced empathy and impaired emotion recognition in patients with arginine vasopressin deficiency

Liv-Helen Lang, Sara-Jessica Camerin, Michelle Müller, Andi Nikaj, Matthias Liechti, Cihan Atila and Mirjam Christ-Crain
University Hospital Basel, Basel, Switzerland

Introduction: Patients with arginine vasopressin (AVP) deficiency (formerly central diabetes insipidus) often report social and emotional deficits and heightened anxiety. Growing evidence suggests that these symptoms may, at least partly, reflect concomitant OXT deficiency. OXT plays a key role in increasing empathy and improving emotion recognition. This analysis aimed to examine empathy and emotion recognition in patients with AVP deficiency compared to controls, and to assess the effects of MDMA (3,4-methylenedioxymethamphetamine), a pharmacological stimulus of OXT, on these measures.

Methods: Analysis of a double-blind, placebo-controlled, crossover study including patients with AVP deficiency and healthy controls matched according to age, sex, BMI, and menopause/hormonal contraceptives. Participants received a single oral dose of MDMA (100mg) and placebo in random order, with a wash-out period of two weeks. A computer-based *Facial Emotion Recognition Task* and a *Multifaceted Empathy Test* were conducted 150 min after drug intake. The statistical analyses were performed using linear mixed-effects models.

Results: Fifteen patients and 15 controls were included (median age 34 [IQR, 25-46] vs 35 [26-48] years; 53% female). Under placebo, OXT levels were comparable between patients and controls (62 pg/mL [55-70] vs 66 pg/mL [56-74]). Following MDMA, OXT increased approximately fivefold in controls but remained unchanged in patients (92 pg/mL [79-110] vs 540 pg/mL [273-844]). Under placebo, direct empathy was lower in patients than controls (median 5.28 vs 5.62), driven by reduced empathy for positive emotions (4.50 vs 5.25). Under MDMA, direct empathy remained lower in patients (4.53 vs 5.58), with MDMA decreasing empathy for positive emotions in patients (3.55) but increasing it in controls (5.85). Linear mixed-effects modeling demonstrated significant effects mainly on the empathy dimension ($P < .001$) and emotional valence ($P = .006$), as well as a significant group × emotional valence interaction ($P < .001$). In emotion recognition, patients showed overall reduced accuracy compared with controls across both placebo and MDMA ($P = .012$), most pronounced for sadness and fear. Mixed-effects analysis confirmed significant effects of facial emotion ($P < .001$) without a significant group × emotion interaction, indicating a global reduction in facial emotion recognition accuracy in patients.

Conclusions: Patients with AVP deficiency exhibit reduced empathy and impaired emotion recognition compared to controls. MDMA amplified these deficits, suggesting an altered response likely linked to OXT deficiency.

Abstract citation ID: lvag096.1270

EP992 - ECE_2106 - Metastatic diffuse large B-cell lymphoma mimicking pituitary apoplexy

Margarida Gonçalves[1], Jorge Henrique Carmona Alexandrino[1], Ana Margarida Sousa[1], Nuno Jesus[1], Luís Gadelho[1], Leopoldina Pereira[2], Rute Caçola[3] and Gustavo Rocha[1]
[1]*Endocrinology, Unidade Local de Saúde de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal;* [2]*Neurosurgery, Unidade Local de Saúde de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal;* [3]*Internal Medicine, Unidade Local de Saúde de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal*

Introduction: Pituitary metastases are rare and involvement by hematologic malignancies is particularly uncommon, with systemic lymphoma being the most frequently reported cause. While lymphoma typically presents with constitutional symptoms, pituitary involvement may lead to atypical endocrine and neurological manifestations, occasionally mimicking acute pituitary disorders.

Case Report: A 59-year-old male with past history of metabolic surgery one year earlier, treated with proton-pump inhibitor and a multivitamin, presented to the emergency room complaining of acute headache, visual deficit and palpebral ptosis. During the preceding week he reported progressive asthenia and had sought emergency care for abdominal pain. Cranial MRI demonstrated an infiltrative lesion involving the anterior floor of the third ventricle, hypothalamic region, pituitary stalk, and posterior pituitary, with extension into the suprasellar cistern, causing anterior displacement and compression of the optic chiasm and molding of the optic tracts. An associated osteolytic lesion was also identified. Further workup revealed: cortisol 1.9 µg/dL (6.2-19.4); TSH 1.04 mIU/L (0.35-4.94); free T4 0.42 ng/dL (0.70-1.48); prolactin 43.0 ng/mL (4.0-15.2). These findings were consistent with adrenal insufficiency and secondary hypothyroidism, raising suspicion for pituitary apoplexy. Corticosteroid replacement was initiated, followed by levothyroxine, with clinical improvement. The patient subsequently developed arginine vasopressin deficiency, treated with desmopressin. As pituitary apoplexy was not confirmed and there was no indication for emergent neurosurgical intervention, he was discharged.

The day after discharge, the patient suffered a cardiopulmonary arrest with successful resuscitation and subsequently developed recurrent sustained ventricular tachycardia. An electrophysiological study identified right bundle branch reentry ventricular tachycardia, which was successfully ablated. Due to recorrent abdominal pain, a thoracoabdominal-pelvic CT scan revealed multiple lesions of probable neoplastic origin, including a left adrenal mass, a lesion in the right renal sinus, multiple abdominopelvic tumor implants and adenopathies, probable pulmonary metastases, intracardiac filling defects and a secondary lytic lesion in the left iliac bone. Cervical lymph node biopsy established the diagnosis of diffuse large B-cell lymphoma. The patient's clinical condition rapidly deteriorated and he died shortly thereafter without receiving lymphoma-directed therapy.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Discussion: This case highlights the diagnostic challenge of infiltrative sellar–suprasellar lesions, which have a broad differential diagnosis. Although the acute presentation initially suggested pituitary apoplexy, radiological features and subsequent clinical evolution were inconsistent with this diagnosis. Pituitary involvement by systemic lymphoma, though rare, should be considered in rapidly progressive cases with atypical imaging findings and carries a high mortality risk.

Abstract citation ID: lvag096.1271

EP993 - ECE_2869 - Evolving Hyponatraemia in Post-Vaccination Inflammatory Demyelinating Neuropathy: From Early ADH Dysregulation to Persistent SIADH

Muhammad Ali and Adhithya Sankar
Department of Endocrinology and Diabetes, Salford Royal NHS Foundation Trust, Manchester, United Kingdom

Background: Hyponatraemia is a recognised complication of Guillain–Barré spectrum (GBS) inflammatory neuropathies and is frequently labelled as SIADH. The mechanism may be time-dependent, and early diagnostic anchoring can misdirect management.

Case: A 79-year-old man developed distal paraesthesiae and progressive ascending weakness with autonomic features (urinary retention and constipation) shortly after COVID-19 and influenza vaccinations. CSF analysis demonstrated albuminocytologic dissociation, supporting an immune-mediated inflammatory demyelinating polyradiculoneuropathy. He developed prolonged hypotonic hyponatraemia with wide fluctuations (serum sodium 115-136 mmol/L; serum osmolality 246-263 mOsm/kg). Early urine indices were discordant, with persistently concentrated urine (urine osmolality 428-638 mOsm/kg) but highly variable urine sodium (<10-118 mmol/L), failing to consistently meet SIADH criteria and suggesting evolving non-osmotic ADH dysregulation related to acute neuroinflammation and autonomic dysfunction. He later deteriorated with symptomatic severe hyponatraemia (nadir 115 mmol/L) with features consistent with established SIADH (hypotonic serum osmolality 246-250 mOsm/kg with inappropriately concentrated urine osmolality 428-638 mOsm/kg and inappropriate natriuresis, urine sodium up to 118 mmol/L). He had received a 5-day course of IVIG prior to presenting to our hospital; pseudohyponatraemia was considered but felt unlikely as serum osmolality confirmed true hypotonic hyponatraemia and total protein was not elevated with IgG within the reference range. Thyroid and adrenal insufficiency and malignancy were excluded. Management required rescue hypertonic saline (250 mL 1.8%) followed by strict 1 L/day fluid restriction, with recurrent sodium decline when restriction was relaxed.

Discussion: Hyponatraemia in GBS can result from various mechanisms, including SIADH, pseudohyponatremia from treatments such as IVIG and, rarely, cerebral salt wasting.

This case illustrates evolving ADH dysregulation in inflammatory neuropathy, progressing from an early non-SIADH state to persistent SIADH.

Pathophysiologically, early sodium volatility likely reflects autonomic-mediated non-osmotic ADH release, possibly due to inflammation of afferent baroreflex pathways or hypersensitivity to volume changes. As the neuropathy progressed, the clinical picture transitioned to established SIADH.

Serial reassessment of tonicity and urine studies is essential in prolonged neuroinflammatory disease, rather than relying on a single early snapshot.

Conclusions: In post-vaccination GBS, hyponatraemia may evolve into sustained SIADH. Understanding the pathophysiological transition supports safer, timely therapy and prevents premature clinical misclassification.

Abstract citation ID: lvag096.1272

EP994 - ECE_3299 - Molecular imaging in Cushing's disease: localization of an ACTH-secreting PitNET with [18F]FET PET-MRI after inconclusive MRI and negative inferior petrosal sinus sampling—a case report

Amber Audhoe[1,2,3], Romy van der Groef[1,2], Sophie Veldhuijzen van Zanten[2,3,4], Layal Chaker[1,2], Sebastian Neggers[1,2] and Julie Celine Refardt[1,2]
[1]*Erasmus Medical Center, Internal Medicine, Section Endocrinology, Rotterdam, The Netherlands;* [2]*Erasmus Medical Center, Pituitary Center Rotterdam, Rotterdam, The Netherlands;* [3]*Erasmus Medical Center, Radiology & Nuclear Medicine, Rotterdam, The Netherlands;* [4]*Erasmus Medical Center, Cancer Institute, Brain Tumor Center, Rotterdam, The Netherlands*

Background: Cushing's disease is a rare disorder caused by an adrenocorticotropic hormone (ACTH)-secreting pituitary neuroendocrine tumor (PitNET) resulting in hypercortisolism. Establishing a central source of ACTH hypersecretion can be challenging, as pituitary MRI is inconclusive in up to 40% of patients with ACTH-dependent hypercortisolism. In these cases, bilateral inferior petrosal sinus sampling (IPSS) is commonly used to differentiate between pituitary and ectopic ACTH secretion. While IPSS is considered the reference standard for confirming a pituitary origin, its ability to localize a PitNET—based on ACTH gradient lateralization—remains limited. Together with the procedure's invasiveness, dependence on venous anatomy, and restricted availability to specialized centers, this highlights the need for complementary diagnostic tools. Molecular imaging techniques, including [^{18}F]FET PET-MRI, have shown promising results for localizing small or MRI-negative PitNETs in patients with Cushing's disease.

Case: A 42-year-old man presented with severe Cushingoid features. ACTH-dependent hypercortisolism was biochemically confirmed. Pituitary MRI revealed a small right-sided pituitary lesion (5.5 mm). Guideline-based IPSS demonstrated no significant central-to-peripheral ACTH gradient (ratio 1.21), suggesting an ectopic ACTH source. In parallel, [^{18}F]FET PET-MRI showed focal increased uptake in the right-sided pituitary lesion, consistent with a functional PitNET. Given the IPSS result, additional imaging including whole-body [^{18}F]FDG PET-MRI, [^{68}Ga]Ga-DOTA-TATE PET-MRI, and CT were performed, without evidence of an ectopic ACTH source. Repeated IPSS with prolactin assessment remained inconclusive (prolactin-adjusted ACTH ratio 1.20), with correct catheter positioning confirmed by an experienced interventional radiologist. After multidisciplinary discussion, the patient underwent transsphenoidal

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

adenomectomy directed at the PET-positive lesion. Postoperatively, cortisol levels became undetectable, and histopathological examination confirmed a corticotroph PitNET.

Conclusions: This case highlights a diagnostic dilemma in which a pituitary source of ACTH hypersecretion could not be confirmed using MRI and technically adequate IPSS, whereas [^{18}F]FET PET-MRI successfully localized the culprit lesion. These findings support the potential added value of molecular imaging in patients with small functional PitNETs and may suggest a future role for [^{18}F]FET PET in reducing reliance on invasive IPSS, improving localization, and shortening the time to diagnosis and definitive treatment in Cushing's disease.

Abstract citation ID: lvag096.1273

EP995 - ECE_3244 - Safety of a corticosteroid-sparing protocol in transsphenoidal surgery and predictive value of copeptin: a prospective cohort study

Ana Rocío Martínez Hartmann[1], Nieves Barceló Álvarez[2], Irene Iglesias-Lozano[3], María Hidalgo-Llorca[3] and Maria del Mar Roca-Rodriguez[1]

[1]Endocrinology and Nutrition Department, Endocrinology and Nutrition, Puerta del Mar Hospital, Puerta del Mar Hospital, Cadiz, Spain; [2]Biochemical Analysis, Puerta del Mar Hospital, Cádiz, Spain; [3]Neurosurgery Department, Neurosurgery, Puerta del Mar Hospital, Puerta del Mar Hospital, Cadiz, Spain

Introduction/Objectives: Routine perioperative corticosteroid coverage in transsphenoidal surgery (TSS) to prevent adrenal crisis is standard practice, though debated for patients with preserved function. The objectives were:

1. To evaluate the safety of a corticosteroid-sparing protocol in patients with intact hypothalamic-pituitary-adrenal (HPA) axis versus standard care.
2. To determine the predictive value of early copeptin, plasma osmolarity, and diuresis for permanent Diabetes Insipidus (DI).

Material and Methods: A prospective observational study included 27 patients undergoing endoscopic TSS for pituitary adenomas. Inclusion criteria required confirmed intact HPA axis (basal/stimulated cortisol >15 µg/dL). Patients were assigned to Standard (with corticosteroids) or Sparing (no corticosteroids) protocols. Analysis included group differences, pre-post clinical/analytical changes, correlations, and multivariate regression models.

Results: The cohort was homogeneous at baseline. The Sparing protocol demonstrated safety: no significant differences were found between groups regarding 1-month adrenal function ($P = 1.000$) or immediate complications, sodium disorders, or desmopressin requirements ($P = .587$).

Linear regression validated the protocol's physiological basis: preoperative ACTH strongly predicted the endogenous cortisol cifre 24 hours after TSS (rho = 0.800, $P = .003$; $\beta = 0.817$), confirming adequate stress response without exogenous steroids in patients with intact basal axes.

Regarding neurohypophysis, early plasma osmolarity (immediately prior to TSS) emerged as the strongest predictor of permanent DI (Linear Regression $R^2 = 0.963$, $P < .001$), outperforming isolated copeptin. Logistic regression identified polyuria as a critical risk factor: risk of permanent DI tripled for every 500 mL increase in maximum 24 h-diuresis ($P = .016$).

Anatomically, larger tumor size was associated with transient "thyroid stunning" (lower 96 hours after TSS T4L, $P < .001$), and posterior extension compromised immediate copeptin reserve (rho = −0.700). Surgery significantly improved visual defects ($P = .011$) and hyperprolactinemia ($P = .005$) without deteriorating other axes ($P > .05$).

Conclusions: Obtained data supports that withholding perioperative corticosteroids is safe for patients with preserved HPA function. Early osmolarity and diuresis are predictors of permanent neurohypophyseal damage. Copeptin emerges as a potential early biomarker for diabetes insipidus prediction, showing strong correlation with anatomical and functional damage, suggesting its future utility in clinical decision algorithms.

Abstract citation ID: lvag096.1274

EP996 - ECE_3380 - Beyond clinical features: the respiratory impact of acromegalic macroglossia

Teodora Vintilă[1], Alexandru Florescu[1,2], Viviana Adam[2], Irina Puscasu[1], Andra Berigoi[1], Stefana Bilha[1,2], Anca Matei[1,2] and Cristina Preda[1,2]

[1]Saint Spiridon County Hospital, Iași, Romania; [2]Iași, Romania

Macroglossia in acromegaly is often perceived as a static phenotypic marker rather than a dynamic contributor to functional morbidity. Clinical attention is therefore usually focused on its diagnostic and morphological value, while its progressive impact on oral cavity anatomy and upper airway configuration remains insufficiently explored. Consequently, the potential role of acromegalic macroglossia in airway compromise and ventilatory dysfunction is frequently underestimated.

We report the case of a 67-year-old woman with no significant chronic comorbidities, admitted to a neurology department for diffuse subarachnoid haemorrhage due to rupture of an anterior communicating artery aneurysm. During hospitalization, the patient's physical appearance raised suspicion of an underlying endocrine disorder, leading to referral for endocrine evaluation. Endocrine assessment confirmed active acromegaly, with elevated GH (10.1 ng/mL) and IGF-1 (383 ng/mL), together with absent GH suppression during oral glucose tolerance testing. Pituitary MRI revealed a 13 × 14 × 10 mm sellar lesion compatible with a pituitary macroadenoma. In line with the well-recognized association between acromegaly and thyroid disease, thyroid evaluation revealed a toxic multinodular goiter, with biochemical hyperthyroidism and autonomously functioning nodules on scintigraphy, requiring antithyroid therapy for metabolic stabilization prior to definitive neurosurgical management.

From a functional perspective, macroglossia emerged as the most clinically relevant physical finding. The tongue exhibited no signs of acute swelling, induration or recent haemorrhage, while the covering mucosa showed normal colour and preserved papillary configuration, supporting a chronic hypertrophic rather than inflammatory or edematous process. Even in passive resting

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

position, without intentional protrusion, the tongue partially extended beyond the lower lip, suggesting a significant contribution to upper airway compromise.

The patient subsequently underwent endoscopic transsphenoidal resection of the pituitary macroadenoma. Persistent postoperative respiratory alkalosis, documented by repeatedly elevated serum bicarbonate levels (43 mmol/L and 45.5 mmol/L), together with ventilatory instability in the setting of severe acromegalic macroglossia, prompted further evaluation of nocturnal respiratory function.

Polysomnography demonstrated severe obstructive sleep apnea (apnea–hypopnea index 47.9 events/hour) with marked nocturnal hypoxemia. In this anatomical and functional context, maxillofacial evaluation identified macroglossia as the principal substrate for airway compromise, and functional reductive tongue surgery using the keyhole glossectomy technique was therefore recommended. This technique, rarely reported in acromegaly and more commonly described in congenital macroglossia, was indicated strictly for ventilatory purposes.

This case illustrates how acromegalic macroglossia may evolve from a phenotypic hallmark into a clinically significant respiratory disorder, underscoring the importance of systematic functional assessment and interdisciplinary management of oral manifestations in acromegaly.

Abstract citation ID: lvag096.1275

EP999 - ECE_1942 - Chordoma mimicking macroprolactinoma in a young female patient

Ieva Baikštienė[1], Saiva Gaidytė[2], Martyna Juškienė[1] and Birutė Žilaitienė[1]
[1]*Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [2]*Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania*

Introduction: Chordomas are relatively rare bone tumors that may lead to hyperprolactinemia when they develop in the sellar or parasellar region and compress the pituitary stalk, thereby interfering with hypothalamic dopamine transport to the pituitary gland. We report a case of a skull base chordoma presenting with an unusually high prolactin concentration.

Case: A 20-year-old patient presented with complaints of an irregular menstrual cycle of up to 60 days and headaches accompanied by generalized muscle weakness and diffuse body pain, patient reported episodes consistent with panic attacks. Marked hyperprolactinemia (4492.0-5104 mIU/L; reference range 102-496 mIU/L) was confirmed on repeat testing, with macroprolactin excluded. Brain MRI was performed due to suspicion of a macroprolactinoma. Imaging demonstrated a sella turcica of normal size and regular configuration, with an area of altered signal intensity in the superior portion of the clivus.

Subsequent brain CT revealed a $13 \times 7 \times 7$ mm lesion radiologically most suggestive of an intraosseous hemangioma. The patient was admitted for transsphenoidal biopsy. Histological examination with immunohistochemistry positive for brachyury, cytokeratin, and S-100 confirmed the diagnosis of chordoma. Six weeks after the biopsy, the patient reported clinical improvement and repeat prolactin concentration was 397.87 mIU/L (reference range 105-548 mIU/L).

Conclusions: Chordoma located in the sellar region can lead to hyperprolactinemia via the stalk effect and should therefore be included in the differential diagnosis of sellar masses associated with elevated prolactin levels.

Abstract citation ID: lvag096.1276

EP1000 - ECE_3057 - Recurrent Crooke cell corticotroph adenoma: diagnostic challenges and multidisciplinary management in complex Cushing's disease

Gergő Csitári and Dóra Sümegi
DBC-SZIEOK, Budapest, Hungary

Background: Recurrent corticotroph pituitary adenomas with Crooke cell morphology present significant diagnostic and therapeutic challenges. Accurate differentiation between silent and manifest ACTH-omas, alongside detailed histopathological assessment and comprehensive anamnesis, is critical for effective management.

Case Presentation: A 54-year-old woman with extreme obesity was treated for recurrent corticotroph pituitary macroadenoma. Initial transsphenoidal surgery took place in 2011 for a $32 \times 31 \times 19.5$ mm tumour compressing the optic chiasm. Histology confirmed partial ACTH secretion. Early biochemical evaluation for Cushing's syndrome was limited due to the urgent clinical situation. In 2017 worsening neurological symptoms and imaging revealed recurrence with infiltration of the right cavernous sinus and carotid artery. The second surgery confirmed Crooke cell corticotroph adenoma with diffuse ACTH positivity. Follow-up care was irregular. Comprehensive endocrinological reassessment began around 2020. Detailed anamnesis and histopathological reviews clarified the clinical scenario. Biochemical results suggested manifest Cushing's disease; however, differentiation between silent and manifest ACTH-oma remained uncertain. Crooke cell morphology indicated aggressive tumour behaviour and increased recurrence risk. In January 2024 the Multidisciplinary Pituitary Committee reviewed the patient's case, based on the MRI showing a Knosp 3B residual tumour with invasive features. The Committee recommended annual MRI follow-up. In December 2024 the patient developed acute right eye ptosis and diplopia. MRI confirmed tumour growth with infiltration into the right cavernous sinus. Urgent third endoscopic transethmoidal-transsphenoidal surgery was performed. Histology reconfirmed a recurrent or residual corticotroph PitNET, with Crooke cell morphology, isolated TPIT positivity and diffuse ACTH expression within the tumour, and low proliferation index.

Conclusions: This case highlights the importance of thorough anamnesis and repeated histopathological assessment in managing recurrent corticotroph adenomas. The aggressive nature of Crooke cell adenomas and the subtle differentiation between silent and manifest ACTH-omas necessitate a multidisciplinary approach. The Multidisciplinary Pituitary Committee's role is central in guiding surveillance and interventions. These findings highlight the need for personalized management strategies in complex Cushing's disease cases.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1277

EP1001 - ECE_3596 - Setmelanotide therapy in hypothalamic obesity following craniopharyngioma: a case series of three patients

Oana Ruxandra Cotta[1], Cesare Morgante[2], Damiano Siligato[1], Carla Paola Costa[1], Elena Sofia Blanca[1], Giordana Siracusano[1], Annalisa Giandalia[1,3], Francesco Ferraù[1,3] and Salvatore Cannavò[1,3]
[1]*Endocrine Unit, University Hospital "G. Martino", MESSINA, Italy;* [2]*PhD Program in Science of Nutrition, Metabolism and Gender-Related Diseases, Università Cattolica del Sacro Cuore-Fondazione Policlinico "A. Gemelli" IRCCS, Rome, Italy;* [3]*Messina, Italy*

Background: Hypothalamic obesity (HO) is a severe, often treatment-refractory complication after craniopharyngioma (CP) surgery. Setmelanotide, a melanocortin-4 receptor agonist (MC4R-A), offers a targeted therapeutic approach, but real-world data are limited.

Methods: We performed a retrospective review of patients with post-CP HO treated with setmelanotide at our center over a period of 3-15 months, collecting clinical, metabolic, and treatment-related data.

Results: Three young adults with HO after surgery for CP were included. Treatment responses were variable: one patient discontinued setmelanotide after continued weight gain over 3 months, while two experienced significant reductions in weight (−14.4% and −25.9%), BMI (−11.9% and −25%), waist circumference (−4% and −20%) and triglycerides levels (−35% and −39%) over 7-15 months. Adverse effects as nausea, vomiting, headache and skin hyperpigmentation, were mild and non-limiting. One patient experienced sclera hyperpigmentation after 2 months of treatment.

Conclusions: Setmelanotide may provide meaningful benefit for selected patients with severe HO following CP surgery. Despite small sample size, this series supports further investigation of MC4R agonism as a targeted therapy for acquired HO.

Abstract citation ID: lvag096.1278

EP1002 - ECE_3406 - Real-world BMI outcomes in adult patients with acquired hypothalamic obesity treated with setmelanotide for up to 9 months in France

Pauline Faucher[1], Sarah Chalopin[1], Emilie Montastier[2], Helena Mosbah[3], Vincent Clotilde[4], Claire Carette[5], Anne-Laure Borel[6], Karine Decaux[7], Frederique Albarel Loy[8], Elsa Fasciglione[9], Thibault Bahougne[9], Agnès Aubourg[7], Benjamin Moreau[10], Lucie Meillet[11], Vianney Demeocq[12], Arnaud De Luca[13], Justine Cristante[6], Nicolas Farigon[14], Marie Michelet[15], Véronique Savey[16], Bérénice Ségrestin[17], Géraldine Vitellius[18], Karine Clément[1], Blandine Gatta-Cherifi[15] and Christine Poitou[1]
[1]*Nutrition Department, La Pitié-Salpêtrière Hospital APHP, Sorbonne University, Paris, France;* [2]*Nutrition Department, University Hospital of Toulouse, Toulouse, France;* [3]*Endocrinology Department, University Hospital of Poitiers, Poitiers, France*
[4]*Nutrition Department, University Hospital of Lille, Lille, France;* [5]*Nutrition Department, Hôpital Européen Georges Pompidou APHP, Paris, France;* [6]*Nutrition and Endocrinology Department, University Hospital of Grenoble, Grenoble, France;* [7]*Nutrition Department, University Hospital of Rouen, Rouen, France;* [8]*Endocrinology Department, Conception Hospital AP-HM, Marseille, France;* [9]*Department of Endocrinology, Diabetology and Nutrition, University Hospital of Strasbourg, Strasbourg, France;* [10]*Department of Endocrinology, Diabetology and Nutrition, University Hospital Rennes, Rennes, France;* [11]*Endocrinology and Diabetology Department, J Minjoz University Hospital of Besançon, Besançon, France;* [12]*Endocrinology and Metabolism Department, University Hospital of Brest, Brest, France;* [13]*Nutrition Department, University Hospital of Tours, Tours, France;* [14]*Clinical Nutrition Department, University Hospital of Clermont-Ferrand, Clermont-Ferrand, France;* [15]*Department of Endocrinology, Diabetology and Nutrition, University Hospital of Bordeaux, Bordeaux, France;* [16]*Hepato-Gastroenterology and Nutrition Department, Caen-Normandy Hospital, Caen, France;* [17]*Endocrinology Department, Lyon Sud Hospital, HCL, Lyon, France;* [18]*Endocrinology, Diabetology and Nutrition Department, Robert-Debré University Hospital of Reims, Reims, France*

Introduction: Acquired hypothalamic obesity (aHO) arises from physical injury to the hypothalamus caused by trauma, tumours, treatment-related damage, inflammation, or developmental abnormalities, leading to disrupted melanocortin-4 receptor (MC4R) signalling and marked by accelerated, sustained weight gain. In a 52-week placebo-controlled Phase 3 trial of the MC4R agonist setmelanotide in patients with aHO aged ≥4 years, the primary endpoint of percent change in body mass index (BMI) at Week 52 was achieved with a 16.5% reduction in the setmelanotide group corresponding to a −19.8% placebo-adjusted difference. Here, we report real-world data from 56 adult patients with aHO treated with setmelanotide for up to 9 months under France's pre-marketing early-access program.

Methods: BMI outcomes and response rates—defined as achieving a ≥10% reduction—are presented for adult patients with aHO in France receiving early-access treatment with setmelanotide for up to 9 months.

Results: Fifty-six adult patients (33 females), aged 18-68 years old, started setmelanotide treatment. Forty-two patients had craniopharyngioma, 5 astrocytoma, 2 Langerhans cell histiocytosis, and 1 each hamartoma, germinoma, histiocytosis, neuroglial tumour, Rathke's pouch cyst, macroprolactinoma or not specified. Patients started treatment at 0.25-2 mg/day, titrated up to 1-3 mg/day at last included visit. For patients with 6-month data ($n = 26$), mean (SD) BMI at baseline was 44.8 (11.4) kg/m^2 which reduced to 39.1 (12.5) kg/m^2 after 6 months of treatment, representing a 12.7% decrease from baseline ($P < .0001$). For patients with 9-month data ($n = 16$), mean (SD) BMI at baseline was 42.8 (7.7) kg/m^2 which decreased to 34.8 (8.5) kg/m^2 after 9 months of treatment, representing an 18.7% decrease from baseline ($P < .0001$). Fifteen of 26 patients (57.7%) had a BMI reduction of ≥10% after 6 months of treatment. This increased to 11 of 16 patients (68.8%) after 9 months of treatment. No new

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

safety concerns were observed and reported adverse events were consistent with phase 3 trial data.

Conclusions: This real-world evidence of 56 patients with aHO, who received up to 9 months of setmelanotide under pre-marketing early access authorization in France showed consistent improvements in BMI. Efficacy and safety outcomes are consistent with Phase 3 trial data. These findings underscore the real-world therapeutic value of setmelanotide as an intervention strategy for patients with aHO.

Abstract citation ID: lvag096.1279

EP1005 - ECE_2451 - Potential role of the overnight dexamethasone suppression test in monitoring medical treatment of Cushing's syndrome

Evangelia Makri, Georgios Kostopoulos and Zoe Efstathiadou
Endocrinology, Hippokration General Hospital of Thessaloniki, Thessaloniki, Greece

Background: The overnight dexamethasone suppression test (ODST) is widely used for the screening and diagnosis of Cushing's Syndrome (CS) but is not included in monitoring medical treatment. Nevertheless, the restoration of the negative feedback of cortisol on corticotroph cells, could serve as a biomarker of successful treatment of endogenous hypercortisolism. The aim of the present study was to examine whether ODST may serve as an index of disease remission in patients with medically-treated CS, when assessed longitudinally.

Methods: We retrospectively evaluated 12 patients with ACTH-dependent Cushing's disease or ectopic ACTH syndrome who were treated with medical therapies including ketoconazole, metyrapone, pasireotide, osilodrostat, or cabergoline. ODST cortisol levels and urinary free cortisol (UFC) were recorded before and, in the majority of patients, approximately one year after initiation of medical treatment. Changes were assessed descriptively on an individual basis.

Results: Following medical therapy, a consistent reduction in ODST cortisol levels was observed across the cohort. Mean ODST cortisol decreased from 18.4 μg/dL before treatment to 5.6 μg/dL after treatment. This decline was accompanied by a marked reduction in UFC levels, which decreased from a mean of 227.7 μg/24 h to 41.8 μg/24 h. Six patients received metyrapone with ODST cortisol levels reduction after treatment in each patient, despite the known interference of metyrapone with cortisol synthesis and hypothalamic–pituitary–adrenal axis feedback. Three patients were treated with pasireotide and ODST cortisol was lower only in one patient compared with baseline values. Additionally, one patient received ketoconazole, one received osilodrostat and one received cabergoline presented decreased cortisol levels after ODST. Directionally concordant decreases in ODST and UFC were observed in most patients. No systematic pattern of paradoxical ODST suppression or discordance between ODST and UFC was evident. In the two patients treated with pasireotide, who did not show a reduction in cortisol levels, cortisol measurements were performed within less than 8 months after treatment initiation.

Conclusions: In this small real-world cohort, ODST cortisol levels decreased in parallel with UFC following medical treatment for Cushing's disease. Although ODST is not validated as a monitoring tool and absolute post-dexamethasone thresholds remain unreliable during therapy, longitudinal changes in ODST may reflect treatment-induced reductions in cortisol secretion. These findings suggest that ODST could provide adjunctive and physiologically relevant information on treatment response when interpreted cautiously.

Abstract citation ID: lvag096.1280

EP1006 - ECE_2935 - A thirsty beginning: AVP deficiency as the isolated presenting symptom of systemic sarcoidosis

Csilla Czékus[1], Krisztian Sepp[1], Kristóf Barath[2] and Zsuzsanna Valkusz[1]
[1]*Albert Szent-Györgyi Health Center, Department of Internal Medicine, Metabolism and Endocrinology Unit, University of Szeged, Szeged, Hungary;* [2]*Albert Szent-Györgyi Health Center, Department of Pulmonology, University of Szeged, Deszk, Hungary*

Introduction: Sarcoidosis is a chronic, multisystemic inflammatory disorder of unknown etiology, characterized by the formation of non-caseating granulomas. While the disease primarily affects the lungs, extrapulmonary manifestations (skin, eyes, liver, and heart) are common. While systemic sarcoidosis is relatively frequent, central nervous system involvement (neurosarcoidosis) is rare (5%). Within the neurosarcoidosis subgroup, involvement of the hypothalamic-pituitary axis is even more infrequent. Sarcoidosis presenting with arginine vasopressin (AVP) deficiency as the sole initial symptom is considered a clinical rarity in the literature.

Case Presentation: A 23-year-old male patient was admitted to our endocrine department due to symptoms of thirst, polydipsia, and polyuria progressing for 2 months. Adenohypophyseal function showed no abnormalities except for a minimally elevated prolactin level. Electrolyte and calcium levels were within the normal range, and carbohydrate metabolism was intact. Fluid intake was approximately 113 mL/body weight kg/day. A water deprivation test demonstrated an inability to concentrate urine. During the DDAVP test, urine volume and concentration normalized. Consequent to the confirmed AVP deficiency, desmopressin was initiated, which successfully regulated urine volume and daily fluid balance. Pituitary MRI described the absence of the physiological T1 hyperintensity of the neurohypophysis (the "bright spot") and irregular thickening of the pituitary stalk, which raised the possibility of eosinophilic granuloma. Laboratory investigations for multiple juvenile autoimmune disease associations were negative, except for slightly elevated total IgG and IgG4 levels. To confirm potential IgG4-related disease, a whole-body 18F-FDG-PET/CT was performed, which revealed granulomatous lung disease. Bronchoscopy with biopsy and bronchoalveolar lavage excluded the infectious etiologies while histopathology confirmed typical sarcoidosis morphology with non-caseating granulomatosis with Langhans-cells. Consequently, given the systemic sarcoidosis with pituitary and lung involvement, systemic corticosteroid therapy with 32 mg

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

methylprednisolone was initiated for both endocrine and pulmonary indications. Currently, the steroid dose is being tapered, but the desmopressin dose cannot yet be reduced. Follow-up pituitary MRI and chest CT scans are planned.

Conclusions: In rare cases, polyuria caused by AVP deficiency can be the sole presenting symptom of sarcoidosis, preceding pulmonary or other organ-specific symptoms. Identifying sarcoidosis in these cases is a diagnostic challenge but remains a crucial step for timely systemic treatment. This case also highlights that mild IgG4 elevation occurring in granulomatous diseases can act as a confounding factor during the diagnostic process.

Abstract citation ID: lvag096.1281

EP1008 - ECE_1700 - A rare case of prolactinoma transformation into a resistant prolactin- and growth hormone-secreting adenoma

Emily Davies, Arshia Beigi and David Shu
Department of Medicine, University of British Columbia, Vancouver, Canada

Background: Mixed prolactin- and growth hormone (GH)-secreting adenomas are well recognized, reflecting a shared somatomammotroph progenitor lineage. In contrast, transformation of a well-controlled prolactinoma on dopamine agonist therapy into a resistant, rapidly enlarging mixed prolactin- and GH-secreting adenoma is rare and carries important implications for long-term surveillance and management.

Case: A 39-year-old male with no personal or family history of pituitary disease presented in 2011 with a four-month history of persistent headache. MRI head showed a large 3.5 cm sellar mass, prompting urgent endocrine assessment. There were no clinical features of acromegaly. Biochemical evaluation demonstrated marked hyperprolactinemia and mild secondary hypogonadism; remainder of pituitary function was normal. Acute surgical intervention was not indicated and cabergoline was initiated with gradual dose escalation, resulting in symptomatic improvement, normalization of prolactin levels and interval tumor shrinkage over two years. From 2014 to 2022, cabergoline was slowly reduced to a low maintenance dose with continued biochemical and radiographic control. In October 2022, a dramatic rise in prolactin levels was noted on routine follow up and repeat pituitary hormone assessment revealed newly elevated insulin-like growth factor 1 (IGF-1). He had no acromegalic features and reported occasional headaches and new left eye visual impairment. Acromegaly was confirmed by failure of GH suppression on oral glucose tolerance testing. Lanreotide was initiated with escalation of cabergoline therapy. Repeat MRI head in September 2023 demonstrated marked tumour growth compared to 2021 imaging, from 1.5 cm to 3.4 cm in maximal diameter, with new compression of the optic chiasm. He underwent transsphenoidal debulking surgery in November 2023. Histopathology confirmed a mixed somatotroph and lactotroph pituitary adenoma. Post-operative imaging showed residual tumour with adequate decompression of the optic apparatus. Prolactin and IGF-1 levels remained elevated after surgery despite escalating doses of cabergoline and lanreotide. He subsequently underwent pituitary radiotherapy in May 2024, and had a brief trial of pegvisomant which was self-discontinued. By October 2025, both prolactin and IGF-1 demonstrated partial improvement, largely attributed to radiotherapy. He remains under close surveillance with ongoing hormone monitoring and interval imaging.

Conclusions: Transformation of a well-controlled prolactinoma into a resistant, mixed prolactin/GH-secreting adenoma is exceedingly rare, with only isolated cases reported. The coexistence of GH excess requires a distinct therapeutic strategy, emphasizing the importance of timely recognition. This case highlights the importance of long-term surveillance and regular comprehensive pituitary hormonal assessment in patients with prolactinomas, even after prolonged biochemical and radiographic stability.

Abstract citation ID: lvag096.1282

EP1010 - ECE_1414 - JY007: a super long-acting growth hormone with potential for Q3W-Q4W dosing

Jianping Huang[1] and Qunhuan Kou[2]
[1]*Shanghai, China;* [2]*Shanghai ClessBio, Shanghai, China*

Objective: JY007 is a novel long-acting human growth hormone (hGH) composed of GH linked to an engineered Fc fragment via a flexible linker. The Fc domain incorporates the YTE mutation to enhance binding to FcRn and three additional amino acid mutations to silence effector functions. Here we present the preclinical comparison data between JY007 and once-weekly hGH, such as somatrogon and TJ101(GX-H9).

Methods: PK, PD and safety studies were conducted in hFcRn transgenic mice and NHPs following subcutaneous administration. Dosing regimens of JY007: mice at 5.8 and 58 mg/kg; cynomolgus monkeys at 1.5 and 15 mg/kg.

Results: ***In vitro* assays.** JY007 and somatrogon exhibited similar affinity to human, cyno and rat GHR and similar cell proliferation activity. Compared to wild-type Fc, JY007 exhibited attenuated binding affinity for FcγRs and abolished ADCC and CDC. YTE mutation resulted in a 33-fold enhancement in FcRn binding affinity over the wild-type Fc. **PK and PD study *in vivo***. In B-hFcRn mice, half-life of JY007 was 16 times that of somatrogon, and its IGF-1 duration was 3 times longer. Despite distinct dosing regimens (Q2W vs BIW), JY007 and somatrogon exhibited similar percentage of body weight gain in mice. The NHP study demonstrated that half-life, AUC, and IGF-1 maintenance duration of JY007 were two times those of TJ101 at an equivalent dose. **Favorable safety profile *in vivo*.** JY007 was well tolerated in mice and NHPs at the high dose. Data were collected in NHPs at day-1, 3, 7, 14, 28, including: body temperature, ophthalmic examination, electrocardiograph and blood biochemical examination. No significant change was observed before and after treatment.

Conclusions: Compared to once-weekly hGH, JY007 demonstrates similar in vitro activity while exhibiting a significantly extended half-life in both mice and NHPs, along with a favorable safety profile. Currently JY007 is under IND stage. The general pattern of YTE mutation: YTE mutation extends half-life more significantly in human (3.1-4.0 times) than in NHPs (2-2.4 times). Based on 5 days half-life of TJ101 in human, half-life of JY007 in human is predicted to be up to 15-20 days and supports Q3W-Q4W SC dosing.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Target	Antibody	NHPs		Human	
		$t_{1/2}$	Times	$t_{1/2}$	Times
IL-4Rα	APG808(YTE)	27 d	2.4	55 d	3.7
	Dupilumab (No YTE)	11 d		15 d	
IL-13	APG777(YTE)	27 d	2.1	75 d	3.1
	Lebrikizumab (No YTE)	13 d		24.5 d	
IGF-1R	VRDN-003(YTE)	12.8 d	2.0	40-50 d	4.0
	VRDN-001(No YTE)	6.3 d		10-12 d	
GHR	JY007(YTE)		2.0	About 15-20 d	About 3-4 times
	TJ101(No YTE)			5 d	

Abstract citation ID: lvag096.1283

EP1011 - ECE_3627 - Functional blockade in silent corticotroph tumors: dissociation between POMC expression and regulation of ACTH secretion

Jorge Navarro[1], Johana Sottile[1], Cristina Guillen[2], María Eugenia Torregrosa-Quesada[2], Francisca María Peiró-Marqués[2], Luís Concepción[2] and Antonio Pico[1]
[1]*Clinical Medicine, ISABIAL (Instituto de Investigación Sanitaria y Biomédica de Alicante), Alicante, Spain;* [2]*Radiology, Hospital General Universitario de Alicantet Emergency Room, Alicante, Spain*

Introduction: Silent corticotroph tumors (SCTs) represent a clinically non-functioning subtype that, despite exhibiting immunohistochemical and molecular features characteristic of the corticotroph lineage, is not associated with clinical hypercortisolism. This dissociation between cellular identity and hormonal function suggests the existence of molecular mechanisms that limit effective ACTH secretion, although these mechanisms have not been fully characterized. In this study, we compared the molecular profile of SCTs with that of functioning corticotroph tumors responsible for Cushing's disease, aiming to identify alterations associated with functional corticotroph blockade.

Methods: Gene expression analysis was performed by RT-qPCR in human pituitary tumor biopsies obtained from 29 patients with Cushing's disease and 28 patients with silent corticotroph tumors, using normal pituitary tissue as reference. Tumor classification was conducted according to the 2022 WHO criteria, based on the expression of the transcription factors TBX19/TPIT and SF-1. Genes involved in corticotroph regulation and ACTH synthesis (*POMC*, *CRHR1*, *AVPR1B*, *TBX19*, *NEUROD1*), post-translational processing of POMC (*PCSK1*, *PCSK2*), glucocorticoid receptor signaling (*NR3C1*, *FKBP5*), and pathways associated with oncogenic signaling, cellular stress, and cell-cycle control (*USP8*, *EGFR*, *STAT3*, *HSF1*, *JUN*) were evaluated. Statistical analysis was performed using the Mann–Whitney test ($P < .05$).

Results: Compared with Cushing's disease tumors, SCTs showed a significant dysregulation of upstream regulators of the corticotroph axis, characterized by decreased *CRHR1* expression ($P < .0001$) and increased *AVPR1B* expression ($P = .0061$), while *POMC* expression remained preserved. In addition, differences in differentiation-related factors were observed, with significantly lower *NR0B1* expression in Cushing's tumors compared with SCTs ($P = .0269$), and no significant changes in *TBX19* or *NEUROD1*. Genes involved in POMC processing (*PCSK1*, *PCSK2*) did not show significant differences between tumor subtypes. In contrast, SCTs exhibited alterations in glucocorticoid receptor signaling, with significant changes in *NR3C1* ($P = .0093$) and *FKBP5* ($P = .0187$). Genes associated with oncogenic signaling, cellular stress, and cell-cycle control (*USP8*, *EGFR*, *STAT3*, *HSF1* and JUN) did not show significant differences between functioning and silent tumors.

Conclusions: Silent corticotroph tumors do not lack corticotroph identity but instead display a functional blockade characterized by dysregulation of upstream mechanisms controlling ACTH secretion, specifically suggesting that in CST the hypothalamic regulation of POMC processing is mediated preferently by AVPR1 than CHRH. Moreover, the preserved glucocorticoid feedback in SCT could contribute to the absence of the clinical Cushing's disease. This molecular dissociation provides a mechanistic basis to explain their clinical silence.

Abstract citation ID: lvag096.1284

EP1012 - ECE_2488 - Efficacy of recombinant human growth hormone therapy in patients with Schaaf-Yang syndrome

Oksana Khyzhnyak[1], Khristina Shchubelka[2], Olga Oleksyk[1], Elena Pop[1] and Miroslava Mykytyk[3]
[1]*Zakarpatska Endoclinica, Uzhhorod, Ukraine;* [2]*Medical Faculty, Uzhhorod National University, Uzhhorod, Ukraine;* [3]*Clinical Department, V. Danilevsky' Institute for Endocrine Pathology Problems of the National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine*

Objective: Schaaf-Yang syndrome (SYS) is an autosomal dominant multisystem disorder with early clinical overlap with Prader–Willi syndrome. Key features include hypotonia, joint contractures, autism spectrum disorders, intellectual disability, and growth retardation. The feasibility and efficacy of recombinant human growth hormone (rhGH) therapy in SYS remain under discussion. This study aimed to evaluate the clinical and laboratory efficacy of rhGH therapy in 2 siblings with SYS.

Materials and Methods: Two siblings with SYS were examined: an 11.10-year-old boy and his 18.2-year-old sister. Serum GH, IGF-1, levels were measured by ELISA. Bone age was assessed using the Greulich–Pyle method. Anthropometric parameters were evaluated according to WHO standards. Molecular genetic testing identified a heterozygous nonsense variant in the *MAGEL2* gene (c.2873G > A, p.Trp958*), inherited from the father, confirming the diagnosis of SYS in both patients. Both received rhGH in pediatric and adult dosage and the efficacy was assessed.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: The boy presented with congenital finger contractures, persistent hypotonia, feeding difficulties in infancy, chronic constipation, gastroesophageal reflux, and severe psychomotor delay (independent sitting at 2.5 years, walking at 3.8 years). Baseline GH was 0.84 ng/mL. rhGH therapy was initiated at 0.035 mg/kg/day. After 15 months, height increased from 116 to 128 cm (SDS −4.8 to −4.2), weight from 21.1 to 26.5 kg, and growth velocity reached +12 cm. IGF-1 increased from 20.0 to 126.0 ng/mL (SDS −5.28 to −2.40), and bone age progressed from 7 to 11 years. Marked improvements were noted in muscle strength, physical activity, speech development, communication, and self-care skills. The sister exhibited intellectual disability, social maladaptation, short stature, muscle weakness, obesity with hyperphagia, atopic dermatitis, and secondary amenorrhea. Baseline height was 134 cm (SDS −4.5), bone age 18 years, IGF-1 80 ng/mL (SDS −2.8), and GH 0.9 ng/mL. She received rhGH 0.3 mg/day combined with estradiol and dydrogesterone. After 15 months, fat mass decreased from 51% to 45%, muscle mass—from 28 to 31.7 kg, and body weight decreased from 68.8 to 58.0 kg. Clinical improvements included reduced appetite, increased physical activity, better social adaptation, reduced behavioral disturbances, and normalization of the menstrual cycle.

Conclusions: Patients with Schaaf-Yang syndrome demonstrate clinical and laboratory signs consistent with growth hormone deficiency. rhGH therapy appears safe and effective in both pediatric and adult patients, significantly improving growth parameters, body composition, and psycho-emotional functioning.

Keywords Schaaf-Yang syndrome, recombinant human growth hormone therapy

Abstract citation ID: lvag096.1285

EP1013 - ECE_1987 - Two siblings with normosmic isolated hypogonadotropic hypogonadism and hearing loss with a KISS1R gene mutation

Daniel Grigorie, Elena Braha and Alina Sucaliuc
National Institute of Endocrinology, Bucharest, Romania

Introduction: Kisspeptin 1 receptor (KISS1R) gene mutations are rare but become an important etiology of normosmic isolated hypogonadotropic hypogonadism (nIHH). IHH with associated hearing loss could be the consequence of a single gene mutation or not.

Cases Presentation: The proband was a male born to nonconsanguineous eugonadal Romanian parents. He was initially referred to our department at the age of 31 years reporting absent pubertal development at 15 yrs (FSH 0.05 mIU/mL, LH 0.17 mIU/mL, testosterone 0.26 ng/mL) and treatment with testosterone undecanoate (1000 mg every 3 months, intramuscular injections) with acquisition of full secondary sexual features and final height (180 cm). Micropenis and cryptorchidism were noticed at birth and treated with HCG for 1 yr. At present time, physical examination showed normal olfaction, small for age intrascrotal testes (15 mL), a penis length of 6 cm, azoospermia. His karyotype was normal (46, XY). Serum LH (<0.2 mIU/mL) and FSH (0.38 mIU/mL) were low and normal testosterone 2.93 ng/mL (1.75 – 7.81 ng/mL). He had hearing loss and difficulties in speech, been diagnosed at 1 yr and considered to be caused by gentamicin administration. His sister was 22 years, tall and eunuchoid, Tanner B4P4, normal olfaction, milder hearing loss (also attributed to gentamicin in childhood). At age 15 she presented with primary amenorrhea and thereafter treated with oral contraceptives. At the present time, FSH = 2.47 mUI/mL, LH = 2.12 mUI/mL, E2 = 15.53 pg/mL and on ultrasound low-normal uterus and bilateral micropolycystic ovaries. Her karyotype was normal (46, XX). Pituitary and olfactory bulb magnetic resonance imaging were normal as the anterior pituitary function in both.

Results of Genetic Testing: We found a heterozygous KISS1R mutation (c.305T > C) by NGS and a 35delG mutation of GJB2 gene by MLPA in both siblings.

Discussion: c.305T > C is a recurrent missense mutation (p. Leu102Pro) of KISS1R gene and was described as homozygous or compound heterozygous mutation of several families with IHH, heterozygous been unaffected. Nevertheless, significantly delayed puberty in heterozygous female patients have been described with another mutation. However, 2 heterozygous missense mutations (KISS1R and IL17RD) were identified in a male patient with IHH (Miraoui, 2013), suggesting oligogenicity. Hearing loss caused by mutations in GJB2 accounts for approximately half of all autosomal recessive forms of hearing loss and is the most common form of hereditary hearing loss.

Conclusions: We described two siblings with nIHH and hearing loss produced by mutations in two unrelated genes.

Abstract citation ID: lvag096.1286

EP1014 - ECE_1999 - Persistent remission after steroidogenesis inhibitor discontinuation in Cushing disease: a case series

Alessandra Mangone[1,2], Elisa Sala[2], Giulia Carosi[2], Giulia Del Sindaco[2], Roberta Mungari[2], Arianna Cremaschi[2], Iulia Petria[1,2], Giovanna Mantovani[1,2] and Emanuele Ferrante[2]
[1]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [2]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Background: Adrenal steroidogenesis inhibitors, such as metyrapone and osilodrostat, represent key treatment options for persistent or recurrent Cushing disease. These drugs have a short half-life and are considered rapidly reversible in their effects, yet recent reports have described prolonged adrenal insufficiency following osilodrostat discontinuation, suggesting potential long-lasting effects. Proposed mechanisms include a direct cytotoxic effect on the adrenal cortex, supported by recent imaging data suggesting possible adrenal shrinkage during osilodrostat treatment. Similar prolonged effects have not been previously reported with metyrapone.

Case Presentation: We describe three female patients with Cushing disease who had previously undergone pituitary surgery and subsequently initiated adrenal steroidogenesis inhibitors (metyrapone or osilodrostat) for documented recurrent disease, defined by elevated 1-mg dexamethasone suppression test, urinary free cortisol and late-night salivary cortisol levels. All three patients experienced an unplanned interruption of therapy due to symptoms consistent with adrenal insufficiency after a mean duration of 6 months and subsequently remained in biochemical remission after treatment withdrawal. Remission was persistent at last follow-up, observed 31 months after

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

metyrapone discontinuation and 19 and 41 months after osilodrostat withdrawal.

Results: Long-term remission persisted despite the short half-life of steroidogenesis inhibitors and in the absence of further active treatment. Biochemical evaluation consistently demonstrated normal UFC and LNSC levels during subsequent follow-up.

Conclusions: We report three cases of prolonged adrenocortical suppression after withdrawal of steroidogenesis inhibitors, contributing to the growing literature on potential long-lasting adrenal effects of these therapies by providing a longer follow-up and including metyrapone among the agents involved. These observations support hypotheses of sustained adrenal effects beyond transient enzyme inhibition and underscore the need for systematic studies to identify predictors and mechanisms underlying this unexpected outcome.

Abstract citation ID: lvag096.1287

EP1015 - ECE_2908 - Two distinct cases of acromegaly with benign and malignant lung tumors

Gokcen Ertuna[1], Berna Evranos Ogmen[1], Meric Coskun[2], Birgul Genc[1], Gulsum Karahmetli[1], Oya Topaloglu[1], Bekir Cakir[1] and Reyhan Ersoy[1]
[1]Endocrinogy and Metabolism, Ankara Bilkent Şehir Hastanesi, Ankara, Türkiye; [2]Endocrinogy and Metabolism, Bartın Devlet Hastanesi, Bartın (Merkez), Türkiye

Introduction: Acromegaly is a rare chronic condition characterised by excessive secretion of growth hormone (GH) and insulin-like growth factor-1 (IGF-1), with an incidence of 30-70 cases per million. It is associated with increased morbidity and mortality due to systemic and metabolic effects, primarily leading to cardiovascular diseases, respiratory issues, and cancers. While it is debated whether acromegaly increases the incidence of benign and malignant tumors, the potential relationship between the GH-IGF-1 axis and tumorigenesis has been documented in various studies. However, the existing literature on the connection between acromegaly and lung tumors remains scarce. This report presents two cases of acromegaly involving pulmonary hamartoma and lung adenocarcinoma and reviews related literature.

Case 1: A 56-year-old male patient presented for evaluation due to concerns about his altered and rough appearance and was subsequently diagnosed with acromegaly. After multiple treatments, including transsphenoidal hypophysectomy, medical drugs and Gamma knife radiosurgery, the patient's IGF-1 level normalised. In a follow-up 12 years after the acromegaly diagnosis, he developed a pulmonary hamartoma followed by lung adenocarcinoma after nine years of hamartoma, ultimately leading to his death from metastatic lung cancer at age 78.

Case 2: A 26-year-old male presented with typical symptoms of acromegaly and was diagnosed with a $14 \times 16 \times 21$ mm pituitary adenoma. After two transsphenoidal adenoidectomies, medical drugs and gamma knife radiosurgery, GH and IGF-1 levels were fixed within normal limits. Eighteen years after the diagnosis, a nodular lesion was discovered in his right lung, later identified as a pulmonary hamartoma during monitoring.

Discussion: The presented cases highlight the complexity of acromegaly and its potential associations with lung tumors. Further research is needed to clarify the relationship between acromegaly and lung tumorigenesis and to ensure comprehensive follow-up care focusing on potential respiratory complications in these patients.

Keywords acromegaly, hamartoma, lung cancer, pituitary

Abstract citation ID: lvag096.1288

EP1017 - ECE_2448 - The renin-angiotensin system is activated by short-term, but repressed by long-term growth hormone excess

Clemens Baumgartner[1], Paul Fellinger[1], Anna Tosin[1], Anne Blanchard[2], Matthaeus Metz[1], Oliver Domenig[3], Dunja Van Oyen[3], Anton Luger[1], Greisa Vila[1], Alexandra Kautzky-Willer[1], Michael Krebs[1], Philippe Chanson[2], Peter Kamenicky[2] and Peter Wolf[1]
[1]Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria; [2]Service d'Endocrinologie et des Maladies de la Reproduction, Université Paris-Saclay, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin-Bicêtre, France; [3]Attoquant Diagnostics, Vienna, Austria

Background: The renin-angiotensin system (RAS) constitutes an important cornerstone in blood pressure (BP) regulation. Previous studies have reported heterogeneous and sometimes contradictory results regarding the relationship between growth hormone (GH), insulin-like growth factor I (IGF-I), and the RAS, depending on study conditions and exposure duration. This study therefore investigated the effects of short- and long-term GH excess on RAS activity.

Methods: RAS activity was assessed in 10 healthy, male volunteers (26 ± 5 years, BMI 23 ± 3.4 kg/m^2) before and after one week of daily, subcutaneous GH treatment serving as model of short-term GH excess. Regarding long-term GH excess, RAS activity in 19 patients with active acromegaly (54 [48-59] years, 10 females, IGF-I/ULN 2.8 [2.3-3.3]) were compared to a cohort of 25 controls (39 [32-47] years, 19 females). In 12 patients measurements were re-conducted after successful treatment of acromegaly.

Results: One week of GH treatment increased overall RAS activity, including angiotensin II levels (117.5 ± 50.3 vs 205.9 ± 135.7, $P = .03$) and the sum of angiotensin I + II (PRA-S) representing a marker for renin activity (149.8 ± 63.3 vs 269.1 ± 177.4, $P = .03$) alongside increased concentrations of insulin and C-peptide in healthy males. In contrast, patients with acromegaly showed lower concentrations of angiotensin II (47.2 [33-145] vs 155.3 [64-326], $P = .017$), aldosterone (118 [71-193] vs 227.8 [165-305], $P = .009$), and PRA-S (84.2 [51-200] vs 230 [85-403], $P = .032$) despite higher mean arterial BP (105 [99-115] vs 91 [85-97], $P < .001$) compared to controls. Biochemical disease control did not change RAS activity in acromegaly, but ΔIGF-I showed a strong negative correlation with Δaldosterone/angiotensin II-ratio ($rho = -0.61$, $P = .04$), a biomarker for adrenal response to angiotensin II signalling.

Conclusions: Short-term GH excess stimulates RAS activity which might be related to the increase in insulin and C-peptide. In contrast, RAS activity is down-regulated in long-term GH excess despite high BP.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1290

EP1019 - ECE_1669 - GHRH and its agonist MR-409 attenuate neurodegeneration and inflammation in experimental Alzheimer's disease

Francesca Pedrolli[1], Giulia Morello[2], Iacopo Gesmundo[1], Federica Bistolfi[1], Gabriella Gruden[1], Medhi Wangpaichitr[3], Wei Sha[3], Elena Tamagno[2], Andrew V. Schally[3], Michela Guglielmotto[2] and Riccarda Granata[4]
[1]*Department of Medical Sciences, University of Turin, Turin, Italy;* [2]*Department of Neurosciences "Rita Levi Montalcini", University of Turin and Neuroscience Institute Cavalieri Ottolenghi, Turin, Italy;* [3]*Endocrine and Polypeptide Institute, Miami VA Healthcare System, Miami, FL, United States;* [4]*Department of Molecular Biotechnology and Health Sciences, University of Turin, Turin, Italy*

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by amyloid-β (Aβ) accumulation and tau hyperphosphorylation, leading to neuroinflammation, neuronal loss, and cognitive decline. Current therapies provide limited symptomatic relief and fail to halt disease progression, highlighting the need for novel therapeutic strategies. Growth hormone-releasing hormone (GHRH), besides promoting the release of pituitary growth hormone (GH), exerts several peripheral functions, including stimulation of cell survival and proliferation. Notably, both GHRH and its agonistic analog MR-409 exert anti-inflammatory, cardioprotective, and neuroprotective effects. However, the role of GHRH in AD remains to be elucidated. Thus, in this study we explored the therapeutic potential of GHRH and its agonist MR-409 in *in vitro* and *in vivo* AD models. *In vitro,* GHRH(1-44)NH_2 enhanced cell survival, proliferation and neuronal differentiation in rat hippocampal neural stem cells (NSCs) and human SH-SY5Y neuroblastoma cells under growth factor deprivation or amyloid-β ($A\beta_{1-42}$) exposure. The underlying molecular mechanisms involved the activation of $G_{\alpha S}$/cAMP/PKA/CREB pathway, as well as ERK1/2 and PI3K/Akt signaling. Furthermore, GHRH mitigated Aβ-induced neurotoxicity by reducing apoptosis, inhibiting GSK-3β activity and tau phosphorylation and suppressing inflammatory cytokines expression and NF-κB phosphorylation. *In vivo*, 3-month-old male transgenic 5xFAD mice were divided into two groups (5xFAD-vehicle [$n = 14$] and 5xFAD-MR-409 [$n = 14$]) and treated daily for 3 months with subcutaneous injection of MR-409 (20 μg) or vehicle. 5xFAD-MR-409 mice showed increased body weight gain compared with vehicle-treated controls. MR-409 markedly reduced brain Aβ deposits compared with vehicle, accompanied by decreased tau phosphorylation and reduced activation of GSK-3β and CDK5. In addition, MR-409 exerted significant anti-inflammatory effects by attenuating microgliosis, astrogliosis, inflammatory cytokine expression, and NF-κB phosphorylation, while also displaying antioxidant activity through modulation of KEAP1–NRF2 pathway. MR-409 also mitigated neuronal and synaptic loss, as evidenced by increased expression of the neuronal marker NeuN, neurotrophic factors and synaptic proteins synaptophysin and PSD-95. These molecular and histological changes were associated with improved cognitive performance, as assessed by novel object recognition and Y-maze tests, in MR-409-treated mice compared with controls. In summary, this study demonstrates that GHRH and its agonist MR-409 modulate multiple aspects of AD pathology, and hold promise for further translational development in neurodegenerative diseases.

Abstract citation ID: lvag096.1291

EP1020 - ECE_2014 - Under-recognition of endocrinopathies among patients with chronic opioid use: a population-based study

Ashley Han, Sara J. Achenbach, Elizabeth Atkinson and Irina Bancos
Mayo Clinic, Rochester, NY, United States

Background: Although opioid use has been associated with several endocrinopathies due to hypothalamus-pituitary axis suppression, biochemical testing is not routinely performed in patients with chronic opioid use. As a result, it is suspected that opioid-induced endocrinopathies remain significantly under-recognized and untreated in this patient population, potentially contributing to adverse clinical outcomes associated with long-term opioid use.

Methods: We performed a large retrospective population-based cohort study with 15-years of follow-up (2005-2021). Patients with ≥3 months of consecutive opioid use were identified as cases and paired 1:1 with age-, sex-, and calendar-year matched referent subjects. Adrenal insufficiency was defined using a composite clinical definition to capture cases identified in routine clinical practice. Hypogonadism and hyperprolactinemia were identified based on International Classification of Diseases (ICD) codes and hypothyroidism was defined by an active prescription for thyroid hormone replacement. Outcomes of interest included incidence of adrenal insufficiency, serum cortisol testing, hypogonadism, hypothyroidism, and hyperprolactinemia during follow-up.

Results: In our cohort of 7805 matched patients, the cumulative incidence of adrenal insufficiency was 11.3% among patients with chronic opioid use compared with 5.9% among referent patients (hazard ratio [HR] 2.13 [95% CI 1.82-2.50]). Although patients with chronic opioid use were more likely to undergo biochemical testing than referent patients, less than 14% of patients with chronic opioid use had at least one serum cortisol level measured during 15-year follow-up. Compared with referent patients, those with chronic opioid use were at increased risk of incident hypogonadism (HR 2.57 [95% CI 1.69-3.91]) and hyperprolactinemia (HR 1.67 [1.04-2.67]), but not hypothyroidism. The cumulative incidence of hypogonadism among male patients with chronic opioid use was 4.3%. Notably, adrenal insufficiency was independently associated with increased risk of inpatient hospitalization (HR 1.48 [95% CI 1.29-1.69]) and mortality (HR 2.21 [95% CI 1.98-2.47]) after adjustment for opioid use, age, sex, comorbidity burden, and prior hospitalization.

Conclusions: Despite a well-established association between opioid use and endocrinopathies such as hypogonadism and adrenal insufficiency, biochemical testing remains uncommon among patients with chronic opioid use. The incidence of endocrinopathies observed in this population-based study was lower than previously reported estimates from smaller studies in which all patients underwent biochemical testing. This real-world data suggests that endocrinopathies are likely substantially underdiagnosed among patients with chronic opioid use due to insufficient biochemical testing, which may contribute to adverse clinical outcomes associated with long-term opioid therapy.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1292

EP1022 - ECE_3537 - Distinct molecular profile of silent corticotroph tumours compared with gonadotroph tumours

Jorge Navarro[1], Johana Sottile[1], Elena Garcia-Garrigos[2], Jorge Frances[3], Francisca María Peiró-Marqués[4] and Antonio Pico[1]

[1]*Clinical Medicine, ISABIAL (Instituto de Investigación Sanitaria y Biomédica de Alicante), Alicante, Spain;* [2]*Radiology, Hospital General Universitario de Alicantet Emergency Room, Alicante, Spain;* [3]*Clinical Analyse, ISABIAL, Alicante, Spain;* [4]*Pathology, ISABIAL, Alicante, Spain*

Introduction: Silent corticotroph tumors (SCTs) are considered clinically non-functioning and, in routine practice, are frequently grouped together with gonadotroph tumors (GTs) within non-functioning pituitary tumors. However, the true biological identity of SCTs and their molecular relationship with GTs remain a matter of debate. The aim of this study was to compare the molecular profile of SCTs with that of gonadotroph tumors in order to determine whether SCTs represent a distinct entity within this group.

Methods: Gene expression analysis was performed by RT-qPCR in human pituitary tumor biopsies obtained from 28 patients with silent corticotroph tumors and 53 patients with gonadotroph tumors, using normal pituitary tissue as a reference for gene expression normalization. Tumor classification was carried out according to the 2022 WHO criteria, based on the expression of the transcription factors TBX19/TPIT for corticotroph tumors and *NR5A1*/SF-1 for gonadotroph tumors. Genes related to tumor identity and differentiation (*TBX19*, *NEUROD1*, *NR5A1*, *GATA2*, *NR0B1*), corticotroph regulation and hormonal function (*POMC*, *CRHR1*, *AVPR1B*), somatostatin-mediated inhibitory signaling (*SSTR2*, *SSTR3*, *SSTR5*), tumor signaling and cellular stress pathways (*EGFR*, *USP8*, *STAT3*, *HSF1*, *JUN*), cell cycle control and genomic stability (*CABLES1*, *MSH6*), and tumor immunomodulation (CD274) were evaluated. Statistical analysis was performed using the non-parametric Mann–Whitney test, considering P values $<.05$ as statistically significant.

Results: Beyond the expected differences related to corticotroph lineage, silent corticotroph tumors displayed a differential molecular profile dominated by alterations in regulatory and signaling pathways. In particular, SCTs showed higher expression of *SSTR5*, whereas *SSTR3* was significantly higher in gonadotroph tumors and *SSTR2* did not differ between groups. In addition, SCTs were characterized by increased expression of genes involved in tumor signaling and cell cycle control, including *EGFR*, *STAT3*, *JUN* and *CABLES1*. *USP8* showed a trend toward higher expression in SCTs without reaching statistical significance. In contrast, *GATA2* and *CD274* were more highly expressed in gonadotroph tumors. No significant differences were observed for *NEUROD1*, *NR5A1*, *NR0B1*, *HSF1*, or *MSH6*.

Conclusions: Silent corticotroph tumors exhibit a molecular profile clearly distinct from that of gonadotroph tumors, characterized by a specific pattern of somatostatin receptor expression and by alterations in tumor signaling and cell cycle–related pathways, independent of classical hormonal identity. These findings support the concept that SCTs constitute a defined molecular entity within non-functioning pituitary tumors, with potential diagnostic and therapeutic implications.

Abstract citation ID: lvag096.1293

EP1023 - ECE_1175 - The pituitary paradigm shift: a multimodal approach to redefining tumor aggressiveness

Ipsita Mishra

Endocrinology, Diabetes and Metabolism, IMS & SUM II, Phulnakhara, Soul Balance, Diabetes and Endocrine Centre of Excellence, Cuttack, India

Background: Pituitary neuroendocrine tumors (PitNETs) are typically benign, but a small subset exhibits aggressive behavior. Accurately predicting which tumors will behave aggressively remains a clinical challenge. We hypothesized that an integrated, multimodal approach combining clinical, radiological, and immunohistochemical (IHC) markers would provide a more robust and accurate prediction of tumor aggressiveness and clinical outcome.

Methods: 250 patients with PitNETs who underwent surgical resection were analyzed on three key domains: 1) **Clinical features**, including patient age, sex, tumor type (functioning vs non-functioning), and presenting symptoms; 2) **Radiological characteristics**, such as maximum tumor diameter, tumor volume, and Knosp grade for cavernous sinus invasion; and 3) **Immunohistochemical markers**, including the proliferative index (Ki-67), p53 expression, and methylguanine-DNA methyltransferase (MGMT) expression. A multivariate predictive model was developed by integrating these markers, and its ability to predict recurrence-free survival (RFS) and progression-free survival (PFS) which was analyzed over a five-year follow-up period.

Results: Univariate analysis revealed that a high Ki-67 index ($\geq$3%), Knosp grade $\geq$3, and strong p53 expression were each significantly associated with shorter recurrence-free survival (RFS) and progression-free survival (PFS) ($P < .01$ for all. However, the most compelling findings emerged from the integrated multivariate model. Our risk stratification system, which assigned scores based on a combination of these markers, identified three distinct prognostic groups. The high-risk group ($n = 55$), characterized by the co-occurrence of a high Ki-67 index ($\geq$3%), Knosp grade $\geq$3, and strong p53 expression, had a median RFS of 1.5 years (95% CI: 1.2-1.8 years) and a 5-year RFS of only 18.2%. This was in contrast to the low-risk group ($n = 120$), which had a 5-year RFS of 92.5%, and the intermediate-risk group ($n = 75$), with a 5-year RFS of 55.1%. The Kaplan-Meier analysis showed a significant separation between the three groups ($P < .001$, log-rank test). Cox proportional hazards modelling demonstrated that our integrated risk score was a powerful independent predictor of recurrence (HR = 4.7; 95% CI: 3.2-6.9; $P < .001$), outperforming any single marker alone. The predictive accuracy (as measured by the concordance index, or C-index) of our model was 0.88, a substantial improvement over a model using only Ki-67 (0.70) or Knosp grade (0.75) in isolation.

Conclusions: The findings of this study underscore the limitations of a single-marker approach for assessing pituitary tumor aggressiveness. Our integrated multimodal model, provides a superior tool for accurate risk stratification. The proposed model represents a crucial step toward personalized medicine in the management of PitNETs.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1294

EP1024 - ECE_2181 - Systemic inflammatory markers discriminate ACTH-secreting PitNET from the other PitNET histotypes with high accuracy

Claudia Campana[1], Giuliana Corica[2], Karol Sagan[3], Diego Criminelli[4], Elżbieta Andrysiak-Mamos[3], Anna Brzeska[3], Anhelli Syrenicz[3], Gianluigi Zona[4], Diego Ferone[1] and Federico Gatto[1]

[1]Endocrinology Unit, Department of Internal Medicine and Medical Specialties, University of Genoa, Genoa, Italy; [2]Endocrinology Unit, IRCCS Ospedale Policlinico San Martino, Genoa, Italy; [3]Department of Endocrinology, Metabolic and Internal Diseases, Pomeranian Medical University, Szczecin, Poland; [4]Division of Neurosurgery, Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Introduction: Systemic **i**nflammatory markers have been shown to properly discriminate adrenal Cushing's syndrome from other adrenal lesions. Moreover, these biomarkers have been reported to be differentially modulated in GH-secreting PitNETs compared to non-functioning (NF)-PitNETs.

Aim: To investigate whether pre-operative systemic inflammatory markers may properly discriminate ACTH-secreting PitNETs from the other PitNET histotypes.

Methods: Retrospective, two-centre study, including patients that underwent surgery for PitNETs. We collected patient pre-operative blood count and calculated the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR) and the systemic immune-inflammation index (SII; platelet count multiplied by neutrophil count, then divided by lymphocyte count). Data concerning pituitary function before surgery we collected, when available. Patients were stratified based on pathology report and clinical/biochemical evaluation (NF-PitNET: NF-group; ACTH-secreting PitNET: ACTH-group; silent corticotroph PitNETs: sACTH-group; GH-secreting PitNET: GH-group; PRL-secreting PitNET: PRL-group).

Results: 295 patients were included; 158 males (56%), mean age at surgery 54.5 ± 15.3 years. Most tumors belonged to the NF-group ($n = 176$, 60.7%), followed by GH-group ($n = 41$, 14.1%), ACTH-group ($n = 39$, 13.4%), PRL-group ($n = 24$, 8.3%) and sACTH-group ($n = 10$, 3.4%). NLR and SII were significantly higher in ACTH-group compared to the other groups, except the sACTH ($P < .001$). SII was significantly higher in the sACTH-group compared to NF-group. PLR was significantly higher in ACTH-group compared to NF-group and GH-group ($P < .001$); PLR was significantly higher in sACTH-group compared to NF-group. LMR was significantly lower in ACTH-group compared to NF-group and GH-group ($P < .001$). Morning plasma cortisol levels were available in 202 patients (36 ACTH-group and 166 of the other groups); overall, we observed a positive correlation between cortisol levels and NLR (rho = 0.227, $P < .002$), SII (rho = 0.258, $P < .001$) and PLR (rho = 0.289, $P < .001$), and a negative correlation with LMR (rho = −0.320, $P < .001$). The evaluation of UFC values (available in 79 patients, 29 from the ACTH-group) showed the same pattern. ROC curve analyses showed that SII was able to differentiate the ACTH-group from all other groups with high accuracy (AUC = 0.854, 95%CI 0.774-0.933; cut-off 538.3 = sensitivity 86%, specificity 78%, accuracy 80%) and it was the best predictor compared to the other systemic inflammation markers ($P < .05$). A similar accuracy of SII was observed when considering together the ACTH + sACTH-groups vs all other tumor types (AUC = 0.847, 95%CI 0.777-0.916).

Conclusions: A dysregulation of systemic **i**nflammatory markers is observed in patients with Cushing's disease and silent ACTH-secreting PitNETs. In particular, SII seems to be an easily available and reliable tool to discriminate patients with ACTH-PitNETs from other PitNET histotypes.

Abstract citation ID: lvag096.1295

EP1025 - ECE_2817 - Impact of CRH shortage on the work-up of ACTH-dependent Cushing's syndrome and usefulness of desmopressin-based diagnostic tests: insights from 54 European expert centres

Annamaria Colao[1], Barbara Altieri[2], Carla Scaroni[3], Elena Valassi[4], Emese Mezosi[5], Frederic Castinetti[6], Leonard Saiegh[7], Manel Puig-Domingo[4], Pedro Marques[8,9] and Timo Deutschbein[10]

[1]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione, Università Federico II di Napoli, UNESCO Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy; [2]Division of Endocrinology and Diabetes, Department of Internal Medicine I, University Hospital of Würzburg, Würzburg, Germany; [3]Endocrinology Unit, Department of Medicine DIMED, University-Hospital of Padova, Padova, Italy; [4]Department of Endocrinology & Nutrition CIBERER Group 747, Germans Trias Research Institute and University Hospital, Universitat Autònoma de Barcelona, Barcelona, Spain; [5]Ist Department of Internal Medicine, Clinical Center, University Medical School of Pecs, Pecs, Hungary; [6]Marseille Medical Genetics, Aix Marseille Univ, INSERM, UMR1251, Institut MarMaRa, Marseille, France; [7]Department of Endocrinology, Bnai Zion Medical Center, The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel; [8]Pituitary Tumor Unit, Endocrinology Department, Hospital CUF Descobertas, Lisbon, Portugal; [9]Scientific Programmes Department, European Society of Endocrinology (ESE), Bristol, United Kingdom; [10]Medicover Oldenburg MVZ, Oldenburg, Germany

Introduction: The main supplier of corticotropin-releasing hormone (CRH) is no longer manufacturing this drug. The European Society of Endocrinology (ESE) provided recommendations on how to deal with this issue (PMID:39005054). The diagnostic work-up of adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome (CS) is now more reliant on desmopressin. We aimed to evaluate the impact of CRH shortage and usefulness of desmopressin-based alternative diagnostic tests across expert centres in Europe.

Methods: A standardized survey (SurveyMonkey®) with 25 questions was created by an ESE Task Force and sent to European expert pituitary centres. Answers were counted as absolute numbers and percentages.

Results: Forty-four of 54 centres (82%) from 17 countries that answered the survey currently have no CRH. The main CRH utilisation was the diagnostic work-up of ACTH-dependent CS (98%), but CRH was also commonly used to distinguish between CS and pseudo-Cushing states (31%). Top investigations for ACTH-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

dependent CS before and after CRH shortage were pituitary MRI and IPSS (>90%), and there was an expected drop in the use of CRH stimulation tests across centres from 80% to 8%, while desmopressin test use increased from 25% to 73%. After CRH shortage there was an increased use of whole-body CT scan (from 41% to 49%) and functioning imaging (from 35% to 41%). Based on their experience, 47% of centres consider the desmopressin test performance worse than CRH stimulation test, while 36% consider these similar. Since CRH shortage, 70% of centres are using desmopressin during IPSS (contrasting with 4% before CRH shortage), and 4% stopped performing IPSS because of CRH shortage. Overall, 57% of centres consider CRH shortage has low impact on the ACTH-dependent CS diagnostic work-up, while 28% and 15% of centres describe CRH shortage as having no and high impact, respectively; 85% of centres agreed that a revised CS diagnostic algorithm without CRH is necessary.

Conclusions: CRH is not available in most European centres, which led to a shift towards desmopressin-based diagnostic tests. In general, CRH shortage seems to have low or no impact on ACTH-dependent CS work-up, but it can create additional diagnostic challenges due to the limited experience with desmopressin and need for more expensive and time-consuming alternative investigations. The performance of desmopressin is regarded as inferior to CRH by most centres, perception that may reflect the lack of data and experience with desmopressin. Further studies to assess the desmopressin diagnostic accuracy, and a revised CS diagnostic algorithm without CRH, are needed.

Abstract citation ID: lvag096.1296

EP1026 - ECE_3194 - Peripheral immune and inflammatory profiles as potential biomarkers of disease activity and treatment response in acromegaly

Dario De Alcubierre[1,2], Ludovica Vincenzi[1], Lorenzo Cerroni[1], Francesca Sciarra[1], Marie-Lise Jaffrain-Rea[2,3], Mary Anna Venneri[1], Emilia Sbardella[1], Andrea Isidori[1,4] and Tiziana Feola[1,2]

[1]Department of Experimental Medicine, Sapienza University, Rome, Italy; [2]Neuroendocrinology, Neuromed IRCCS, Pozzilli, Italy; [3]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [4]Centre for Rare Diseases, Policlinico Umberto I, Rome, Italy

Background: Acromegaly is associated with a distinct circulating immunophenotype, characterized by reduced monocytes, enrichment of non-classical subsets, and decreased NK cells with $CD56^{dim}$ predominance. However, longitudinal data on peripheral immune and inflammatory profiles and their relationship with therapeutic response are lacking.

Objective: To characterize baseline immune and inflammatory profiles in patients with newly-diagnosed acromegaly, to assess their longitudinal modulation and evaluate their association with biochemical response to medical therapies.

Methods: Patients with newly-diagnosed acromegaly (January 2022-June 2025) were evaluated at diagnosis and during follow-up after neurosurgery or, in the absence of remission, during medical therapy (first-line somatostatin analogues [SSA] and pegvisomant add-on in SSA non-responders). Clinical, hormonal, and radiological data were collected. Peripheral immunophenotyping was performed by multiparametric flow cytometry to quantify T-cell subsets, NK cells, and monocyte populations. Systemic inflammation indices derived from routine blood counts—neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), and systemic immune–inflammation index (SII)—were assessed.

Results: Twenty-one patients (11 males, mean age 51 ± 16 years) were included; follow-up ranged from 6 to 12 months. At baseline, NLR and SII correlated with increased IGF-1 levels × ULN (NLR: $r = 0.769$, $P = .002$; SII: $r = 0.723$, $P = .005$) and tumor volume (NLR: $r = 0.738$, $P = .015$). Eighteen patients (85.7%) underwent neurosurgery; five had not yet completed longitudinal evaluation at the time of data collection. Following surgical remission ($n = 4$), a significant reduction in circulating $CD56^{dim}$ NK cells was observed ($P = .042$). Twelve patients received SSA therapy, out of whom 7 achieved biochemical control and 5 required second-line treatment. Noteworthy, higher circulating $CD8^+$ T-cell percentages were significantly associated with greater IGF-1 reduction after SSA therapy ($r = -0.699$, $P = .011$), with a similar non-significant trend toward GH reduction ($r = -0.517$, $P = .085$). Accordingly, $CD8^+$ T-cell levels were higher in SSA responders than in non-responders (0.27 ± 0.13 vs 0.09 ± 0.04, $P = .024$). In contrast, baseline inflammatory indices did not differ between SSA responders and non-responders. SSA responders also exhibited a significant longitudinal increase in intermediate monocytes ($P = .029$) and a progressive reduction in $CD56^{dim}$ NK cells ($P = .001$), whereas patients requiring pegvisomant add-on showed an increase in total monocytes ($P = .014$) and a reduction in $CD56^{dim}$ NK cells ($P = .004$). No significant longitudinal changes in lymphocyte subsets were observed in either group.

Conclusions: In acromegaly, baseline systemic inflammatory indices reflect disease burden, whereas higher circulating $CD8^+$ T cells are associated with better response to SSA. The treatment of acromegaly was found to dynamically modulate innate immunity, partially restoring the distribution of innate immune cells subpopulations.

Abstract citation ID: lvag096.1297

EP1027 - ECE_3565 - Comparison of ACTH responses to CRH and desmopressin during inferior petrosal sinus sampling in confirmed Cushing's disease

Diogo Brandão Neves[1], Beatriz Tavares Da Silva[1], Andreia Martins Fernandes[2], Maria Teresa Pereira[1], Carolina Noronha[3], Isabel Ribeiro[3] and Claudia Amaral[1]

[1]Division of Endocrinology, Centro Hospitalar e Universitário de Santo António, ULSSA, Porto, Portugal; [2]Clinic, Endocrinology Department, Portuguese Oncology Institute of Coimbra, Coimbra, Portugal; [3]Neurossurgery, Centro Hospitalar e Universitário de Santo António, ULSSA, Porto, Portugal

Background: Inferior petrosal sinus sampling (IPSS) with corticotropin-releasing hormone (CRH) is considered the gold standard for differentiating pituitary from ectopic ACTH-dependent Cushing's syndrome and may assist in tumor lateralization. Due to worldwide shortages of CRH, desmopressin (ddAVP) has increasingly been used as an alternative stimulus, despite concerns regarding its potentially lower ACTH stimulatory capacity.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Objective: To assess whether differences exist in the magnitude of ACTH response—evaluated by peak ACTH ratios and peak ACTH concentrations—between patients with confirmed Cushing's disease undergoing IPSS with CRH or desmopressin, and to describe lateralization concordance with pituitary imaging and procedural safety.

Methods: We performed a retrospective analysis of patients with ACTH-dependent Cushing's syndrome who underwent IPSS with CRH or desmopressin and in whom Cushing's disease was subsequently confirmed. ACTH responses, lateralization results, and procedural safety were evaluated.

Results: Forty-seven patients were included (66% female; mean age 44.8 ± 15.0 years). IPSS stimulation was performed with CRH in 39 patients (83%) and desmopressin in 8 patients (17%). Baseline characteristics, including age, lesion size, and baseline ACTH ratios, were comparable between stimulation groups. Median peak ACTH ratios were 24.95 (IQR 10.2-22.8) in the desmopressin group and 47 (IQR 23.9-155) in the CRH group ($P = .156$). Median peak ACTH concentrations were 1174 pg/mL (IQR 932.8-1897.0) versus 1983 pg/mL (IQR 1170-12 382), respectively ($P = .111$). Among patients with informative imaging and successful bilateral catheterization ($n = 27$), lateralization concordance between IPSS and pituitary MRI was 70.4% ($n = 19$). In operated patients, histopathology most frequently demonstrated corticotroph PitNET (46.8%), while normal adenohypophysis was observed in a subset, consistent with the known limitations of histological detection in Cushing's disease. Procedural complications were infrequent: transient oxygen desaturation occurred in 1 patient (2.1%), and minor post-procedural adverse events were observed in 8 patients (17.0%), including inguinal hematoma in 7 (14.9%) and subconjunctival hemorrhage in 1 (2.1%). No major complications were recorded.

Conclusions: In our study, desmopressin stimulation during IPSS resulted in ACTH responses comparable to those obtained with CRH in patients with confirmed Cushing's disease, which shows it appears to be a safe and feasible alternative stimulus for IPSS in settings where CRH is unavailable. As described previously in literature, lateralization concordance with imaging was limited and frequently not assessable.

Abstract citation ID: lvag096.1298

EP1028 - ECE_3963 - Tenascin C as a predictor of progression during somatostatin analogue therapy in patients with stage IV well-differentiated gastroenteropancreatic neuroendocrine tumors

Dorota Kaczmarska-Turek, Zbigniew Bartoszewicz and Tomasz Bednarczuk
Clinic of Internal Medicine and Endocrinology, University Clinical Center of the Medical University of Warsaw, Warsaw, Poland

Introduction: Long-acting somatostatin analogues (SSA) are recommended as first-line systemic therapy in patients with advanced, well-differentiated gastroenteropancreatic neuroendocrine tumors (GEP-NET). Despite their proven antiproliferative activity, a considerable proportion of patients experience early disease progression. Identification of biomarkers predicting reduced effectiveness of SSA could support early treatment optimization. Data addressing this issue in homogeneous populations of stage IV GEP-NET are limited. To assess the incidence of progression during SSA therapy and to identify biomarkers predicting progression, with particular emphasis on tenascin C (TNC), in patients with stage IV well-differentiated GEP-NET.

Material and Methods: This prospective observational study enrolled 30 patients with stage IV, well-differentiated GEP-NET (G1-G2, Ki-67 < 20%), all with liver metastases and confirmed somatostatin receptor expression on ^{68}Ga-PET/CT. Patients received octreotide LAR or lanreotide Autogel as first-line therapy and were followed for up to 12 months or until disease progression, assessed according to RECIST 1.1. Serum concentrations of TNC and selected biomarkers were measured at baseline and at predefined follow-up time points. Based on clinical course, patients were classified into progression and non-progression groups. A control group consisted of 28 healthy volunteers.

Results: During 12 months of SSA therapy, disease progression occurred in 56.7% of patients, with a median time to progression of 6 months. Baseline TNC concentrations were significantly higher in patients with GEP-NET compared with controls and were highest in patients who subsequently progressed. In the progression group, TNC concentrations increased significantly between 6 and 3 months before radiological progression, whereas no significant longitudinal changes were observed in patients without progression. ROC analysis identified a TNC cut-off value of 4.93% at progression, predicting disease progression with an AUC of 0.76, sensitivity of 70% and specificity of 80%. Progression was also associated with G2 grading and higher Ki-67 index in liver metastases, as well as the presence of extra-abdominal and extraskeletal metastases at baseline.

Conclusions: In patients with stage IV well-differentiated GEP-NET treated with SSA, more than half experience disease progression within the first year. Tenascin C demonstrates dynamic changes preceding radiological progression and may serve as a promising biomarker of reduced SSA effectiveness in this homogeneous population. Further studies in larger cohorts are required to validate its clinical utility for early risk stratification and treatment personalization.

Keywords tenascin C, GEP-NET, somatostatin analogues, biomarkers, disease progression

Abstract citation ID: lvag096.1299

EP1029 - ECE_1026 - Serum neurofilament light chain: a candidate biomarker of neuroaxonal injury in patients with dysnatremia, associated with functional outcomes and mortality

Fabio Bioletto, Daniela Cuboni, Emanuele Varaldo, Michela Sibilla, Valentina Gasco, Ezio Ghigo, Silvia Grottoli, Nunzia Prencipe and Alessandro Maria Berton
Turin, Italy

Background: Both hypo- and hypernatremia are associated with neurocognitive and neuromuscular dysfunction. However, specific biomarkers for these complications are lacking. In the present study, we aimed to explore the association between serum sodium levels and serum neurofilament light chain (sNfL), an emerging circulating biomarker of neuroaxonal injury.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Methods: sNfL levels were evaluated in serum obtained from stored specimens from subjects that participated in the population-based 2013-2014 cycles of the National Health and Nutrition Examination Survey (NHANES). Cognitive function was evaluated using the Consortium to Establish a Registry for Alzheimer's Disease-Word Learning, the Animal Fluency Test, and the Digit Symbol Substitution Test. Muscle strength was measured through a handgrip dynamometer. All-cause mortality was evaluated by linking NHANES data with data from the National Death Index. All analyses were adjusted for relevant confounders.

Results: The study population consisted of 2071 subjects. Serum sodium levels were low (≤135 mmol/L), normal (136-144 mmol/L), or high (≥145 mmol/L) in 47, 1999, and 25 participants, respectively. Patients with hyponatremia had higher sNfL levels compared to normonatremic subjects, independent of potential confounders (mean difference in log-transformed sNfL values: +0.44, 95%CI:[+0.06,+0.81], $P = .03$). Conversely, no significant alteration of sNfL levels was observed in hypernatremic patients. Evaluating sodium as a continuous predictor, a significant non-linear association was observed between sodium levels and sNfL ($P < .01$ for association; $P < .01$ for non-linearity), with an inflection at 138 mmol/L; below this threshold, an increase of +0.09 (95%CI:[+0.01,+0.16], $P = .02$) in log-sNfL was observed for each 1 mmol/L serum sodium decrease. Higher sNfL levels were associated with worse cognitive performance and muscle strength, independent of sodium levels and other potential confounders ($P < .05$ for all functional tests). Hyponatremia (HR = 2.18 compared to normonatremia, 95%CI:[1.13, 4.21], $P = .02$) and sNfL (HR = 2.63 per 1-unit increase in log-transformed sNfL, 95%CI:[1.91, 3.64], $P < .01$) were independent predictors of all-cause mortality. No significant differences in the predictive value of sNfL were observed across sNa categories ($P = .13$ for interaction). The predictive value of sNfL levels was also confirmed in a subgroup analysis limited to hyponatremic patients (HR = 2.89 per 1 unit increase in log-transformed sNfL, 95%CI:[1.76, 4.76], $P < .01$).

Conclusions: We provide first-time evidence of an association between hyponatremia and increased sNfL levels. Conversely, albeit with the limitations imposed by the small number of hypernatremic participants, no significant increase in sNfL was observed in hypernatremia. sNfL could serve as a novel biomarker of neuroaxonal injury in patients with hyponatremia, correlated with functional outcomes and mortality.

Abstract citation ID: lvag096.1300

EP1030 - ECE_1516 - Risk factors and clinical outcomes associated with hyperglycemia-adjusted serum sodium in a large cohort of hospitalized patients

Alessandro Maria Berton[1], Anna Castiglione[2], Sonia Barello[3], Emanuele Varaldo[1], Matteo Baldi[3], Nunzia Prencipe[1], Fabio Bioletto[1], Francesco Biagini[3], Andrea Benso[1], Silvia Grottoli[1], Ezio Ghigo[1], Emanuela Arvat[4], Giulio Mengozzi[5], Giovannino Ciccone[2] and Luca Scaglione[3]

[1]Division of Endocrinology Diabetology and Metabolism, Department of Medical Sciences, Città della Salute e della Scienza di Torino University Hospital, Torino, Italy; [2]Unit of Clinical Epidemiology, Città della Salute e della Scienza di Torino University Hospital and CPO Piemonte, Torino, Italy; [3]Division of Internal Medicine 5, Department of General and Specialist Medicine, Città della Salute e della Scienza di Torino University Hospital, Torino, Italy; [4]Division of Oncological Endocrinology, Department of Medical Sciences, University of Turin, Torino, Italy; [5]Clinical Biochemistry Laboratory, Department of Medical Sciences, University of Turin, Torino, Italy

Introduction: Dysnatremia is the most common electrolyte disorder in hospitalized patients. Both hypo- and hypernatremia are associated with neurological complications, increased morbidity and mortality. This study aimed to assess the prevalence of dysnatremia at admission and its impact on hospitalization outcomes, and to identify factors associated with the development of dysnatremia within the first 10 days of hospitalization among patients with normal s-Na at admission.

Methods: This retrospective study considered for inclusion all adult patients discharged between 2016 and 2021 from the Molinette University Hospital of Turin, the largest tertiary center in Piedmont. A s-Na measurement obtained on the day of admission or within two days was required to classify natremia at presentation. Administrative discharge records were linked with laboratory data. Comorbidity burden was assessed using the Charlson Comorbidity Index (CCI). S-Na was corrected for hyperglycemia using the Katz formula, and analyses were based on corrected sodium (c-Na).

Results: A total of 148 692 admissions were recorded, of which 128 114 (86.2%) had available s-Na and glycemia measurements, with 98.7% of these taken at admission. Patients were predominantly male (57.9%), with a mean age of 66.2 years; 63.2% were admitted to medical wards. Overall, 31.1% of hospitalizations experienced at least one episode of hyponatremia. Correction for hyperglycemia led to reclassification of 37.5% of cases initially labeled as hyponatremia into normonatremia. At admission, corrected hyponatremia was present in 9.3% of hospitalizations, while hypernatremia accounted for 2.0%. These prevalences were stable over time, with a modest increase in hyponatremia during summer months. Both dysnatremias were more frequent in older patients, those with higher CCI, and in medical compared with surgical admissions, with no major sex-related differences. Admission c-Na showed a U-shaped association with in-hospital mortality, ICU transfer, and length of stay, with the lowest risk around 140 mmol/L and a steeper risk increase at higher s-Na levels. Among 86 482 admissions with normal c-Na at entry and repeated measurements, 18.5% developed hyponatremia and 4.0% developed hypernatremia within 10 days. New-onset hyponatremia was associated with male sex, higher comorbidity burden, and surgical admission, whereas hypernatremia was more frequent in older patients and those admitted to medical wards.

Conclusions: Glucose-corrected dysnatremia is common and prognostically relevant in hospitalized patients. Routine correction of s-Na for hyperglycemia is essential to avoid misclassification, particularly in mild cases. Distinct demographic and clinical predictors of hospital-acquired dysnatremia support the concept that acquired hyponatremia and hypernatremia are pathophysiologicallly and prognostically distinct entities.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1301

EP1031 - ECE_1800 - Efficiency of cannulated prolactin test in differential diagnosis of hyperprolactinemia

Natalia Karlovich[1], Maryia Malyshko[2], Tatiana Mokhort[1], Alena Yurenia[2] and Romashko Angela[2]
[1]Belarusian State Medical University, Minsk, Belarus; [2]Minsk City Clinical Endocrinological Centre, Minsk, Belarus

Precise diagnosis of hyperprolactinemia (HP) is essential for choosing appropriate approach for its management. This is particularly important in cases with moderate elevation of prolactin (PRL), when we have to exclude functional (stress-induced) HP.

Aim: The aim was to determine the efficacy of cannulated prolactin test (CPT) in patients of reproductive age with mild HP and to analyze etiological structure and reproductive manifestations of HP.

Materials and Methods: We examined 178 patients with moderate HP, 154 w, 24 m; 31 ± 8.8 yrs. After cannula insertion, prolactin (PRL) was measured at P0, 60 (P1), and 120 minutes (P2). The results of the CPT were considered as positive when HP persisted all three samples (persisted HP), negative—in other cases (stress-induced HP). The presence of reproductive manifestations of HP (galactorrhea, menstrual cycle disorders, decreased libido, and infertility) and pituitary MRI were assessed.

Results: At baseline, the median PRL was 788.4 mIU/L (583.6-1187.0). PRL >1000 mIU/L found in 64 (35.9%) patients, >2000 mIU/L—in 14 patients (7.8%). A positive CTP detected in 60.1% of patients, and significantly more often associated with a baseline PRL >1000 mIU/L. In patients with positive CTP, the baseline PRL was 2 times higher than in those with negative CTP. In patients with a baseline PRL >2000 mIU/L, CTP was negative in 92.9% of cases. The decrease of PRL at P1 compared to P0 occurred in 78.1% of patients. At P2, compared to P1, the PRL value decreased in 84.8% of patients. Stress-induced HP was detected in 71 (39.9%) patients, pituitary microadenoma occurred in 65 (36.5%), and non-tumorous HP (other causes)—in 42 (23.6%) patients. Patients with microadenoma had significantly higher PRL levels and a higher frequency of PRL >2000 mIU/L. Reproductive manifestations of HP were detected in 91 (51.1%) patients, with equal frequency in both stress-induced and pathological HP. In women the most common complaint was menstrual irregularities (23.4%), in men—gynecomastia (29.2%). Also, pituitary microadenoma was detected in 33 (46.5%) patients with stress-induced HP and no reproductive manifestations.

Conclusions: The CTP is specific for the differential diagnosis of stress-induced (39.9% of cases) and pathological HP (60.1%). The baseline PRL is a key factor influencing the CTP result. CTP can be used to exclude stress-induced HP in patients with PRL <1000 mIU/L and is not mandatory for patients with PRL >2000 mIU/L. Visualization of pituitary microadenoma in case of negative CTP and absence of reproductive manifestations indicates a combination of hormonally inactive adenoma and stress-induced HP.

Abstract citation ID: lvag096.1302

EP1032 - ECE_1816 - Glycemic and lipidic profiles of patients with acromegaly long-term treated with pasireotide LAR after dose downtitration

Flavia Costanza[1], Sabrina Chiloiro[1], Antonella Giampietro[1], Laura De Marinis[1], Antonio Bianchi[1], Maria Fleseriu[2] and Alfredo Pontecorvi[1]
[1]Catholic University of the Sacred Heart, Rome, Italy; [2]Oregon Health and Science University, Portland, OR, United States

Introduction: Pasireotide LAR (PAS-LAR) has demonstrated higher efficacy in controlling acromegaly; however, it results in glycometabolic deterioration in many patients. This can lead to early discontinuation of PAS-LAR therapy, even in patients with biochemically controlled acromegaly. The purpose of this real-world study is to investigate the effects of PAS-LAR dose downtitration on glucose and lipid metabolism in patients with acromegaly.

Methods: A retrospective, single-center, longitudinal study was conducted on 27 patients with acromegaly on PAS-LAR monotherapy. Data on glucose and lipid metabolism were collected 6 months after dose downtitration and at 6 months of treatment in patients on a stable PAS-LAR dose. PAS-LAR dose reduction was performed in patients with remission of acromegaly symptoms and IGF-I values in the lower-normal age-adjusted reference range, with a concomitant clinically relevant worsening of the glucose and lipidic control, applying ADA 2024 criteria, therapeutic targets recommended by the ESC/EAS guidelines, and/or the necessity for a therapeutic intervention with glucose-lowering or lipid-lowering medications.

Results: The total duration of PAS-LAR therapy was 8.5 (IQR:5.2) in patients that underwent PAS-LAR dose reduction, and 7.8 (IQR:5.8; $P = .266$) in the stable dose group. The mean duration of PAS-LAR therapy before dose reduction was 7 years (IQR:5.0). PAS-LAR dose down-titration was conducted in 11 out of 27 patients (40.7%). In this group, glucose profile improved in all patients (100%); lipid profile improved in five patients (45.4%), remained stable in four patients (36.3%) and worsened in two patients (18.1%). As compared to patients who underwent PAS-LAR dose reduction, glucose profile did not improve in patients on treatment with stable dose of PAS-LAR ($P < .001$), worsened in 12 patients (75%) and remained stable in 4 patients (25%); lipid profile improved in a patient (6.2%), remained stable in six patients (37.5%) and worsened in nine patients (56.2%) ($P = .033$). After dose downtitration, IGF-I levels showed a slight increase, but remained in the normal range.

Discussion: In acromegaly, the impairment of glucose and lipid metabolism should be carefully managed due to the increased overall mortality risk associated with multiple comorbidities. This study suggests that PAS-LAR dose reduction in patients with acromegaly allows maintenance of biochemical disease control with improved glycemic profiles. Furthermore, we showed for the first time that lipid metabolism also improves with dose downtitration. In selected patients on long-term PAS-LAR therapy with good biochemical disease control, but metabolic deterioration, cautious dose reduction initially should be considered, rather than direct discontinuation of the drug.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1303

EP1033 - ECE_1930 - Pituitary insufficiency in Rathke's cleft cysts—a retrospective analysis

Lucas Steckel, Mirjam Pichler and Susanne Kaser
Medical University Innsbruck, Innsbruck, Austria

Background: The clinical presentations of Rathke's cleft cysts (RCC) vary widely across a spectrum from asymptomatic to generalized hypopituitarism. Data on the frequency of endocrine abnormalities during the course of disease are limited.

Methods: We conducted a retrospective, single-center analysis of patients with neuroradiologically confirmed Rathke's cleft cyst. Data regarding possible pituitary insufficiencies, clinical presentations, and comorbidities was analyzed for a follow-up period of a minimum of 5 years.

Results: 72 patients were enrolled in the study (age = 44.3 ± 16.8 years; female = 67%; BMI = 25.9 ± 5.9 kg/m^2), the diagnosis of RCC was classified as an incidental finding in 94.4% of cases. At baseline, anterior total or partial pituitary insufficiency was diagnosed in 7 out of 72 patients (9.7%), with only one person suffering from total anterior hypopituitarism and non with generalized hypopituitarism. Hypogonadism occurred in all 7 patients followed by insufficiencies of the thyrotropic axis (n = 4), adrenal deficiency (n = 4) and somatotropic axis (n = 3). Arginine vasopressin deficiency was found in one patient and hyperprolactinemia in 6 patients. Regular MRT scans performed during follow-up showed a progression in cyst size in 10 out of 72 patients, 9 of these patients had intact pituitary function at baseline. None of the 65 patients with intact pituitary function at baseline developed hypopituitarism during the follow-up period.

Conclusions: Our study indicates that pituitary insufficiency affects about 10% of patients with RCC, emphasizing the need of endocrinological assessments at time of diagnosis. Patients with intact pituitary function did not develop pituitary insufficiency regardless of whether the cyst increased in size or not. Thus, our data argue against regular endocrine follow-up checks in patients with RCC.

Abstract citation ID: lvag096.1304

EP1034 - ECE_1953 - Early postoperative cortisol as a predictor of remission in Cushing's disease: experience from a tertiary referral center

Sebnem Burhan[1], Aysel Unver Ozkahraman[1], Ebubekir Akpinar[2,3], Mutlu Niyazoğlu[1,3] and Esra Hatipoglu[1,3]
[1]*Department of Endocrinology and Metabolism, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye;* [2]*Department of Neurosurgery, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye;* [3]*Pituitary Disorders Research Center, University of Health Sciences, Istanbul, Türkiye*

Objective: Cushing's disease (CD) is the most common cause of endogenous Cushing's syndrome. Transsphenoidal surgery (TSS) is first-line treatment, yet early predictors of remission remain essential. Early postoperative cortisol has been proposed as a prognostic marker, but optimal cutoffs vary widely among centers.

Materials and Methods: This retrospective single-center study included 58 CD patients undergoing TSS (May 2020-December 2025). 08:00 AM cortisol and ACTH were measured on postoperative days 1-3. Remission was defined as cortisol <5 µg/dL requiring replacement or sustained eucortisolism for ≥12 months. ROC analysis assessed day-3 cortisol's predictive value for 3- and 6-month remission.

Results: Median follow-up was 24 months (IQR: 15.8-39.8). Mean UFC was 346 ± 993 µg/day. Remission rates were 73.6% (43/58) at month-3 and 77.6% (45/58) at month-6. with 100% sustained remission through month-12. No recurrence occurred during follow-up. Preoperative biochemical parameters, tumor size, invasiveness, pathological subtype, Ki-67 index, and surgery count were similar across remission and non-remission groups (P > .05 for all). Conversely, postoperative 3-month basal cortisol, ACTH, and glucocorticoid therapy duration showed significant differences (P < .01). ROC analysis was performed to evaluate the ability of early postoperative cortisol levels to predict remission. Postoperative day 1 cortisol showed poor discriminatory performance for predicting remission at 3 months (AUC = 0.586, 95% CI: 0.435-0.737; P = .264) and postoperative day 2 cortisol levels demonstrated limited predictive value for remission at 3 months (AUC = 0.597, 95% CI: 0.425-0.769; P = .270). Day-3 cortisol moderately predicted both 3-month (AUC 0.69, 95%CI: 0.55-0.83, P = .03) and 6-month remission (AUC of 0.69, 95% CI: 0.52-0.87, P = .028). Optimal cutoff <6.27 µg/dL yielded 78% sensitivity and 64% specificity.

Discussion: Day-3 postoperative cortisol (<6.27 µg/dL) is an independent, practical predictor of sustained remission in CD. Although moderate (AUC 0.69), it enables early risk stratification within 72 hours. Institution-specific thresholds may enhance postoperative management, guide glucocorticoid replacement strategies, and improve patient counseling regarding long-term prognosis.

Keywords Cushing's disease, remission, early cortisol, remission prediction

Abstract citation ID: lvag096.1305

EP1035 - ECE_2423 - Real-world effectiveness and safety of lanreotide autogel in patients with acromegaly in China: primary results and post-hoc analysis from a multicenter prospective observational study

Lian Duan[1], Songyun Zhang[2], Yongjian Wang[3], Wei Wang[4], Huiling Chen[5], Ping Li[6], Yanbing Li[7], Gaofei Ren[8], Juan Chen[9], Xiaoli Wang[10], Jianglong Lu[11], Jun Yang[12], Christelle Pommie[13], Xiaoxi Pan[14] and Huijuan Zhu[1]
[1]*Peking Union Medical College Hospital, PUMCH, Beijing, China;* [2]*The second hospital of Hebei Medical University, Shijiazhuang, China;* [3]*The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, Zhejiang, China;* [4]*West China Hospital, Sichuan University, Chengdu, Sichuan, China;* [5]*Xiangya Hospital Central South University, Changsha, Hunan, China;* [6]*The affiliated hospital of Nanjing University Medical School Nanjing Drum Tower Hospital, Nanjing, Jiangsu, China;* [7]*The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China;* [8]*The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan, China;* [9]*Tongji Hospital, Tongji Medical College of HUST, Wuhan, Hubei, China;* [10]*The First Hospital of China Medical University, Shenyang, Liaoning, China;* [11]*The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, China;* [12]*Peking University Third Hospital, Beijing, China;* [13]*Ipsen, Paris, France;* [14]*Ipsen Pharma, Shanghai, China*

Background: Acromegaly is a chronic condition with substantial comorbidities and impaired life quality. Although Lanreotide

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Autogel (LAN) was effective in previous clinical trials, IGF-1 normalization varies by ethnicity and assay. Real-world evidence in Chinese patients remains limited.

Aim: To assess real-world effectiveness, safety, treatment patterns, and predictors of response to LAN over 12 months in Chinese acromegaly patients.

Methods: Prospective, multicenter, non-interventional study (NCT05431803) enrolled 129 LAN-naïve acromegaly patients. Under protocol-specific IGF-1 local ranges, primary endpoint: full biochemical control (fasting GH <2.5 μg/L and normalized IGF-1) at M12; secondary endpoints included biochemical control based on narrower (GH <1 μg/L and normalized IGF-1) and broader ranges (GH ≤2.5 μg/L and IGF-1 ≤1.3 × ULN), hormonal changes, symptom relief, AcroQoL score, treatment patterns, and safety. Post-hoc analysis: biochemical control assessed with China-specific IGF-1 ranges (normalized IGF-1 ± 2 SD for Chinese adults) (PLoS One 12(10):e0185561) including normal, narrower and broader criteria, versus those with protocol-specific IGF-1 local ranges; explored predictors of response using multivariate logistic regression with protocol-specific IGF-1 local ranges.

Results: Effectiveness was assessed in 120 patients (59.2% female; mean ± SD age: 42.3 ± 12.7 years). Among 102 patients with fasting GH and IGF-1 data at M12, under protocol-specific IGF-1 local ranges, 19.6% achieved full biochemical control; 11.8% and 34.3% met narrower and broader criteria, respectively. Proportion of participants with any reported symptom declined from 87.5% (105/120) to 77.9% (81/104) at M12, with reduction on headache (38.3% [46/120] to 21.2% [22/104]), soft tissue swelling (65.8% [79/120] to 57.7% [60/104]) and excessive sweating (20.0% [24/120] to 13.5% [14/104]). AcroQoL global score improved (LSM change [95%CI]: 5.7 [3.1, 8.2]). Patients received a mean ± SD of 8.2 ± 3.7 LAN injections during the study (mean ± SD LAN exposure duration: 283.9 ± 132.4 days). 19.2% were treated with extended dosing intervals (EDIs); biochemical control was achieved in 26.1% of EDI patients versus 17.7% of non-EDI patients. Overall, 60.5% experienced treatment-emergent adverse events (TEAEs): 41.9% were mild. 28.7% reported treatment-related TEAEs, with 2.3% being serious events. Most frequent TEAE was diarrhea (17.1%). Among 86 patients assessed using IMMULITE-2000®, 24.0% achieved full biochemical control (narrower: 10.7%; broader: 34.7%) applied China-specific IGF-1 ranges, versus 18.7% (narrower: 12.0%; broader: 30.7%) using protocol-specific IGF-1 local ranges. Lower fasting GH at M3, lower baseline IGF-1, excessive sweating, and naïve from prior treatment significantly increased biochemical response rate.

Conclusions: In real-world clinical practice in China, LAN provides effective biochemical control and clinical improvement across multiple assessment methods, with a favorable safety profile, supporting long-term use in acromegaly.

Abstract citation ID: lvag096.1306

EP1036 - ECE_2203 - Postoperative muscle strength decline in Cushing's syndrome is associated with higher circulating activin A concentrations

Moritz Schrenk, Michael Haenelt, Elisabeth Nowak and Martin Reincke
Department of Medicine IV, Endocrinology, LMU University Hospital, Munich, Germany

Context: Cushing's syndrome (CS) is associated with myopathy that may paradoxically worsen after curative surgery despite biochemical remission and contributes to a reduced quality of life. However, the mechanisms underlying this postoperative deterioration in muscle strength remain largely unknown.

Objective: To evaluate serum myokines during active CS and the postoperative remission phase.

Patients and Methods: In this single-center, longitudinal observational cohort study, serum myokine profiles, including activin A, myostatin, and follistatin, were analyzed in 28 patients with endogenous CS prospectively enrolled at LMU Hospital Munich. All patients underwent successful curative surgery. Biochemical and clinical data were collected at baseline and six months postoperatively and compared with those of 28 age-, body mass index, and sex-matched controls in whom hypercortisolism had been ruled out. Handgrip strength was measured in a standardized manner using a JAMAR hand dynamometer (Patterson Medical, Nottinghamshire, UK) and was normalized to age- and sex-specific normative values.

Results: During glucocortcoid excess, median normalized handgrip strength was reduced 91.2% (IQR: 77.9; 100) and further declined six months postoperatively 77.6% (IQR: 62.4; 90.0). Patients younger than 35 years showed no postoperative decline in median normalized handgrip strength 1.3% (IQR: −5.8; 17.9), whereas patients aged 35-50 years exhibited a median decline of −16.3% (IQR: −28.4 to 9.4) and patients older than 50 years a more pronounced decline of −31.5% (IQR: −57.0; −15.3). Baseline activin A concentrations were similar between patients with active CS and controls, whereas myostatin and follistatin concentrations were significantly lower in patients with active CS. Six month following surgery, serum concentrations of myostatin ($P < .0001$), activin A ($P < .0001$), and follistatin ($P = .0044$) increased significantly, accompanied by a significant increase in the activin A-to-follistatin ratio ($P = .0001$). Activin A exhibited age-dependent patterns in CS. Baseline median activin A concentrations were lowest in patients <35 years 61.5 pg/mL (IQR: 31.4-112.0) and highest in patients >50 years 234.0 pg/mL (IQR: 145.3-321.0). Six months postoperatively, activin A increased markedly to 514.9 pg/mL (IQR: 422.8-562.9) in patients >50 years of age. Postoperative activin A concentrations inversely correlated with the decline in normalized handgrip strength (*Spearman's* $\rho = -0.40$; $n = 26$; $P = .042$).

Discussions and Conclusions: The postoperative decline in muscle strength in CS was associated with an age-dependent increase in circulating activin A levels, suggesting that elevated activin A may contribute to postoperative muscle dysfunction through activation of the activin-receptor-type IIB and subsequent induction of atrogenes resulting in muscle atrophy.

Abstract citation ID: lvag096.1307

EP1037 - ECE_1085 - The forgotten face of acromegaly: oral–maxillofacial clues and a possible IGF-1-mediated protection against periodontal breakdown

Marco Puma Duque[1,2] and Paulina Posso Salgado[3]
[1]*Obesity and High Cardiovascular Risk, Endocrinology, Hospital Universitario Sanitas La Zarzuela, Madrid, Spain;* [2]*Medicine and*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Dentistry, Health Sciences, Universidad Europea de Madrid, Madrid, Spain; [3]Primary Care and Community Health Centre, Centro de Salud El Espinar, Castilla y León Health Service (SACYL), El Espinar, Spain

Background: Oral and maxillofacial manifestations of acromegaly remain under-recognised despite their potential to provide early diagnostic cues and insights into disease biology. Beyond the well-known systemic effects of GH and IGF-1, recent evidence suggests that these anabolic hormones may exert local actions on the periodontium, influencing bone remodelling, collagen synthesis, and inflammation.

Objective: To systematically evaluate oral and maxillofacial manifestations of acromegaly and to analyse periodontal outcomes, exploring a potential protective role of the GH/IGF-1 axis in periodontal integrity.

Methods: A PRISMA-based systematic review was conducted (2004-April 2025). Major medical and scholarly databases (PubMed, MEDLINE, Google Scholar, Scopus) were searched for studies reporting oral or periodontal findings in patients with acromegaly. Inclusion criteria encompassed clinical, observational or review studies with clearly defined diagnostic criteria. Studies with insufficient case definition or very small, non-standardised samples were excluded for methodological quality reasons. Data extracted included design, sample characteristics, oral signs, periodontal parameters, and comorbidities. Risk of bias was appraised using JBI for cross-sectional and ROBINS-I for non-randomised designs, and AMSTAR-2 for systematic reviews.

Results: Fourteen studies met inclusion criteria. The most frequent oral features were macroglossia (**54%-58%**), interdental diastemas (**40%-62%**), and mandibular prognathism (**20%-56%**), typically associated with increased lower facial height and Angle Class III malocclusion. Periodontal assessment was reported in seven studies. Across these, **advanced periodontitis was less prevalent than expected**, with reduced probing depth and clinical attachment loss compared to controls, despite similar plaque indices. Other cohorts—particularly those with concomitant diabetes or hypogonadism—did not confirm this pattern, indicating heterogeneous outcomes. Experimental data support that IGF-1 enhances viability and osteogenic differentiation of periodontal ligament and gingival stem cells, up-regulates COL1A1 expression, and modulates inflammatory balance in alveolar bone. Collectively, this evidence outlines a plausible biological framework for **GH/IGF-1-related periodontal preservation** in certain acromegaly phenotypes.

Conclusions: Oral–maxillofacial features are clinically significant yet often overlooked in acromegaly. Their recognition by dental and primary-care professionals may facilitate earlier referral to endocrinology. Moreover, the paradoxically mild periodontal damage observed in some patients opens a new translational perspective: IGF-1 may contribute to maintaining periodontal architecture through regenerative and anti-inflammatory pathways. Prospective, standardised studies integrating endocrine control status and periodontal biomarkers are warranted to validate this hypothesis and to foster true interdisciplinary management.

Abstract citation ID: lvag096.1308

EP1039 - ECE_1807 - Growing too fast: a rare case of gigantism diagnosed during childhood

Daniela-Georgiana Amzar[1,2], Mihaela Maria Vlad[1], Melania Balas[1], Ioana Golu[1], Stoian Dana[1], Oriana Pelineagră[1] and Laura Cotoi[3]

[1]Endocrinology, Spitalul Clinic Județean de Urgență Timișoara, Timișoara, Romania; [2]Endocrinology, Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania; [3]Endocrinology, Centre Hospitalier de Luxembourg, Luxembourg, Luxembourg

Introduction: Gigantism is a rare pathology in children characterized by growth hormone (GH) excess prior to epiphyseal fusion. It is associated with significant morbidity and reduced life expectancy in the absence of appropriate treatment.

Case Presentation: O.D., a male patient, now 18 years old, has been followed in our clinic since 2016, having been diagnosed with gigantism at the Pediatric Department of our horspital at the age of 12 years and 9 months. In 2014, the patient presented with visual disturbances, headaches, swelling of soft tissues, accelerated growth (weight 85 kg, height 171 cm, SD = +2.6 to mid-parental height). Laboratory data confirmed high levels of IGF-1 and basal GH, associated with unsuppressed GH levels following oral glucose tolerance test. No other pituitary insufficiencies were found. MRI of the pituitary gland showed a 3.9 cm pituitary macroadenoma. Transsphenoidal adenomectomy was performed, but only part of the tumour could be removed (tumour remnant volume: 10.2 cm^3). Somatostatin analogue treatment with Octreotide was started postoperatively. Later, due to incomplete response (with persistent sleep apnoea and headaches), dopamine agonist (cabergoline) was added. In 2016, the patient underwent further surgery without complete removal of the tumour. He also developed partial pituitary insufficiency (gonadotropic and thyrotropic). An MRI of the pituitary gland showed a tumour remnant of 1.9 cm^3. Pegvisomant was added to treatment with somatostatin analogues and cabergoline. In 2017, due to persistence of symptoms and unsatisfactory response to medical treatment, Gamma Knife radiosurgery was performed. The somatostatin analogue was also changed to Pasireotide. To date, the disease is well controlled under treatment.

Conclusions: Advances in pharmacotherapy and radiosurgery in patients with acromegaly and gigantism allow successful control of the disease. Early diagnosis is important because many of the complications are reversible in the early stages.

Abstract citation ID: lvag096.1309

EP1040 - ECE_2427 - Effectiveness of organized transition of care pathway in patients with rare endocrine conditions

Savi Shishkov[1], Zhenya Ruseva[1], Mira Siderova[1], Radina Dimitrova[1], Sevim Zekerie[2], Sonya Galcheva[2] and Violeta Iotova[2]

[1]Clinic of Endocrinology and Metabolic Disease, UMHAT "St. Marina", Varna, Bulgaria; [2]First Pediatric Clinic, UMHAT "St. Marina", Varna, Bulgaria

Introduction: Coordinating the transition of patients reaching adulthood with chronic diseases represents significant difficulties for both healthcare providers and patients. In the context

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

of rare endocrine diseases, the requirement for multidisciplinary follow-up in specialized centers can create additional barriers to accessing expert services. Even though transition pathways are implemented in many centers, local regulatory and organizational aspects require tailored center-specific approach.

Objective: To describe and evaluate the existing transition pathway for patients with rare endocrine diseases from a pediatric to an adult endocrinology clinic between 2021 and 2025.

Materials and Methods: The study has a retrospective design. The structure and components of the transition care pathway were described in detail. Included in the analysis were patients over 18 years of age referred to the endocrinology clinic by their treating pediatric endocrinologists. Clinical data, age at transfer, status at transfer, transition readiness assessment, and follow-up status were examined. Success of transition intervention is measured by retention in care after transfer to adult clinic. Lost to follow-up was defined as absence of visit in a period of 24 months.

Results: Over a 4-year period, 53 patients (31, 58.5%—women) with rare endocrine diseases were transferred. All patients were discussed in multidisciplinary team meetings as part of their transition care pathway. The mean age of transfer is 19.5 years (range, 18-37 years). Among them 15 (28.3%) have congenital and acquired hypopituitarism, 7 (13%) patients had Prader-Willi syndrome, 8 (15.1%)—with Turner syndrome, 9 (17%) have congenital adrenal hyperplasia, and 14 (26.4%)—other rare genetic syndromes. Follow up status was evaluated in all patients: eleven patients (20.8%) were lost to follow-up. Continuous medical care was suspended in five (9%), two patients were transferred to another centre. Assessment of transition readiness was conducted in 29 (54.7%). The main condition was stable in 47 (88.7%) of the patients, without acute complications, and in 35 (66%) the medical goals were met at the time of transfer.

Discussions and Conclusions: One-fifth of transferred patients do not continue their regular follow-up. This could lead to deterioration in the condition, especially in cases where treatment goals are not reached. These results are comparable to other published cohorts, but direct comparison is obstructed by possible differences in healthcare settings and protocols. More detailed identification of risk factors for dropout from patient follow-up is needed to prevent adverse health outcomes in a vulnerable group of patients.

Abstract citation ID: lvag096.1310

EP1041 - ECE_3716 - GH–IGF1 axis dysregulation in children with short stature: a tertiary center experience

D Amulya Reddy[1,2], Bhanusree Kalava[1], Vijay Sheker Danda[1], Vivek Kyatham[1], Ann Elias[1] and Venu Gopal Reddy K[1]
[1]*Hyderabad, India;* [2]*Department of Endocrinology, Gandhi Medical College, Hyderabad, India*

Introduction: Short stature resulting from abnormalities of the growth hormone (GH)–insulin-like growth factor 1 (IGF1) axis represents a heterogeneous group of disorders with diverse clinical, radiological, and genetic bases. Differentiating these etiologies is essential for accurate diagnosis, prognostication, and individualized therapy. We aimed to characterize the clinical, hormonal, imaging, and genetic spectrum of GH–IGF1 axis disorders in children presenting with proportionate short stature.

Methods: This retrospective cross-sectional study was conducted at a tertiary pediatric endocrinology center. Thirty children with proportionate short stature and suspected GH–IGF1 axis abnormalities were evaluated. Data retrieved from medical records included auxological parameters, GH stimulation test results, serum IGF1 levels, brain magnetic resonance imaging (MRI) findings, and genetic analyses performed using targeted gene panels and/or whole-exome sequencing.

Results: The cohort comprised 30 children (16 males, 14 females) with a mean age of 9.35 years. Isolated GH deficiency (IGHD) was the predominant diagnosis, identified in 24 patients, while multiple pituitary hormone deficiency (MPHD) and GH insensitivity were less common. Genetic analysis revealed substantial molecular heterogeneity, with **GHRHR mutations emerging as the most frequent genetic etiology**, indicating a major contribution to GH–IGF1 axis dysfunction in this population. Additional pathogenic variants involved genes associated with GH synthesis, pituitary development, and syndromic growth disorders, including GH1, LTBP3, WDR4/LARP7, and LHX3. Neuroimaging demonstrated structural abnormalities of the hypothalamic–pituitary region in a significant proportion of patients. Pituitary stalk interruption syndrome (PSIS) was the most frequent radiological finding and was observed across both IGHD and MPHD phenotypes. Other abnormalities included septo-optic dysplasia and anterior pituitary hypoplasia. Overall, a strong concordance was noted between radiological abnormalities and hormonal phenotypes. From a nutritional perspective, 18 of the 30 children exhibited greater compromise in weight age compared with height age, suggesting concomitant undernutrition. Importantly, GH deficiency was confirmed in several of these children despite nutritional impairment, indicating that undernutrition and GH–IGF1 axis disorders may coexist.

Conclusions: Children with short stature related to GH–IGF1 axis dysfunction demonstrate marked clinical, radiological, and genetic heterogeneity. GHRHR mutations were the most common genetic cause identified in this cohort. The presence of undernutrition should not preclude evaluation for GH deficiency, particularly in resource-limited settings. A comprehensive diagnostic approach integrating hormonal testing, imaging, and genetic analysis is essential for precise diagnosis and individualized management.

Abstract citation ID: lvag096.1311

EP1042 - ECE_2368 - Hormonal staining patterns and clinical outcomes in acromegaly: a 15-year single-center study

Sinem Başak Tan Öksüz[1], Esra Eraslan Aydemir[1], Aylin Okçu Heper[2], Cevriye Cansız Ersöz[2], Murat Erdogan[1], Rıfat Emral[1], Mustafa Sahin[1], Özgür Demir[1], Asena Gökçay Canpolat[1] and Sevim Güllü[1]
[1]*Department of Endocrinology and Metabolism, Ankara University School of Medicine, Ankara, Türkiye;* [2]*Department of Pathology, Ankara University School of Medicine, Ankara, Türkiye*

Background: Acromegaly exhibits marked pathological and clinical heterogeneity. While a substantial proportion of pituitary somatotroph adenomas co-secrete prolactin (PRL), the prognostic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

implications of GH/PRL adenomas remain controversial due to inconsistent diagnostic definitions and limited comparative data. This study evaluated the relationships between immunohistochemical (IHC) patterns, clinical characteristics, radiological features, and surgical/medical outcomes in acromegaly.

Methods: We retrospectively analyzed 96 surgically treated patients with acromegaly between 2010 and 2025. Adenomas were classified based on IHC as GH-only (50.0%), GH/PRL (40.6%), or other patterns (9.4%). Biochemical remission was assessed 3-6 months postoperatively and in patients receiving subsequent somatostatin analogs (SSAs). Radiological invasiveness, T2-MRI signal, cytokeratin (CK8/18) patterns, and Ki-67 indices were examined. Logistic regression was used to identify predictors of surgical remission and SSA responsiveness.

Results: GH/PRL adenomas demonstrated higher proliferative activity, with Ki-67 ≥3% in 79.5% versus 47.9% of GH-only tumors ($P = .003$), yet surgical remission rates were similar (94.9% vs 85.4%). Postoperative remission occurred in 37.5% of the cohort and was associated with smaller tumors, lower baseline GH and PRL levels, T2 hypointensity, and absence of invasion. Optic chiasm compression independently reduced surgical remission by 85% (OR 0.152, $P = .010$). Among 48 patients treated medically, 56.3% achieved SSA response. Responders were older and exhibited lower baseline IGF-1, smaller residual tumors, T2 hypointensity, and perinuclear CK8/18 staining. In multivariable analysis, perinuclear CK8/18 independently predicted SSA response (OR 6.16, $P = .021$). Tumor volume correlated with PRL levels only in GH/PRL adenomas (rho 0.351, $P = .028$), while no correlation existed with GH or IGF-1 in any subgroup.

Conclusions: Although GH/PRL adenomas show higher proliferative indices, they do not confer inferior surgical or medical outcomes. Classical clinical and radiological markers—particularly optic chiasm compression and CK8/18 staining patterns—better predict remission and SSA response than hormone co-secretion status. PRL correlated with tumor burden only in GH/PRL adenomas, suggesting subtype-specific biomarkers. These findings support individualized treatment strategies emphasizing anatomical and pathological features rather than PRL co-secretion alone.

Abstract citation ID: lvag096.1312

EP1044 - ECE_2825 - Endocrine dysfunctions and osteometabolic complications in adult patients with non-transfusion-dependent thalassemia and sickle cell disease: a monocentric cross-sectional study

Giulia Carosi[1], Elisa Sala[1], Roberta Mungari[1], Giulia Del Sindaco[1], Arianna Cremaschi[1], Alessandra Mangone[1], Marta Codegoni[1,2], Giorgia Grassi[1], Cristina Eller Vainicher[1], Irene Motta[2,3], Giovanna Graziadei[3], Emanuele Ferrante[1] and Giovanna Mantovani[1,2]

[1]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [3]SC Medicina ad Indirizzo Metabolico, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Background: Hemoglobinopathies are genetic disorders affecting hemoglobin's structure or production. Research in endocrinology primarily focused on young patients with transfusion-dependent β-thalassemia, while endocrine complications in adults with non-transfusion-dependent thalassemia (NTDT) and sickle-cell-disease (SCD) are less studied. This study aims to assess hormonal and osteometabolic alterations in aged NTDT and SCD patients.

Methods: This cross-sectional study included 83 patients (50 NTDT, 18 sickle-thalassemia or HbS-Thal and 15 SCD) who never received chronic blood transfusions. Patients were screened for hypopituitarism, hypothyroidism, hypoparathyroidism, hypoadrenalism, and growth hormone deficiency (GHD). Dynamic evaluations included ACTH and glucagon stimulation tests for hypoadrenalism/GHD and oral-glucose-tolerance-test (OGTT) for glycometabolic alterations. DEXA scans and vertebral X-ray were performed, along with osteometabolic biochemical assessments. Anamnestic data included history of iron overload based on hepatic-cardiac MRI-T2*.

Results: In the whole group, mean age was 46.7 ± 13 years, with 57.8% females (age and sex distribution were comparable in NTDT, HbS-Thal, and SCD). Iron overload on MRI-T2* was reported in 44%, 20%, and 17% patients with NTDT, HbS-Thal, and SCD, respectively ($P = .06$). Endocrine dysfunction occurred in 27%, with no significant difference between subgroups ($P = .667$). ACTH stimulation test was available in 36 patients, and glucagon test in 10. We diagnosed hypothyroidism (10.8%), secondary hypoadrenalism (6%), and hypogonadism (6%), with no cases of hypoparathyroidism. GHD was present in 1/10 patients tested. We found impaired fasting glucose in 6%, impaired glucose tolerance in 4%, and diabetes mellitus in 2.4%. Endocrine dysfunctions were correlated with iron overload on MRI-T2* ($P = .019$) while splenectomy, hydroxyurea, and age showed no association. Hypoadrenalism was more commonly observed in males ($P = .006$) and in patients with primary hypothyroidism ($P = .001$). Osteoporosis was diagnosed in 42.2%, and osteopenia in 34.9%. Clinical fractures occurred in 26.5%, and morphometric vertebral fractures were detected in 25.4%. Fracture rates were similar in patients with NTDT, HbS-Thal, and SCD. A positive correlation existed between bone-mineral-density (BMD) and TBS with frailty fractures in the groups of NTDT, HbS-Thal (T-score: lumbar $P = .03$, femoral-neck $P = .03$, total-hip $P = .029$, TBS $P = .002$), but not in SCD. No other variables, including urinary calcium, bone turnover markers, and iron overload, were associated with fractures.

Conclusions: Adult patients with NTDT and SCD, especially those with documented iron overload on MRI-T2*, are at risk for hormonal alterations and skeletal fragility. TBS appears to be associated with fractures in all patients, while BMD is an effective predictor for NTDT and HbS-Thal patients, but not for SCD.

Abstract citation ID: lvag096.1313

EP1045 - ECE_3123 - Temporal patterns and evolution of endocrine immune-related adverse events in patients treated with immune checkpoint inhibitors: beyond a static phenotype

Stavroula Asimakopoulou[1], Georgia Tsirou[2], Vasiliki Siampanopoulou[2], Petros Papalexis[2], Alexandros Lafioniatis[2], Varvava Chalmantzi[2], Despoina Tsopouzidou[2], Paschalia Bekiaridou[2],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Dimitroula Stephanou[1], Dimitrios Ziogas[1], Helen Gogas[1] and Anna Angelousi[2]
[1]First Department of Medicine, Laiko General Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [2]First Department of Medicine, Unit of Endocrinology, Laiko General Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Background: Endocrine immune-related adverse events (irEAEs) are common complications of immune checkpoint inhibitor (ICI) therapy and may lead to long-term or permanent hormone deficiencies. Identifying clinical and biochemical markers that predict the timing, phenotype, and risk of sequential endocrine involvement is essential to optimize patient management. This study investigated the temporal development of endocrine irEAEs in a cohort of oncological patients treated with ICIs.

Methods: We retrospectively evaluated 125 oncology patients (52.1% male), with a mean age of 62.27 ± 13.76 years, who developed endocrine irEAEs during ICI treatment. Melanoma was the predominant malignancy (85.3%). The time from ICI initiation to the first and any subsequent endocrine event was recorded. Hormonal profile, thyroid autoantibodies, and baseline metabolic comorbidities were also collected. Associations between autoimmunity, treatment modality, and temporal patterns of endocrine toxicity were analyzed.

Results: Primary thyroid toxicity was the most frequent endocrine irEAE, occurring in 60.6% of patients, followed by hypopituitarism in 30.9%. Thyroid toxicity tended to develop earlier than hypopituitarism (15.59 ± 11.43 vs 22.73 ± 16.14 weeks, $P = .067$). Anti-thyroglobulin antibody (anti-Tg) positivity at irEAE diagnosis was associated with significantly earlier onset of endocrine toxicity ($P = .04$), whereas anti-thyroid peroxidase (anti-TPO) positivity showed no significant association with timing. Baseline metabolic comorbidities—hypertension (36.6%), dyslipidemia (35.5%), and diabetes mellitus (9.7%)—did not significantly affect time to irEAE onset. Sequential endocrine irEAEs occurred in 11.7% of patients. Those who subsequently developed corticotropic axis deficiency presented with earlier primary endocrine toxicity compared with patients who experienced a single endocrine irEAE (11.43 ± 6.29 vs 18.40 ± 13.78 weeks, $P = .055$). Combination ICI therapy was associated with higher rates of initial multi-endocrine involvement (14.3% vs 5.8%) and a greater incidence of sequential endocrine irEAEs (26.7% vs 10%, $P = .136$) compared with monotherapy. Persistence varied by endocrine axis. Functional recovery was observed only in a small subset of patients with primary thyroid toxicity. In contrast, hypopituitarism—particularly corticotropic deficiency—was entirely irreversible during follow-up.

Conclusions: Anti-Tg positivity and early onset of endocrine toxicity identify patients at increased risk of rapid and sequential endocrine involvement, particularly affecting the corticotropic axis. Endocrine irEAEs should not be viewed as a static phenotype, as presentation may evolve over time with axis-specific temporal patterns and reversibility. Patients receiving combination ICI regimens, and those presenting with early or multi-axis toxicity, require intensified and prolonged endocrine monitoring to ensure timely diagnosis and appropriate hormone replacement.

Abstract citation ID: lvag096.1314

EP1046 - ECE_1886 - Comparison of French and PANOMEN-3 classifications for predicting post-operative evolution in paitents with prolactinoma

Anais Job[1], Lina Daoud[2], Orsalia Alexopoulou[1], Fomekong Edward[3], Christian Raftopoulos[3], Stefan Matei Constantinescu[1] and Dominique Maiter[1]
[1]Department of Endocrinology and Nutrition, Cliniques Universitaires Saint-Luc, Brussels, Belgium; [2]Department of Neuropathology, Cliniques Universitaires Saint-Luc, Brussels, Belgium; [3]Department of Neurosurgery, Cliniques Universitaires Saint-Luc, Brussels, Belgium

Background: The French five-tiered clinicopathological classification is used to assess the risk of recurrence/progression of pituitary tumors after surgery, but few studies focused on the post-operative evolution of patients with prolactinoma. Furthermore, clinical validation of the new PANOMEN-3 classification is needed in patients with prolactinoma.

Aim/Objective: We sought to compare the French and PANOMEN-3 classifications in predicting the post-operative evolution of patients with prolactinoma.

Methods: We retrospectively analyzed medical files of patients operated for prolactinoma between 2006 and 2024, with a confirmed histological diagnosis of prolactinoma, available histological markers (Ki 67, p53, mitosis) and at least 12 months of post-operative follow up. We defined recurrence as a new increase in prolactin above the upper limit of normal occurring >3 months after curative surgery. We defined progression as a >20% increase in any tumor diameter during follow-up of a post-operative residue. We defined disease free status at last visit as a normal prolactin without dopamine agonist treatment.

Results: 71 patients were included in the final analysis, 44 women and 27 men. 35 patients were initially cured by surgery, of which 7/35 (20%) suffered recurrence after a median of 18 months (range 5-41). 36 patients were not cured by surgery, 12/36 (33%) of which suffered disease progression during follow-up after a median of 12 months (range 2-82 months, 11/12 during the first 4 years). Progression or recurrence (19/71 or 27%) was significantly associated with the proliferative nature of the tumor as defined by the French classification ($P = .003$) but not with invasiveness ($P = .734$). The overall French grade was significantly associated with the risk of progression ($P = .027$) but not with recurrence ($P = .201$) or the pooled outcome of progression and recurrence ($P = .163$). PANOMEN-3 grade was associated with neither recurrence ($P = .528$), nor progression ($P = .440$) nor the pooled outcome of recurrence and progression ($P = .378$). However, disease free status at last visit was significantly associated with both the French (58%, 66%, 0% and 0% for grades 1a, 1b, 2a and 2b respectively, $P < .001$) and PANOMEN-3 grades (86%, 58%, 14% and 0% for grades 0, 1, 2 and 3 respectively, $P < .001$).

Conclusions: The proliferative nature of the tumor, as assessed by the French classification, was the most important predictor of progression/recurrence after surgery in patients with prolactinoma, highlighting the need for careful follow-up of proliferative tumors especially during the first 4 years after surgery. Both the French and PANOMEN-3 classifications predict long-term disease free status.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1315

EP1047 - ECE_3129 - Thyroid abnormalities in acromegaly in the era of improved disease control: a two-stage study

Gustavo Leite[1], Luciana Pedral S.D. Leite[2], Gabriel Leite[1], Roberto Salvatori[3], Juliana Drummond[4], Beatriz Santana Soares[4], Lucas Freitas[1], Izabella Freitas[1], Angela Leal[2], Arthur Oliveira[5,6] and Manuel H. Aguiar Oliveira[2]

[1]Faculty of Medicine, Medicine, Federal University of Minas Gerais, Belo Horizonte, Brazil; [2]Clinic, Medicine, Federal University of Sergipe, Aracaju, Brazil; [3]Clinic, Medicine, The Johns Hopkins University, School of Medicine Baltimore, Baltimore, MD, United States; [4]Division of Endocrinology, Department of Internal Medicine, Faculty of Medicine, Federal University of Minas Gerais, Belo Horizonte, Brazil; [5]Health Sciences Graduate Program, Federal University of Sergipe, Aracaju, Brazil; [6]Division of Neurosurgery, Medicine, Hospital de Cirurgia, Aracaju, Brazil

Introduction: The somatotropic and thyroid axes are interrelated, with the thyroid acting as a relevant site for extrapituitary circuits via autocrine production of growth factors. In acromegaly, such continuous stimulation has traditionally resulted in a high prevalence of diffuse or nodular goiter and thyroid cancer. This study aimed to verify whether these findings persist in the current scenario of greater availability of pharmacologic agents and better biochemical control of the disease.

Methods: A multicenter study was conducted with 92 acromegaly patients from two tertiary centers in Brazil. The protocol included a retrospective analysis of the clinical and laboratory data and a cross-sectional thyroid ultrasound in a subset of 74 patients. Disease control was calculated based on the ratio of IGF-1/Upper Limit of Normal (ULN) over the follow-up. Thyroid nodules were classified using ACR-TIRADS. Cluster analysis was performed to identify phenotypic patterns in the 74 patients with ultrasound data.

Results: The total cohort (71.7% females and 81.5% macroadenomas) exhibited a median biochemical control rate of 50%, with a median follow-up of 13 years and a well differentiated thyroid carcinoma prevalence of 4.3%, lower than in historical series. Among the 74 patients that underwent thyroid ultrasonography, 63.5% of them had nodules, and 27% goiter. There was a significant positive correlation between the percentage of biochemical control rate and the follow-up duration ($r = 0.378$; $P = .001$). In contrast, a negative trend correlation was observed between thyroid volume and control percentage ($P = .077$). Three clusters were identified: Cluster 1 ($n = 18$; 83.3% female; median age 64 years), Cluster 2 ($n = 36$; 100% female; median age 60 years), and Cluster 3 ($n = 20$; 100% male; median age 52.5 years). Significant differences were observed between clusters regarding sex and echotextural alterations ($P < .0001$ in both cases). Age, number of nodules, thyroid volume and follow-up time were similar across clusters, although the biochemical control rate showed a decreasing trend from Cluster 1 to the others.

Conclusions: In this cohort, massive goiter and increased risk of thyroid malignancy were not observed. The natural history of acromegaly appears to have changed due to therapeutic evolution and improved biochemical control. These advances are associated with a reduction in thyroid manifestations, contributing to an improved overall prognosis for patients with acromegaly. This reinforces that strict control during follow-up effectively attenuates these thyroid abnormalities.

Abstract citation ID: lvag096.1316

EP1048 - ECE_3369 - Misleading performance of clinical risk scores for Cushing's syndrome in partial lipodystrophy: results from a multicenter study

Stella Pigni[1], Carolina Cecchetti[2], Marina Caputo[3], Maria Francesca Birtolo[4], Gherardo Mazziotti[4], Andrea Lania[4], Alessandra Gambineri[2] and Flavia Prodam[3,5]

[1]Department of Translational Medicine, University of Eastern Piedmont, Novara, Italy; [2]Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy; [3]Department of Health Sciences, University of Eastern Piedmont, Novara, Italy; [4]Department of Biomedical Sciences, Humanitas University, Milan, Italy; [5]Department of Health Science, University of Piemonte Orientale, Novara, Italy

Background: Partial lipodystrophies (PLD) frequently overlap with Cushing's syndrome (CS) for clinical manifestations. Simplified clinical risk scores have been developed to estimate the pre-test probability of CS; however, their ability to discriminate between CS and other overlapping conditions such as PLD remains unclear. Moreover, reduced leptin action in lipodystrophy may influence the hypothalamic–pituitary–adrenal (HPA) axis, although human data are limited.

Methods: Retrospective, multicenter study, including 61 patients (91.8% females; mean ± SD age 50.2 ± 13.2 years) with PLD (54 familiar partial lipodystrophy, 4 acquired partial lipodystrophy, 3 progeroid syndromes) and 56 patients with CS (62.5% females; age 55.1 ± 14 years). Clinical and laboratory data were retrieved from medical records. To estimate the probability of hypercortisolism, the Cushing score was calculated considering main clinical predictors of CS (age <59 years, facial fullness, facial plethora, proximal muscle atrophy, dorsocervical fat pad, hirsutism/seborrhoea, non-obesity, hypertension, diabetes, osteopenia/osteoporosis). Clinical and metabolic features of PLD and CS were compared. Leptin–HPA axis interactions in PLD were also explored.

Results: Most PLD patients (93.4%) exhibited at least one clinical feature suggestive of CS. Facial fullness, facial plethora, dorsocervical fat pad, and hirsutism ($P < .001$) were more frequent in PLD, whereas proximal muscle atrophy and osteoporosis ($P < .015$) were more common in CS. PLD patients also showed a higher prevalence of diabetes and hypertriglyceridemia ($P < .001$). Mean Cushing score values were higher in PLD than in CS (9.6 ± 2.5 vs 8.6 ± 2.8 points, $P = .04$), particularly in patients with monogenic familiar partial lipodystrophy. In multivariable regression analysis, proximal muscle atrophy and osteoporosis were independently associated with CS, whereas diabetes and hypertriglyceridemia were associated with PLD ($P < .001$). Leptin levels were inversely correlated with Cushing score values (rho −0.41, $P = .009$).

Conclusions: PLD patients often exhibit cushingoid features, limiting the specificity of simplified clinical risk scores for CS. By identifying distinguishing clinical and metabolic features, this study underscores the need for greater awareness of lipodystrophy phenotypes to reduce misdiagnosis and supports an integrated diagnostic approach to improve patient recognition and management.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1317

EP1049 - ECE_2445 - Low work ability and high disability in Cushing's syndrome: a multicenter observational Cohort study in Germany

Annika Steinkogler[1], Stephanie Zopp[1], Kathrin Moser[1], Júnia Ribeiro De Oliveira Longo Schweizer[1], Isabel Stüfchen[1], Friederike Völter[1,2], Katrin Ritzel[1], German Rubinstein[1], Leah Braun[1], Marily Theodoropoulou[1], Rolf Holle[3], Birgit Linkohr[4], Tina Kienitz[5], Marcus Quinkler[5], Martin Reincke[1] and Elisabeth Nowak[1]

[1]*Department of Medicine IV, LMU University Hospital, LMU Munich, Munich, Germany;* [2]*Department of Nuclear Medicine, LMU University Hospital, LMU Munich, Munich, Germany;* [3]*Munich, Germany;* [4]*Institute of Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Munich-Neuherberg, Germany;* [5]*Endocrinology, Endocrinology in Charlottenburg, Berlin, Germany*

Objective: Data on the social and occupational impact of Cushing's syndrome (CS) remain scarce. In Germany, disability assessment guidelines consider surgically treated patients as "cured," which may fail to capture persistent functional impairment. We assessed work ability, as well as social and employment status, in patients with newly diagnosed and remitted CS.

Methods: This national observational study comprised two arms. Cohort 1 was a monocentric prospective study including patients evaluated for suspected endogenous glucocorticoid excess. Cohort 2 was a multicenter cross-sectional study of patients in remission from CS, comparing individuals with recovered versus persistent adrenal insufficiency. In both cohorts, participants underwent standardised clinical and biochemical evaluations and completed validated questionnaires addressing socioeconomic status, work ability, and fatigue.

Results: In cohort 1, patients with active CS ($n = 28$) and those in whom CS was excluded ($n = 56$) showed similar clinical characteristics, comorbidities, educational levels, and employment status. However, work ability scores were significantly lower in active CS (median 22.5 vs 28.5, $P = .008$) and were inversely associated with the degree of biochemical cortisol excess. In cohort 2 ($n = 89$; 39 with recovered and 50 with persistent adrenal insufficiency), overall employment was 69%. Work ability was frequently classified as "poor" (42% in recovered vs 58% in persistent adrenal insufficiency), and weekly working hours tended to be lower in patients with persistent insufficiency (33 h vs 39 h, $P = .051$). Across cohort 2, 76% reported illness-related absenteeism in the preceding year, 47% had a formally recognised disability, and 15% received a reduced earning capacity pension. Fatigue was strongly and negatively correlated with work ability ($r = -0.73$, $P < .0001$).

Conclusions: Despite high educational attainment, individuals with CS experience considerable occupational impairment, particularly during active disease and persistent adrenal insufficiency. Given that CS predominantly affects young women, a group already subject to occupational gender disparities, this population is especially vulnerable. The mismatch between documented functional limitations and current German disability assessments highlights a structural gap, underscoring the need for targeted rehabilitation and reintegration to improve long-term socioeconomic outcomes.

Abstract citation ID: lvag096.1318

EP1050 - ECE_1598 - A rare case of TSH-secreting pituitary adenoma showing discordant dynamic tests with eventual curative resection

Melvin Kok Seng Lee[1,2]

[1]*Singapore, Singapore;* [2]*Endocrinology, Singapore, Singapore*

Introduction: TSHoma is a rare functioning pituitary tumour that causes hyperthyroidism. This case report highlights the complexity of diagnosing TSHOma through dynamic tests and the eventual successful medical optimization and surgical removal of such a tumour.

Case Report: A 38-year-old woman was noted to have hyperthyroxinemia and high thyroid stimulating hormone on routine health screening. On further questioning, she reported heat intolerance and increased appetite over 1 year. She had regular menses and had no personal or family history of thyroid disorders. She was clinically euthyroid on examination and had no significant goiter. Visual fields were intact on direct confrontation. Her pulse was regular at 92 beats per minute. An electrocardiogram showed normal sinus rhythm. Her thyroid function tests were repeated on a separate assay platform. Free thyroxine and triiodothyronine levels remained elevated at 24 pmol/L (normal 8-16) and 7.6 pmol/L (normal 2.4-6.0) in the presence of elevated thyroid stimulating hormone levels 4.83 mIU/L (normal 0.45-4.50). The alpha subunit to TSH molar ratio was also elevated at 2.3. Further dynamic tests with oral thyroxine suppression over 7 days showed no suppression of TSH consistent with TSHoma. However, thyrotropin stimulation showed a 2-fold rise of TSH which was discordant. MRI pituitary revealed a 1.4 cm × 2.2 cm × 1.4 cm sellar mass with early compression of the optic chiasm. She was given 2 doses of long-acting octreotide over 8 weeks with improvement in free thyroxine levels and normalization of TSH. She subsequently underwent transsphenoidal resection of the pituitary adenoma. Thyroid function tests repeated 2 weeks post-surgery showed normal thyroid function tests with a significantly decreased TSH level of 0.94 mIU/L.

Conclusions: Discordant dynamic tests can be observed in TSHoma and both tests should be interpreted in context. Response to octreotide treatment is a use adjunct for diagnosis and can guide treatment decisions.

Abstract citation ID: lvag096.1319

EP1051 - ECE_2866 - Panhypopituitarism associated with ectopic posterior pituitary presenting as delayed puberty in an adolescent male

Aye Me Me Ko[1,2] and Fiona Smeeton[1]

[1]*Diabetes and endocrinology, Nevill Hall Hospital, Abergavenny, United Kingdom;* [2]*Aneurin Bevan University Health Board, Abergavenny, United Kingdom*

Background: Ectopic posterior pituitary (EPP) is a rare congenital malformation caused by abnormal migration of neurohypophyseal tissue during embryogenesis. It is commonly associated with varying degrees of hypopituitarism. Clinical presentation may be subtle, resulting in delayed diagnosis, particularly in adolescence.

Case Presentation: A 17-year-old male was referred for assessment of delayed puberty and chronic fatigue. He reported a complete lack of energy, muscle aches, back pain, reduced exercise

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

tolerance, and inability to participate in sports. Examination revealed a prepubertal appearance with absent secondary sexual characteristics, puffy hands, and height below the 50th centile. Hormonal evaluation demonstrated panhypopituitarism. IGF-1 was profoundly low at 2 nmol/L. Gonadotropins were suppressed (LH 0.1 IU/L, FSH 0.4 IU/L) with testosterone <0.2 nmol/L. Thyroid function tests showed inappropriately normal TSH of 4.4 mIU/L with low free T4 of 7.9 pmol/L, consistent with secondary hypothyroidism. Random cortisol was 47 nmol/L, and a short Synacthen test confirmed secondary adrenal insufficiency. MRI of the pituitary revealed an ectopic posterior pituitary, identified as a 4-mm T1-hyperintense focus at the median eminence, with absence of the posterior pituitary bright spot in the sella. Bone age was significantly delayed at 12.6 years compared with a chronological age of 16.8 years. The patient was commenced on hormone replacement therapy including prednisolone, levothyroxine, and intramuscular testosterone (Sustanon 250 mg every four weeks), with planned follow-up at six months. Prednisone was chosen by the patient to simplify dosing and improve adherence.

Conclusions: This case illustrates a rare but important cause of delayed puberty and chronic fatigue in adolescence. Recognition of ectopic posterior pituitary and associated hypopituitarism is essential, as early diagnosis and timely hormone replacement can significantly improve growth, pubertal progression, and overall quality of life.

Abstract citation ID: lvag096.1320

EP1053 - ECE_3873 - TSH-secreting pituitary macroadenoma presenting with thyrotoxicosis: a case report

Violeta Hoxha[1], Megi Lekbello[2], Dorina Ylli[1], Klodi Poshi[1], Marjeta Kermaj[2,3], Edenisa Shahinas[2] and Agron Ylli[1]
[1]*University of Medicine Tirana, University Hospital Centre "Mother Teresa", Tirana, Albania;* [2]*University Hospital Centre "Mother Teresa", Tirana, Albania;* [3]*Endocrinology, University Hospital Center "Mother Tereza", Tiranë, Albania*

Background: Thyrotropin-secreting pituitary tumors (TSHomas) are rare causes of hyperthyroidism, accounting for approximately 1% of pituitary adenomas. Increased awareness has led to improved recognition, but early diagnosis remains challenging and is essential to prevent inappropriate treatment and disease progression.

Case Presentation: A 55-year-old woman was admitted with headache, generalized weakness, weight loss, and palpitations. Her medical history included osteoporosis under treatment, gluten intolerance, and a family history of thyroid disease. One year earlier, she had been diagnosed with hypothyroidism and treated with levothyroxine 25 µg daily. Reevaluation one month prior to admission showed persistently elevated thyroid hormone levels with inappropriately high TSH (TSH 11.38 µIU/mL, FT3 7.42 pg/mL, FT4 2.38 ng/dL). Thyroid autoantibodies were negative, excluding autoimmune hyperthyroidism and raising suspicion of a TSH-secreting pituitary adenoma. Pituitary MRI revealed a 22 × 23 × 27 mm macroadenoma with heterogeneous enhancement, extension into the right cavernous sinus, and compression of the optic chiasm. Visual field testing demonstrated partial temporal quadrantanopia in the left eye. Pituitary hormonal evaluation showed hypogonadotropic hypogonadism and mildly elevated prolactin levels, with normal ACTH and cortisol. Antithyroid therapy with methimazole was initiated. The patient underwent transsphenoidal surgical excision on 19 November 2025 without complications. Postoperatively, TSH and thyroid hormone levels normalized, cortisol and growth hormone remained normal, gonadotropins stayed low, prolactin was mildly elevated, and IGF-1 was reduced. The patient was discharged on 27 November 2025.

Conclusions: TSHomas are rare functional pituitary adenomas that may be misdiagnosed as primary thyroid disease. Recognition of central hyperthyroidism and a multidisciplinary diagnostic approach are essential for optimal management.

Abstract citation ID: lvag096.1321

EP1054 - ECE_3987 - Coexistence of Fahr's syndrome and Sheehan's syndrome: a case report of complex metabolic encephalopathy

Raysha Shirley Silva Jordan[1], Luz Marina Medina Puma[2] and Paolo Augusto Romero Merino[3]
[1]*Universidad Nacional de San Antonio Abad del Cusco, Cusco, Peru;* [2]*Hospital Nacional Sergio E. Bernales, Lima, Peru;* [3]*Hospital Clinico Universitario of Valladolid, Valladolid, Spain*

Background and Objective: Fahr syndrome is a rare clinico-radiological condition characterized by bilateral and symmetric calcium deposits in the basal ganglia and other subcortical structures. Its occurrence is commonly associated with endocrine disorders that disrupt calcium metabolism, with hypoparathyroidism and pseudohypoparathyroidism being the most frequently reported causes.[1] Sheehan syndrome, in turn, is a form of hypopituitarism resulting from ischemic necrosis of the adenohypophysis following severe obstetric hemorrhage. Although its incidence has declined in recent decades, it remains an underdiagnosed cause of complex endocrine dysfunction, with clinical manifestations that may go unrecognized for years.[2,3] The relevance of this case lies in the simultaneous presentation of both conditions, in which severe panhypopituitarism and a secondary disorder of mineral metabolism converged to manifest as a neuropsychiatric emergency. This unusual coexistence represents a multiorgan diagnostic challenge that has been scarcely documented in recent literature.

Case Presentation: A 51-year-old woman with a history of hypothyroidism and a severe obstetric hemorrhage occurring 24 years earlier presented to the emergency department with a four-week history of vomiting, abdominal pain, and constipation, which progressed to psychomotor agitation, disorientation, and emotional lability. Initial laboratory investigations revealed severe hypoglycemia, hyponatremia, and hypocalcemia. Non-contrast brain computed tomography demonstrated bilateral calcifications in the basal ganglia (putamen and globus pallidus) and dentate nuclei, confirming the radiological diagnosis of Fahr syndrome. An extended hormonal profile showed decreased levels of TSH, T4, FSH, LH, and cortisol, consistent with panhypopituitarism secondary to Sheehan syndrome. Further evaluation of hypocalcemia revealed elevated parathyroid hormone levels with normal vitamin D concentrations, establishing the diagnosis of pseudohypoparathyroidism type II as the underlying metabolic cause of Fahr syndrome.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: The patient was managed using a multidisciplinary approach, initiating hormone replacement therapy with prednisone and levothyroxine, along with correction of electrolyte disturbances using calcium carbonate and calcitriol. This treatment led to normalization of glucose and electrolyte levels, resolution of neuropsychiatric symptoms, and stabilization of gastrointestinal function. The patient showed favorable clinical evolution and was discharged with follow-up by endocrinology and neurology services.

Conclusions: This case highlights the critical importance of considering endocrine and metabolic causes in the presence of intracranial calcifications. Sheehan syndrome should be suspected in women with a history of postpartum hemorrhage and multisystem involvement, even decades after the initial event. The coexistence of panhypopituitarism due to Sheehan syndrome and secondary Fahr syndrome underscores the need for a multidisciplinary approach to ensure appropriate management of complex neuroendocrine disorders.

Abstract citation ID: lvag096.1322

EP1055 - ECE_1515 - The long-term effect of denosumab on bone mineral density in the treatment of pituitary disease-driven osteoporosis

Alessandra Vicari[1], Sabrina Chiloiro[1], Flavia Costanza[1], Antonella Giampietro[1], Chiara Palumbo[1], Amato Infante[2], Consolato Gullì[2], Mario Rigante[3], Pier Paolo Mattogno[4], Laura De Marinis[1], Antonio Bianchi[1], Francesco Doglietto[4] and Alfredo Pontecorvi[1]

[1]Endocrinologia e Malattie del Metabolismo, Università Cattolica del Sacro Cuore, Policlinico Universitario Agostino Gemelli IRCCS, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy; [2]Radiology, Università Cattolica del Sacro Cuore, Roma, Italy; [3]Dipartimento di Neuroscienze, Organi di Senso e Torace, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy; [4]Neurosurgery, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy

Background: The management of skeletal fragility in patients with pituitary diseases represents a relevant clinical challenge. Treatment with denosumab, an antiresorptive bone active drug, has been shown to significantly increase bone mineral density (BMD) and reduce the incidence and risk of fractures. The long-term efficacy of denosumab has been well demonstrated in primary osteoporosis; however, to date, no studies have been conducted on osteoporosis driven by pituitary disease. The aim of this study was to evaluate the efficacy of denosumab in patients with osteoporosis driven by pituitary disease.

Methods: A retrospective, monocentre, observational cohort study was conducted to investigate the frequency of incident vertebral (i-VFs) and femoral (i-FFs) fractures and the percent BMD changes at 1-, 2-, 5-, and 10-years of treatment with denosumab, in patients with pituitary disease-driven osteoporosis and in patients with primary osteoporosis.

Results: 35 patients with pituitary disease-driven osteoporosis and 35 patients with primary osteoporosis were included in the study. The frequency of i-VFs and i-FFs was similar in both treatment groups at all fixed-term evaluations. Percent BMD changes in the lumbar spine and femur were similar in both treatment groups at all fixed-term evaluations. Among patients with pituitary disease-driven osteoporosis, lumbar spine BMD significantly increased at 2 years and at 5 years of treatment (respectively +6% IQR: 14.3 $P < .001$, and +7.8% IQR: 12.6 $P = .002$); femoral neck BMD significantly improved at 5 and 10 years of treatment (respectively +4.3% IQR: 16 $P < .001$ and 9% IQR: 17, $P = .002$). No drug-related adverse events occurred in both treatment groups.

Conclusions: This study demonstrated for the first time that long-term treatment with denosumab is effective and safe in patients with pituitary disease-driven osteoporosis.

Abstract citation ID: lvag096.1323

EP1056 - ECE_2558 - Reduced circulating humanin in patients with acromegaly and concomitant diabetes

Daniela Dadej, Dorota Filipowicz, Marianna Cemel and Marek Ruchala

Poznan, Poland

Introduction: Diabetes and insulin resistance belong to the most common metabolic complications of acromegaly, resulting from the chronic impact of growth hormone excess on glucose homeostasis. Humanin, a mitochondrial-derived peptide, has been shown to exert insulin-sensitizing properties, enhance insulin secretion and improve pancreatic B-cell viability, potentially delaying the onset of diabetes. However, existing evidence derives predominantly from experimental studies and mechanisms underlying these effects remain unclear. The aim of this study was to assess circulating humanin concentrations in patients with acromegaly in relation to glycaemic status and metabolic parameters.

Material and Methods: A cross-sectional analysis was performed in 122 adults: 42 with active acromegaly, 40 with biochemically controlled acromegaly following surgical or pharmacological treatment, or both, and 40 controls without acromegaly. Anthropometric, biochemical, and clinical data were collected. Humanin concentrations were evaluated using commercially available Elisa kit (Human Putative Humanin Peptide MT-RNR2; Cusabio). Statistical analyses were conducted using PQStat Software v.1.8.6.126. A P-value <.05 was considered statistically significant.

Results: Among the study population, 25 participants had diabetes, 30 had prediabetes, 59 had hypertension, and 67 had dyslipidaemia. Humanin concentrations were significantly lower in acromegalic patients with diabetes compared with those with normoglycaemia, but not with prediabetes (Kruskal–Wallis $P = .01$; Dunn–Bonferroni $P = .03$). In the entire cohort, humanin concentrations correlated inversely with fasting glucose (Spearman r $= -0.20$; $P = .03$). This association, however, was not significant when analyses were limited to patients with acromegaly ($P = .11$). No correlations were observed between humanin and HbA1c ($P = .48$), insulin ($P = .26$) or HOMA-IR ($P = .17$). Humanin concentrations did not differ according to the presence of hypertension ($P = .24$) or dyslipidaemia ($P = .83$) and showed no associations with blood pressure, lipid profile or cardiovascular risk assessed by the SCORE2 model.

Conclusions: Circulating humanin concentrations were reduced in patients with acromegaly and concomitant diabetes, while no associations were observed with other metabolic or

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

cardiovascular parameters. These findings indicate that alterations in humanin concentrations may be primarily related to glycaemic status. Additional studies are required to clarify the underlying mechanisms and determine the diagnostic or prognostic value of humanin in metabolic complications of endocrine disorders.

Abstract citation ID: lvag096.1324

EP1057 - ECE_3083 - Prolactin levels, but not T2-weighted tumor signal, discriminated between non-functioning PitNETs and lactotroph PitNETs

Beatrice Crasta[1,2], Luigi Demarchis[1,2], Sabrina Chiloiro[1,2], Antonella Giampietro[1,2], Pier Paolo Mattogno[2,3], Rosalinda Calandrelli[2,4], Marco Gessi[2,5], Simona Gaudino[2,4], Laura De Marinis[1,2], Antonio Bianchi[1,2], Francesco Doglietto[2,3] and Alfredo Pontecorvi[1,2]
[1]Endocrinology and Metabolism Unit, Department of Medical and Surgical Sciences, Fondazione Policlinico Universitario Agostino Gemelli, Roma, Italy; [2]Università Cattolica del Sacro Cuore, Roma, Italy; [3]Neurosurgery Unit, Department of Neurosciences, Fondazione Policlinico Universitario Agostino Gemelli, Roma, Italy; [4]Radiology and Neuroradiology Unit, Department of Radiological Sciences, Fondazione Policlinico Universitario Agostino Gemelli, Roma, Italy; [5]Pathology Unit of Head and Neck, Lung and Endocrine Systems, Fondazione Policlinico Universitario Agostino Gemelli, Roma, Italy

Introduction: Both prolactin-secreting PitNETs (PRL-PitNETs) and non-functioning PitNETs (NF-PitNETs) can cause different grades of hyperprolactinemia, the first ones by directly producing it, the other ones by compression of the pituitary stalk. This study aimed to investigate the usefulness of biochemical and radiological features in differentiating between non-functioning PitNETs and secreting lactotroph Pit-NETs.

Patients and Methods: 166 patients with clinical suspicion of NF-PitNET or PRL-PitNET and histological confirmation were included in the study. For all patients were collected prolactin levels at diagnosis, tumor volume and consistency, ratio between MRI-based T2-weighted tumor signal and T2-weighted white matter intensity.

Results: 143 NF-PitNETs and 23 PRL-PitNETs were included in the study. 16 cases were microPitNETs (8 NF-PitNETs, 8 PRL-PitNETs) and 150 were macro-PitNETs (135 NF-PitNETs, 15 PRL-PitNETs). Tumor consistency was cystic in 47 cases (39 NF-PitNETs, 8 PRL-PitNETs) and solid in 119 cases (104 NF-PitNETs; 15 PRL-PitNETs). As T2-ratio significantly differed between cystic and solid PitNETs ($P < .001$), we separately analyzed the two groups. Among cystic PitNETs, T2-ratio didn't differ in NF-PitNETs and PRL-PitNETs, both micro- ($P = .2$) and macro-PitNETs ($P = .248$); instead, prolactin levels were significantly higher in PRL-PitNETs than in NF-PitNETs, both micro- (respectively, 500 ng/mL SD: 125 and 28.7 ng/mL SD: 25 $P < .001$) and macro-PitNETs (respectively, 428 ng/mL SD: 321 and 28.2 ng/mL SD: 25 $P < .001$). Likewise, among solid PitNETs, T2-ratio didn't differ in NF-PitNETs and PRL-PitNETs, both micro- ($P = .977$) and macro-PitNETs ($P = .243$); instead, prolactin levels were significantly higher in PRL-PitNETs than in NF-PitNETs, both micro- (respectively 162 ng/mL SD: 91 and 21 ng/mL SD: 24 $P = .003$) and macro-PitNETs (respectively 195 ng/mL SD: 428 and 20 ng/mL SD: 193 $P < .001$).

Discussion: In this study, serum prolactin levels confirmed their reliability as a biochemical marker in distinguishing PRL-PitNETs from NF-PitNETs, independently of tumor size or consistency. Conversely, MRI-based T2-weighted signal ratios didn't help differentiate the secretory status, highlighting the limited diagnostic role of conventional MRI features. Advanced MRI modalities (such as radiomics, DWI, susceptibility imaging, and molecular imaging) could further improve diagnostic accuracy by providing quantitative, microstructural, and functional data beyond standard imaging and serum prolactin levels.

Conclusions: Prolactin levels at diagnosis, but not T2-weighted tumor signal, predict the diagnosis of secreting lactotroph tumors rather than non-functioning PitNETs.

Abstract citation ID: lvag096.1325

EP1058 - ECE_3304 - Long-term treatment patterns and biochemical control rates in patients with acromegaly: a 5-year landmark analysis from a large tertiary pituitary center

Jon Rasmussen, Mathilde Damm, Amanda Sørensen, Yeliz Bulut, Mikkel Andreassen and Caroline Kistorp
Department of Nephrology and Endocrinology, Rigshospitalet, København Ø, Denmark

Objective: To describe treatment strategies and biochemical control rates in patients with acromegaly five years after diagnosis at a tertiary pituitary centre, and further to evaluate whether patient outcomes are in accordance with standard of care of the Pituitary Tumor Centers of Excellence (PTCOE).

Methods: A retrospective cohort study from Copenhagen University Hospital, Rigshospitalet including patients diagnosed with acromegaly between January 1, 2000, and November 30, 2025. Data was recorded from patient electronic records. Baseline characteristics included age, sex, maximal pituitary adenoma diameter, and serum IGF-1 values (absolute and SD scores). During five years following the diagnosis, treatment modalities, pituitary surgery, use of medical therapy (somatostatin analogues [SSA], pegvisomant [PEGV], cabergoline, pasireotide, and combination regimens), and radiotherapy, were recorded. Biochemical control was defined as serum IGF-1 $\leq$2 SD.

Results: A total of 176 patients with acromegaly are followed in our specialized outpatient clinic. Mean (SD) age at diagnosis was 51 (14) years, and 52% were women. Of these, 104 patients were eligible for five-year evaluation; 45 patients (26%) had insufficient follow-up duration, and 27 (15%) were excluded due to missing data. At five years from diagnosis, 80 (77%) of acromegaly patients were on medical therapy, whereas 24 (23%) were only treated with pituitary surgery of the GH secreting adenoma. A minor part, 14 (13%), of the patients were on medical therapy, without prior surgery. In 15 (14%) patients, radiotherapy was used after surgery and medical therapy. Overall, biochemical control at five years was achieved in 84% of patients and did not differ significantly between treatment groups, $P = .259$, but control rates were numerically highest in the surgery-only group (96%) and lowest in the multimodality treated group (73%). In patients treated with pituitary surgery alone ($n = 24$), 5-year remission rates were similar for macroadenomas and microadenomas, $P = 1.00$. Among patients receiving medical therapy at five years from baseline, 59% were treated with SSA monotherapy

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and 30% with combined SSA and PEGV. Biochemical control was achieved in 89% of patients treated with SSA monotherapy.

Conclusions: Treatment patterns and biochemical control rates five years after diagnosis in acromegaly patients at our centre are consistent with PTCOE standard of care and with their reported patient outcomes.

Abstract citation ID: lvag096.1326

EP1059 - ECE_3459 - Non-invasive evaluation of hepatic steatosis in active versus biochemically controlled acromegaly

Hamza El Hadi, Maximilian Brol, Eric Suero Molina, Walter Stummer, Jonel Trebicka and Elena Vorona
Münster University Hospital, Münster, Germany

Introduction: Growth hormone (GH) and insulin-like growth factor-1 (IGF-1) exert important physiological effects on hepatic lipid metabolism and suppress intrahepatic profibrotic pathways. The impact of disease activity in acromegaly on hepatic steatosis, however, remains incompletely understood. This study aimed to non-invasively evaluate the relationship between acromegaly disease activity and hepatic steatosis and fibrosis.

Materials and Methods: Hepatic steatosis and fibrosis were assessed using transient elastography (FibroScan Mini 430), measuring the controlled attenuation parameter (CAP) and liver stiffness (LSM), respectively. 33 patients with acromegaly (12 with active disease and 21 in biochemical remission) followed at our endocrinology outpatient clinic at University Hospital in Münster between March and December 2025 were enrolled. All patients had undergone prior transsphenoidal surgical resection of GH-secreting pituitary adenomas. Fat mass index (FMI) was assessed non-invasively using bioelectrical impedance analysis (BIA).

Results: Patients with active disease and those in biochemical remission did not differ significantly in terms of age, sex distribution, body mass index (BMI), LDL cholesterol/triglycerid levels, or the prevalence of diabetes mellitus, hypertension, obstructive sleep apnea, or cardiovascular disease. Although not statistically significant, patients with biochemically controlled acromegaly exhibited a higher FMI. CAP values, reflecting hepatic steatosis, were significantly lower in patients with active acromegaly compared to those with biochemically controlled disease (227 ± 37 vs 261 ± 55 mmol/L, $P < .05$ respectively). No significant difference in LSM values was observed between the two groups. CAP scores showed positive correlations with age ($r = 0.49$, $P = .002$), BMI ($r = 0.53$, $P = .001$), body weight ($r = 0.44$, $P = .01$), and hepatic steatosis index (HSI) ($r = 0.63$, $P < .001$), while a negative correlation was identified between CAP score and GH levels ($\rho = -0.48$, $P = .005$).

Conclusions: Our findings demonstrate that patients with active acromegaly exhibit lower non-invasive markers of hepatic steatosis compared with those in biochemical remission, supporting a protective role of the GH–IGF-1 axis against hepatic fat accumulation. The absence of significant differences in overall body composition highlights the need for further studies to clarify the mechanisms by which GH and IGF-1 influence hepatic lipid metabolism.

Abstract citation ID: lvag096.1327

EP1060 - ECE_3613 - Proteins of the neutrophil degranulation pathway may regulate invasiveness and proliferation in somatotroph tumors

Sabrina Chiloiro[1,2], Luigi Demarchis[1,2], Pier Paolo Mattogno[2], Michela Cicchinelli[1], Federico Valeri[2], Flavia Angelini[1,2], Antonella Giampietro[1,2], Domenico Milardi[1,2], Quintino Giorgio De Alessandris[1,2], Laura De Marinis[1,2], Andrea Urbani[1,2], Alfredo Pontecorvi[1,2], Francesco Doglietto[1,2], Antonio Bianchi[1,2] and Federica Iavarone[1]
[1]School of Medicine and Surgery, Università Cattolica del Sacro Cuore, Rome, Italy; [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Introduction: The tumor microenvironment is composed of non-tumor cells, blood vessels, extracellular matrix and soluble factors, and generates a complex network with tumor cells, regulating tumor proliferation, invasiveness, and response to medical therapies.

Patients and Methods: A liquid chromatography-mass spectrometry was conducted on samples of somatotroph pituitary tumor (after processing and digestion of the sample) to identify and assay the expression of proteins involved in immune system pathways. The differential expression of identified proteins was compared and investigated according to the tumor pattern of growth, tumor proliferation, and persistence of post-surgery tumor residual. Biological functions were investigated for proteins that were found differentially expressed, with a ratio of variation based on Fold-Change (FC) > |1.50| and statistical significance (*P*-value <.05).

Results: Eleven patients with acromegaly were included. Seven patients were females (63.6%). Mean age at diagnosis was 45 years (SD:18). Mean serum GH levels at diagnosis were 10.5 ng/mL (SD:9.3), and mean IGF-I levels were $2.6 \times$ ULN (SD:0.8). Ten patients carried a tumor >1 cm (90.9%). An invasive growth was identified in 5 tumours with an invasion of the cavernous sinus (45.4%). Ten patients were diagnosed with a sparsely granulated somatotroph tumor (90.9%). Two tumors (18.2%) were proliferative, according to Ki-67 and p53 expressions and the number of mitoses. Six patients (54.5%) underwent curative surgery, and five patients (45.4%) required adjuvant treatment with first-generation somatostatin analogues. In this cohort, a total of 590 proteins were identified. A total of 10 proteins (mainly involved in the neutrophil degranulation pathway) were differently expressed, comparing groups of somatotroph tumors based on established criteria. The proteins 26S proteasome non-ATPase regulatory subunit 3 and mitochondrial antiviral-signaling protein were more expressed in invasive tumors than in non-invasive ones. The proteins phosphoglucomutase-2, keratin, adenylyl cyclase-associated protein 1, and guanylate-binding protein 1 were significantly more expressed in proliferative somatotroph tumors than in non-proliferative ones. The proteins alpha-1-antichymotrypsin, clusterin, phosphoglucomutase-2, glutathione S-transferase omega-1, prosaposin, keratin, and the guanylate-binding protein 1 were significantly more expressed in tumours that underwent radical surgery than in patients carrying a residual disease.

Conclusions: Our results provided that specific proteins involved in the neutrophil degranulation pathway may impact

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

somatotroph tumor behaviour, in terms of invasive growth and proliferation, and consequently surgical outcome.

Abstract citation ID: lvag096.1328

EP1061 - ECE_3807 - Incidence of acromegaly a nationwide study through 11 years in Iceland

Iðunn Valgerður Pétursdóttir[1] and Helga Sigurjónsdóttir[1,2]
[1]Department of Medicine, Landspítali University Hospital, Reykjavík, Iceland; [2]School of Medicine, University of Iceland, Reykjavík, Iceland

Background: A study on the incidence and prevalence of Acromegaly in Iceland from 1955 through 2013 found the incidence to be higher than anticipated compared to studies from other countries. Therefore, we were interested in conducting a similar study for the following 11 years, from 2014 through 2024.

Methods: In a retrospective study, results on patients diagnosed with Acromegaly during the years 2014-2024 were sampled from electronic medical records at Landspitali University Hospital (LUH), Reykjavik, Iceland. LUH is the only tertiary hospital in Iceland housing the only Neurosurgery Department. All work up and diagnosis of Acromegaly in Iceland is performed at the Department of Endocrinology at LUH. The number of patients diagnosed with Acromegaly in Iceland is therefore found in the medical records of LUH. This is thus a nationwide study. Patients diagnosed in Iceland during the study period were included. Two of the patients had immigrated to Iceland after the diagnosis abroad before the year 2014. They were included in the study as they recieved all their treatment in Iceland during the study period.

Results: Sixteen patients (10 men) were diagnosed with the average age of 50.8 years ± 18.8 years. Two patients died during the study period. Most patients had experienced symptoms for 2 years or less before diagnosis, however two patients had experienced symptoms for up to 10-20 years before the diagnosis.

Conclusions: The incidence of Acromegaly in Iceland during the years 2014-2024 was 4.1 patients per million per year. These results are lower than previously reported from Iceland and more in line with the incidence of Acromegaly in other countries.

Abstract citation ID: lvag096.1329

EP1062 - ECE_3812 - From resistance to response: pasireotide efficacy in previously treated acromegaly patients—a real-world analysis

Iulia Florentina Burcea[1,2], Dobre Ramona[1,2], Ioana Postelnicu[2], Căpăţînă Cristina[1,2], Simona Galoiu[1,2], Ionela Baciu[1,2], Serban Radian[1,2], Raluca Trifanescu[1,2], Nicoleta Baculescu[1,2] and Catalina Poiana[1,2]
[1]Department I, "C. I. Parhon" National Institute of Endocrinology, Bucharest, Romania; [2]Endocrinology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Introduction: Pasireotide LAR (PAS) is a second-line therapy for acromegaly in patients inadequately controlled with first-generation somatostatin receptor ligands (fgSRLs) ± growth hormone (GH) receptor antagonist ± dopamine agonist. This study evaluates PAS efficacy in previously treated patients from a single tertiary center.

Methods: We retrospectively analyzed 30 patients (66.7% female, mean age 37.9 ± 12.8 years) previously treated with other medical therapy, surgery, radiotherapy. All tumors measured >10 mm at diagnosis. We collected biochemical data: GH, insulin-like growth factor-1 (IGF-1), tumor dimensions from imaging, glycemic parameters: fasting plasma glucose (FPG), glycated hemoglobin (HbA1c) and body mass index (BMI). The mean treatment duration with PAS was 44.6 ± 31.9 months. The mean baseline BMI was 29.08 ± 4.82 kg/m^2, indicating a predominantly overweight cohort.

Results: Early Biochemical Response: PAS demonstrated rapid efficacy. At 3 months, mean GH decreased by 57.9% (from 4.28 to 1.80 ng/mL) and IGF-1 decreased by 30.3%, from 1.65 to 1.15 × Upper limit of normal (ULN). Biochemical control was achieved in 41.4% of patients at 3 months. **Progressive Improvement:** At 6 months, control improved to 54.2%. By last follow-up (>6 months), mean GH was 1.54 ± 1.48 ng/mL (64% reduction) and IGF-1 normalized to 0.96 ± 0.44 × ULN (41.8% reduction), with 64.3% achieving control. Prior therapy duration did not correlate with GH or IGF-1 reduction at any timepoint ($P < .05$), indicating PAS efficacy is independent of prior treatment history. Patients with longer prior therapy (>6 years) showed numerically higher biochemical control rates at 3 months (58.3% vs 29.4%), suggesting extensive prior treatment does not impair PAS response. **Tumor Volume:** Mean tumor diameter decreased from 16.9 ± 10.0 mm to 15.1 ± 9.8 mm. Significant shrinkage (≥20%) occurred in 33.3% of patients, with 60% stable and 6.7% progressive. **Glycemic Profile:** Mean FPG increased from 100.5 ± 18.0 to 118.0 ± 29.1 mg/dL; mean HbA1c rose from 5.91 ± 0.88% to 6.54 ± 0.98%. Diabetes prevalence increased from 6 to 10 patients.

Conclusions: Pasireotide LAR demonstrates significant efficacy in achieving biochemical control and tumor shrinkage in previously treated acromegaly patients. Importantly, PAS efficacy is independent of prior therapy duration—patients treated for extended periods respond as well as those with shorter histories. While secretory and morphological responses are favorable, treatment is associated with worsening glycemic control, requiring careful metabolic monitoring.

Abstract citation ID: lvag096.1330

EP1063 - ECE_1347 - Somapacitan in Japanese adults with growth hormone deficiency: an interim analysis of post-marketing surveillance

Fumio Otsuka[1], Hidenori Fukuoka[2], Shigeyuki Tahara[3], Shingo Fujio[4], Takaaki Endo[5], Michael Højby[6], Anne Helene Olsen[7], Beverly M.K. Biller[8] and Gudmundur Johannsson[9,10]
[1]Dentistry and Pharmaceutical Sciences, Department of General Medicine, Okayama University Graduate School of Medicine, Okayama, Japan; [2]Division of Diabetes and Endocrinology, Department of Internal Medicine, Kobe University Hospital, Kobe, Japan; [3]Department of Neurological Surgery, Nippon Medical School, Musashikosugi Hospital, Kanagawa, Japan; [4]Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan; [5]Medical Affairs Department, Novo Nordisk Pharma Ltd., Tokyo, Japan; [6]Medical & Translational Science, Novo Nordisk A/S, Søborg, Denmark; [7]R&D Real World Evidence, Novo Nordisk A/S, Søborg, Denmark; [8]Neuroendocrine & Pituitary Tumor Clinical Center, Massachusetts General Hospital, Boston, MA, United States; [9]Sahlgrenska University

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Hospital, Department of Endocrinology, Gothenburg, Sweden; [10]*Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*

Introduction: Somapacitan is approved for the treatment of adult growth hormone (GH) deficiency (AGHD) yet real-world reports in this population remain limited. We report interim results from a post-marketing study of Japanese patients (pts) with AGHD treated with somapacitan.

Methods: Eligible pts had AGHD, had not previously enrolled in the study and had no safety contraindications. Pts exposed to somapacitan comprised the safety analysis set (SAS) and were analysed according to treatment status at enrolment (GH-naïve or switched [SW] from another GH product within 180 days of registration). Primary endpoint was incidence of adverse events (AEs), including serious AEs (SAEs), adverse reactions (ARs) and serious ARs (SARs).

Results: At data cutoff (16 January 2025) 223 pts had enrolled in the study, of whom 53 with complete case report forms comprised the SAS (23 GH-naïve; 30 SW). Pts were female (54.7%) and male (45.3%); mean (standard deviation [SD]) age was 54.3 (15.0) years and mean (SD) insulin-like growth factor-I SD score was −3.2 (2.9) and −0.7 (1.8) for GH-naïve and SW pts, respectively. Mean weekly somapacitan dose was 1.3 and 1.5 mg/week at baseline, 1.8 and 2.3 mg/week at 1 year, and 1.5 and 1.7 mg/week at 2 years in GH-naïve and SW pts, respectively. Most pts missed ≤1 somapacitan dose every 2 months at 1 year (22/23 [95.7%] GH-naïve and 30/30 [100.0%] SW) and 2 years (5/5 [100%] and 8/9 [88.9%], respectively). One GH-naïve patient missed >1-<3 doses per 2 months after 1 year versus no SW pts. Seven AEs were reported by 5 pts (headache; brain fog; arthralgia; injection site pain and malaise); of these, six were ARs in 4 pts. No SAEs or SARs occurred.

Conclusions: Somapacitan is a valid treatment option for Japanese pts with AGHD, with real-world data showing good treatment adherence and a safety profile in agreement with that previously seen in clinical trials.

Abstract citation ID: lvag096.1331

EP1064 - ECE_2090 - Neurophysin-I, a surrogate biomarker of oxytocin, and cortisol interaction during psychological stress

Andi Nikaj[1,2], Elin Broman[1,2], Cihan Atila[1,2], Joachim Heuberger[1,2], Carla Walti[1,2], Judith Siegenthaler[1,2], Sandrine A. Urwyler[1,2], Deborah Rudin[3], Dino Lüthi[3], Schuetz Philipp[4] and Mirjam Christ-Crain[1,2]

[1]*Departments of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland;* [2]*Department of Clinical Research, University Hospital Basel, Basel, Switzerland;* [3]*Clinical Pharmacology and Toxicology, Department of Biomedicine and Department of Clinical Research, University Hospital Basel, Basel, Switzerland;* [4]*Department of Internal Medicine, Kantonsspital Aarau, Aarau, Switzerland*

Background: Oxytocin (OXT) is a neuropeptide that is synthesised in the hypothalamic paraventricular and supraoptic nuclei and released into circulation from the posterior pituitary. Among others, OXT is involved in psychological and socio-behavioural processes. Beyond its known role in these processes, evidence from both animal and human studies suggests that OXT might also regulate neuroendocrine stress responses within the central nervous system. OXT is thought to suppress the stress-induced activation of the hypothalamic-pituitary-adrenal (HPA) axis by exerting an inhibitory effect on cortisol secretion.

Design: This is a secondary analysis of a prospective observational study, which was conducted to investigate the relationship between copeptin concentration and psychological stress.

Methods: Twenty healthy adults (ten female) underwent the Trier Social Stress Test (TSST) which included a 30-minute waiting period, a 10-minute anticipation period, a 10-minute test period, and a 40-minute recovery period. For this analysis, plasma Neurophysin-I (NP-I), a surrogate biomarker of OXT, and plasma cortisol were measured at baseline (T0), 20 minutes (ie, right after the stress, T1) and 40 minutes (ie, 20 minutes into recovery, T2).

Results: At T0, median (IQR) NP-I levels were 1237 pg/mL (693, 3143), decreasing to 1166 pg/mL (767, 3360) at T1. At T2, NP-I levels increased again to 1199 pg/mL (717, 3063). Median cortisol levels were 435 nmol/L (385, 547) before psychological stress (T0) and peaked at 529 nmol/L (494, 701) at T1. At T2, cortisol levels decreased again to 507 nmol/L (438, 632). Linear mixed-effects model analysis revealed that in healthy individuals, higher NP-I levels measured at both T1 ($P = .004$) and T2 ($P < .001$) were associated with lower plasma cortisol concentrations compared to T0.

Conclusions: In healthy volunteers, higher NP-I levels were associated with a blunted cortisol response to psychological stress, suggesting a cortisol-buffering effect of NP-I mirroring OXT. These findings support the idea of an inverse relationship between NP-I concentrations and cortisol responses over time following stress exposure.

Abstract citation ID: lvag096.1332

EP1066 - ECE_2469 - Not all empty sella are the same: baseline clinical and endocrine differences between primary and secondary empty sella

Vanessa Caccin[1], Francesca Paglia[1], Nicolò Bacchi[1], Gianluca Margiotta[2], Chiara Diazzi[3], Bruno Madeo[3], Maria Chiara Decaroli[1], Maria Laura Monzani[1], Sara De Vincentis[1] and Vincenzo Rochira[1]

[1]*Department of Biomedical, Metabolic and Neurosciences, Endocrinology Unit, University of Modena and Reggio Emilia, Modena, Italy;* [2]*Local Health Authority (ASL) CN1, Cuneo, Italy;* [3]*Modena, Italy*

Background: Empty Sella (ES) is a neuroradiological condition characterized by partial or complete occupation of the sella turcica by cerebrospinal fluid, resulting in compression of the pituitary gland. Primary (PES) and Secondary ES (SES) share similar neuroradiological appearances but originate from different pathophysiological mechanisms. The clinical and endocrine implications of these differences at baseline have not been systematically evaluated in large cohorts.

Methods: We retrospectively evaluated 258 adult patients with ES followed at a tertiary endocrinology center between 2007 and 2025. Demographic characteristics, clinical presentation, MRI findings, comorbidities, and comprehensive pituitary

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hormonal assessments were collected at diagnosis. ES was classified as PES or SES based on clinical history. Determinants of pituitary dysfunction severity were explored using ordinal logistic regression.

Results: In the overall cohort (64.3% women; median age 51.5 years; median follow-up 58.5 months), PES was more prevalent than SES (61.6% vs 38.4%). At presentation, ES was incidentally detected more frequently in PES (66%), whereas SES was diagnosed mainly following clinical suspicion (87.9%) ($P < .001$). While headache was the most frequent symptom overall, visual field defects were significantly more common in SES than PES ($P = .021$), highlighting a more overt clinical presentation. Radiological grade (partial vs complete ES) did not differ between groups and was not associated with endocrine burden. Striking differences emerged at endocrine evaluation. At baseline, 41.1% of patients had at least one pituitary hormone deficiency, significantly more frequent in SES than PES (62.6% vs 27.7%, $P < .001$), with gonadotropic deficiency the most common alteration. SES was characterized by a significantly higher prevalence of multiple pituitary deficiencies, involving the gonadotropic, corticotropic, thyrotropic, and GH axes (all $P < .001$). Complete anterior hypopituitarism and arginine vasopressin deficiency were observed exclusively in SES ($P < .001$). In contrast, preserved pituitary function predominated in PES (72.3%). At ordinal logistic regression analysis, male sex ($P = .002$), secondary ES ($P = .006$), clinically driven diagnosis ($P = .030$), and older age at both diagnosis ($P = .010$) and first evaluation ($P = .017$) independently predicted a higher burden of pituitary hormone deficiencies.

Conclusions: Despite similar imaging features, PES and SES display profoundly different baseline endocrine and clinical profiles. SES is associated with a significantly higher and more complex pituitary dysfunction at diagnosis, while PES is largely characterized by preserved hormonal function. These findings emphasize that ES should not be considered a single entity and support systematic endocrine evaluation in all patients, with particular attention to secondary forms.

Abstract citation ID: lvag096.1333

EP1067 - ECE_2795 - Changes in cognitive and psychological functioning in patients with prolactinoma after treatment

Iris Pelsma, Willem Verbeek, Victoria van Trigt, Leontine Bakker, Cornelie Andela and Nienke Biermasz
Endocrinology, Leiden University Medical Center, Leiden, The Netherlands

Objective: To examine the reversibility of cognitive impairment and psychological complaints in patients with prolactinomas following treatment and subsequent biochemical control.

Methods: Sixteen patients, among whom 13 (81.3%) females, with active hyperprolactinemia and without any comorbidities potentitally affecting cognition (depressive disorders, anxiety disorders, subtracne abuse) were included. In this prospective longitudinal study, 16 patients, underwent comprehensive neuropsychological assessment (8 cognitive tests and 7 validated questionnaires) at baseline. All 16 patients were re-evaluated after a mean of 19.8 months of follow-up.

Results: Following biochemical remission, significant improvements were observed in delayed verbal memory (Rey 15-words delayed recall: 11.0 ± 2.5 vs 12.3 ± 2.7, $P = .004$) and executive functioning, specifically planning (D-KEFS Tower Test: 10.8 ± 2.9 vs 12.9 ± 2.6, $P < .001$) and cognitive flexibility (TMT-B 59.5[49.3 − 71.5] vs 47.4[40.3 − 60.0] sec, $P = .011$). Also, selective attention errors (Digit Deletion Test) decreased significantly (3.5[2.0-5.0] vs 1.0[0.0-3.8]), $P = .014$). Disease-specific quality of life improved significantly at both burden (LBNQ-Bothers: 22.4[10.8-33.5] vs 13.4[5.3-15.9], $P = .001$) and care needs (LBNQ-Needs: 23.5[7.8-36.6] vs 13.9[1.5-23.5], $P < .001$). Furthermore, reductions were seen in fatigue (FSS: 41.4 ± 14.8 vs 31.3 ± 15.5, $P = .026$) and depressive symptoms (HADS-D: 5.5[2.0-7.8] vs 1.0[1.0-7.0], $P = .013$). Higher baseline prolactin levels were associated with less improvement in verbal memory (immediate learning phase, Verbal Learning Test of Rey: $r_S = -0.58$, $P = .019$).

Conclusions: Cognitive deficits in prolactinoma patients are largely reversible state-dependent impairments that resolve significantly upon biochemical control. While substantial recovery occurs in memory and executive functioning, severe baseline hyperprolactinemia may reduce the recovery trajectory of immediate verbal memory.

Abstract citation ID: lvag096.1334

EP1068 - ECE_3253 - Evaluation of endocrinological disorders in pediatric patients with empty sella

Eda Boz Öncel[1], Çiğdem Öztunalı[2], Coşkun Yarar[3] and Birgul Kirel[4,5]
[1]*Pediatrics, Eskişehir Osmangazi University Faculty of Medicine, Eskişehir, Türkiye;* [2]*Radiology, Eskisehir Osmangazi Univercity Faculty of Medicine, Eskişehir, Türkiye;* [3]*Pediatric Norology, Eskisehir Osmangazi Univercity Faculty of Medicine, Eskişehir, Türkiye;* [4]*Pediatric Endocrinology, Eskisehir Osmangazi Univercity Faculty of Medicine, Eskişehir, Türkiye;* [5]*Pediatric Endocrinology, Eskisehir Osmangazi University Hospital, Eskisehir, Türkiye*

Background: Empty sella (ES) is an anatomical condition resulting from herniation of the subarachnoid space into the sella turcica, leading to cerebrospinal fluid filling and flattening of the pituitary gland. Endocrinological abnormalities are frequently reported in pediatric patients with ES, even in those without clinical symptoms.

Objective: To evaluate the clinical, radiological, and endocrinological characteristics of pediatric patients diagnosed with empty sella and to investigate the relationship between pituitary morphology and hormonal dysfunction.

Methods: A retrospective analysis was performed in 56 patients (24 females, 32 males) aged 6 months to 17 years with radiologically confirmed ES. Pituitary anatomy, etiology, classification, and endocrine findings were reviewed. Hormonal profiles were assessed for isolated and multiple pituitary hormone deficiencies. The association between pituitary height and the presence of multiple hormone deficiencies was analyzed.

Results: Isolated pituitary hormone deficiencies included growth hormone deficiency in 10 patients, isolated hypothyroidism in 1, hyperprolactinemia in 8, and hypogonadism in 2. Multiple pituitary hormone deficiencies were detected in 19.6% of cases. A significant correlation was observed between decreased pituitary height and the presence of multiple pituitary hormone deficiencies ($r = 0.654$, $P = .001$). Empty sella was incidentally detected in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

38 patients (68%); however, 20 of these had hormonal abnormalities at diagnosis, and 7 developed hypopituitarism (hypothyroidism, hypogonadism, or precocious puberty) during follow-up.

Conclusions: Pediatric patients with empty sella, including those who are asymptomatic, should undergo comprehensive endocrine evaluation at diagnosis. Regular long-term follow-up is essential for early detection and management of evolving pituitary hormone deficiencies.

Abstract citation ID: lvag096.1335

EP1069 - ECE_3591 - Effects of prolactin insufficiency in a monocentric cohort of patients

Francesco Padovano Sorrentino[1,2], Antonella Giampietro[1,2], Paola Pagano[2], Pier Paolo Mattogno[2,3], Liverana Lauretti[2,3], Francesco Doglietto[2,3], Laura De Marinis[1,2], Antonio Bianchi[1,2], Sabrina Chiloiro[1,2] and Alfredo Pontecorvi[1,2]

[1]Endocrinology, Diabetology, and Internal Medicine, Fondazione Policlinico Agostino Gemelli (IRCCS), Rome, Italy; [2]Catholic University of the Sacred Heart (UCSC), Rome, Italy; [3]Neurosurgery, Fondazione Policlinico Agostino Gemelli (IRCCS), Rome, Italy

Introduction: Prolactin's functions in the human body are not fully understood. Therefore, the impact of the prolactin insufficiency is often overlooked in people with hypopituitarism. We present the preliminary data of our study on the pleiotropic effects of prolactin insufficiency.

Materials and Methods: A retrospective monocentric study was conducted on patients attending our clinic between the 2021 and 2024. Prolactin insufficiency (PRL-insufficiency) was defined for serum prolactin <3 ng/mL. Prolactin deficiency (PRL-deficiency) was defined for serum prolactin <5 ng/mL. For the control group we considered patient with serum prolactin within the normal range.

Results: The study group consists of 101 patients (55 males, 46 females), 31 with PRL-insufficiency, 40 with PRL-deficiency and 30 controls. They suffered from non-secreting macroadenoma (55 patients), non-secreting microadenoma (6 patient), Rathke's cleft cyst (5 patients), craniopharyngioma (11 patients), hypophysitis (5 patients), primary empty sella (11 patients) and other sellar tumors (8 patients). PRL-insufficiency and PRL-deficiency are both associated with a higher prevalence of hypopituitarism ($P < .001$; $P = .018$) and male sex ($P = .001$; $P = .045$). PRL-insufficiency is individually associated with a larger prevalence of secondary hypoadrenalism ($P < .001$), secondary hypothyroidism ($P < .001$), GH-deficiency ($P < .001$) and secondary hypogonadism ($P < .001$). Furthermore, patients with PRL-insufficiency were younger than patients with PRL-deficiency ($P < .001$) and showed a lower prevalence of primary hypertension (PH) ($P = .006$) and a better bone mineral density (BMD) on the hip ($P = .04$). No significant differences were found between the two study groups and controls regarding age, body mass index, BMD, prevalence of diabetes mellitus, dyslipidaemia, cardiovascular and cerebrovascular diseases or primary hypertension.

Conclusions: Patients with PRL-insufficiency tend to be younger, suggesting a more impactful disease and a greater pituitary damage. This data can also explain our findings regarding PH, even though there are some studies showing positive correlation between PRL levels and endothelial disfunction, whilst our results on the BMD seems to be in contrast with the literature. Our study shows that PRL-insufficiency is often associated with other pituitary deficiencies and should be evaluated not individually, but as a whole with patients' hormonal picture.

Abstract citation ID: lvag096.1336

EP1070 - ECE_3935 - Investigation of lower extremity venous Doppler ultrasound parameters in patients with acromegaly

Simge Saydam[1], Fatma Zulal Ozek[1], Zeynep Elüstü Belten[1], Ozge Sahin Kimyon[1], Hasan Toz[2], Hayriye Gulsah Ozkan[3], Suna Nur Gündoğan[3], Hamide Piskinpasa[1], Meral Mert[1] and Sema Ciftci[1]

[1]Endocrinology and Metabolism Clinic, Department of Endocrinology and Metabolism, Sağlık Bilimleri Üniversitesi Bakırköy Doktor Sadi Konuk Eğitim Ve Araştırma Hastan, Bakırköy, Türkiye; [2]Cardiovascular Surgery, Bakırköy Sadi Konuk Hastanesi Onkoloji Merkezi, Istanbul, Türkiye; [3]Radiology, Sağlık Bilimleri Üniversitesi Bakırköy Doktor Sadi Konuk Eğitim Ve Araştırma Hastan, Bakırköy, Türkiye

Background: Acromegaly is a chronic disease characterized by excess growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Although the effects of GH and IGF-1 on structural changes in tissues are well-documented, the specific implications of this hormonal excess for the venous system have not been sufficiently investigated in the literature. This study aims to evaluate lower extremity venous Doppler ultrasonography findings in patients with acromegaly and to examine the relationship between venous structural changes and clinical parameters.

Methods: The study included 50 acromegaly patients followed in our clinic. Color Doppler ultrasonography (CDUS) was performed to measure the diameters of the Vena Saphena Magna (VSM) and Vena Saphena Parva (VSP) in all patients, and the presence of venous reflux was assessed. The CDUS data were analyzed in relation to age, gender, body mass index (BMI), mean disease duration (calculated from symptom onset), biochemical remission status (post-surgery or medical treatment), and somatostatin receptor ligand (SRL) use.

Results: The study population consisted of 50 patients (25 women, 25 men) with a mean age of 52.7 ± 11.6 years and mean disease duration of 10.4 ± 6.3 years. Venous reflux was detected in 64% ($n = 32$) of the patients. Among those with reflux, 68.9% ($n = 22$) exhibited "grade 4" reflux. Regarding vessel diameters, 27 patients (54%) had a VSM diameter >5 mm and 22 patients (44%) had a VSP diameter >2.5 mm. The groups with ($n = 32$) and without ($n = 18$) venous reflux showed no significant differences regarding age, gender, BMI, mean disease duration, SRL use, or remission status ($P > .05$). Correlation analysis revealed that VSM diameter was significantly associated with mean disease duration ($r = 0.29$; $P = .044$) and BMI ($r = 0.43$; $P = .003$). In contrast, VSP diameter was independant of age, gender, BMI, mean disease duration, remission status, or SRL use ($P > .05$).

Conclusions: Our study demonstrated a high prevalence of venous reflux in acromegaly, independent of classic risk factors (age, gender, and BMI), with the majority of these cases

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

exhibiting advanced (Grade 4) reflux. The finding that venous damage and increased vessel diameters are not affected by biochemical remission or medical treatment suggests that structural changes in the venous system in acromegaly may represent a permanent process. Larger series studies are needed to further elucidate the frequency and clinical determinants of venous insufficiency in acromegalic patients.

Abstract citation ID: lvag096.1337

EP1073 - ECE_2377 - Incidental sellar arachnoidocele: a prospective study in Argentina

Simone Cordovez[1], Bibiana Coca[1], Stella Orce[2], Alessandro Locatelli[2], Valeria Reynaldo[1], Nicole Soledispa[1], Diego Ceballos[2], Juan Carlos Treviso[2], Susana Mallea-Gil[1] and Carolina Ballarino[1]

[1]Endocrinology, Hospital Militar Central, Buenos Aires, Argentina; [2]Department of Imagin, Hospital Militar Central, Buenos Aires, Argentina

Empty Sella (ES) is a radiological finding, most often incidental, characterized by the presence of cerebrospinal fluid within the sella turcica due to herniation of the sellar diaphragm, resulting in flattening of the pituitary gland. Primary Empty Sella (PES) is defined in patients with no history of pituitary tumor, surgery, or radiotherapy. The main associated conditions are increased intracranial pressure, obesity, traumatic brain injury (TBI), multiparity, and arterial hypertension (AH).

Our objective is to determine the frequency of primary complete or partial sellar arachnoidocele incidentally detected on magnetic resonance imaging (MRI), to identify the most frequent hormonal disorder, and to assess the possible association between arachnoidocele's degree and hormonal impairment.

Materials and Methods: A prospective observational study is currently being conducted at the Hospital Militar Central (Buenos Aires, Argentina) over a one-year period (May 2025-April 2026). This report presents preliminary results from the first eight months. Patients >18 years who underwent brain MRI for indications unrelated to ES were followed. Pituitary hormonal profiles, degree of arachnoidocele, and predisposing factors (age, sex, clinical features, body mass index, parity, TBI and AH) were evaluated. Statistical analysis was performed using SPSS software.

Results: During the first eight months, a total of 1906 brain MRI scans were performed in a population with an average age of 58.1 ± 16.7 years at the diagnosis, of which 121 (6.3%) ES was found. Of these, 26 (21.4%) were men and 95 (78.6%) were women; among the latter, 82 (77.2%) had a history $\geq$2 deliveries. Main indication for MRI was headache, accounting for 23.1% of cases. Imaging assessment demonstrated the incidence of PES grade III (33.1%) followed by grade II (26.4%). Obesity and HTA were present in 45% and 22.8% patients respectively and 16.5% reported a history of TBI. We could perform biochemical pituitary profile in (57/121) and we found hormonal deficiency in only 2 patients (3.51%): one case of hypogonadism and one case of central hypothyroidism.

Conclusions: In this study, preliminary findings suggest a low incidence of incidentally detected PES on MRI and a low prevalence of associated hormonal deficiencies. Based on these findings, systematic hormonal evaluation and follow-up may be necessary only in patients with incidentally identified PES who present a high clinical suspicion based on symptoms consistent with pituitary dysfunction. The relationship between the degree of arachnoidocele and pituitary dysfunction and final conclusions will be fully elucidated upon completion of the study.

Abstract citation ID: lvag096.1338

EP1074 - ECE_2605 - Granulomatous hypophysitis in sarcoidosis: a rare cause of panhypopituitarism

Nevena Radić[1], Dusan Zivanovic[1], Danilo Lazarevski[1], Đurđina Dronjak[1], Danka Jeremic[1,2], Snezana Polovina[1] and Mirjana Sumarac-Dumanovic[1,2,3]

[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Center of Serbia, Belgrade, Serbia; [2]School of Medicine, University of Belgrade, Belgrade, Serbia; [3]Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Center of Serbia, Belgrade, Serbia

Introduction: Hypophysitis is a rare inflammatory disorder of the pituitary gland, that may be primary or secondary, often occurring in association with systemic diseases. Clinical manifestations include headache, anterior and/or posterior pituitary dysfunction, and enlargement of the pituitary gland or infundibulum on MRI. Diagnosis is based on clinical, hormonal, and imaging findings and can be confirmed histopathologically.

Case Presentation: We report the case of a 37-year-old woman presenting with a four-month history of fatigue, generalized weakness, bone and muscle pain, numbness in the feet, loss of appetite, headaches, marked polydipsia (~6 L/24 h), and secondary amenorrhea. Her medical history was significant for Hashimoto's thyroiditis. Initial thyroid function tests showed low TSH, FT4 and T3. During hospitalization, panhypopituitarism was confirmed and central diabetes insipidus was diagnosed by water deprivation test. Laboratory evaluation showed very low gonadotropins (FSH <2.5 IU/L, LH <0.6 IU/L), low estradiol (23.3 ng/L), markedly elevated prolactin in profile (>2500 mIU/L) without macroprolactin, low-normal cortisol (193.6 nmol/L) and ACTH (13.9 ng/L), low IGF-1 (85.9 ng/mL), and low TSH (0.8 mIU/L). Pituitary MRI demonstrated a markedly enlarged pituitary gland with a thickened infundibulum, raising suspicion of autoimmune hypophysitis. Replacement therapy with hydrocortisone, levothyroxine, and desmopressin resulted in rapid clinical improvement. Further evaluation for an underlying systemic disorder revealed elevated 24-hour urinary calcium, angiotensin-converting enzyme (ACE), and chitotriosidase. Pituitary biopsy confirmed granulomatous hypophysitis, consistent with sarcoidosis. Chest CT demonstrated mediastinal lymphadenopathy, and brain/cervical MRI revealed mild dilation of the central canal from C5 caudally, suggestive of neurosarcoidosis. The patient was treated with pulse methylprednisolone (1000 mg daily for 5 days), followed by oral prednisone 60 mg daily, along with hormone replacement therapy using norgestrel/estradiol valerate. Corticosteroids were gradually tapered during follow-up under pulmonology supervision. After 14 months of therapy, hormonal reevaluation (2 months off norgestrel/estradiol) demonstrated partial recovery of anterior pituitary function, with increase in gonadotropins and estradiol profile (FSH 3.1 IU/L, LH 6.8 IU/L, estradiol 37.5 ng/L), normalized IGF-1 (117.8 ng/mL), ACTH

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(23.8 ng/L), cortisol (386 nmol/L), and prolactin (LTH 466-540 mIU/L). Follow-up MRI showed postoperative changes, a slightly asymmetric heterogeneous gland, and no focal lesion. The patient continued replacement therapy with levothyroxine and a low dose of hydrocortisone (10 mg daily) and the desmopressin dose was adjusted according to clinical response.

Conclusions: This case highlights the importance of timely recognition of nonspecific symptoms that may indicate rare disorders such as granulomatous hypophysitis in sarcoidosis. It also emphasizes the critical role of a multidisciplinary approach in the diagnosis and management of complex systemic diseases with pituitary involvement.

Abstract citation ID: lvag096.1339

EP1075 - ECE_1915 - Quality-of-life improvements in patients with Cushing's syndrome: results from an ad hoc analysis of new osilodrostat users in a prospective, non-interventional study (LINC 6)

Stéphanie Espiard[1], Jérôme Bertherat[2], Frederic Castinetti[3], Richard Feelders[4], Elisabeth Nowak[5], Chiara Simeoli[6], Günter Stalla[7], Annenienke van de Ven[8], Amandine Ferriere[9], Laura Dichtel[10], Elena Varlamov[11], Eliza Geer[12], Jeannie Le Mouhaër[13], Peppi Raunioniemi[14], Beatrice Gueron[13] and Nicolas Scheyer[15]

[1]CHU de Lille, Lille, France; [2]Hôpital Cochin, AP-HP, and Université Paris-Cité, Centre de Référence des Maladies Rares de la Surrénale, Paris, France; [3]Department of Endocrinology, Aix-Marseille University, INSERM, MMG, La Conception Hospital, Assistance Publique Hôpitaux de Marseille, Marseille, France; [4]Department of Internal Medicine, Endocrine Section, Erasmus Medical Center, Rotterdam, The Netherlands; [5]Department of Medicine IV, LMU University Hospital, LMU Munich, Munich, Germany; [6]Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Diabetologia, Andrologia e Nutrizione, Università Federico II di Napoli, Naples, Italy; [7]Medicover Neuroendocrinology, Munich, Germany; [8]Division of Endocrinology, Department of Internal Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands; [9]CHU de Bordeaux and Centre de Référence des Maladies Rares de la Surrénale, Bordeaux, France; [10]Neuroendocrine and Pituitary Tumor Clinical Center, Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States; [11]Pituitary Center, Departments of Medicine and Neurological Surgery, Oregon Health & Science University, Portland, OR, United States; [12]Departments of Medicine and Neurosurgery, Memorial Sloan Kettering Cancer Center, Multidisciplinary Pituitary and Skull Base Tumor Center, New York, NY, United States; [13]Recordati Rare Diseases, Puteaux, France; [14]Recordati AG, Basel, Switzerland; [15]Département d'Endocrinologie, Diabétologie et Nutrition, CHRU de Nancy, Hôpital Brabois et Université de Lorraine, Vandœuvre-lès-Nancy, France

Introduction: LINC 6 (NCT05382156), an ongoing prospective, non-interventional, multinational study, evaluates the long-term safety and effectiveness of osilodrostat in patients with Cushing's syndrome. Data are reported from an *ad hoc* analysis describing changes in patient-reported outcomes with osilodrostat.

Methods: Responses of patients (new osilodrostat users) treated for ≥6 months (M) who completed two validated questionnaires—the Cushing's Quality of Life (CushingQoL) questionnaire at baseline and CushingQoL and/or Patient Global Impression of Change (PGIC) questionnaire 6-18 M after treatment initiation—were analysed. Raw CushingQoL total score range was 12-60 and was converted into a 0- to 100-point scale; higher score indicates improvement in QoL. PGIC score ranged from 1 (very much improved) to 7 (very much worse); three classes were computed based on PGIC assessment: improvement (PGIC ≤3); no change (PGIC = 4); worsening (PGIC ≥5). Analyses are descriptive, with no formal statistical testing.

Results: 29 patients from five countries (Europe and USA) were included (female: $n = 23$, 79.3%; mean [SD] age: 51.0 years [16.4]). Median (min–max) osilodrostat exposure: 14.9 M (7.8-26.8). Overall, mean CushingQoL score increased over time (baseline: 37.7, $n = 29$; 6-12 M: 45.3, $n = 24$; 12-18 M: 47.2, $n = 18$). The minimal clinically important difference in CushingQoL (10.1-point change) was achieved by 41.7% ($n = 10/24$) and 55.6% ($n = 10/18$) of patients at 6-12 M and 12-18 M, respectively. Based on PGIC, from baseline to 6-12 M and 12-18 M, respectively, 60.9% ($n = 14/23$) and 50.0% ($n = 8/16$) of patients reported an improvement in their condition, 17.4% ($n = 4/23$) and 31.3% ($n = 5/16$) reported no change, and 21.7% ($n = 5/23$) and 18.8% ($n = 3/16$) reported worsening. Mean urinary free cortisol (mUFC; xULN) decreased from 1.7 ($n = 17$) at baseline to 0.8 ($n = 19$) at 6-12 M and 0.6 ($n = 11$) at 12-18 M. Mean late-night salivary cortisol (LNSC; xULN) decreased from 3.2 ($n = 13$) at baseline to 1.3 ($n = 9$) at 6-12 M and 1.0 ($n = 6$) at 12-18 M. At 6-12 M and 12-18 M, respectively, 88.9% ($n = 16/18$) and 90.0% ($n = 9/10$) of patients had mUFC ≤ULN, and 44.4% ($n = 4/9$) and 80.0% ($n = 4/5$) had LNSC ≤ULN. Overall, mean systolic blood pressure (SBP; mmHg) decreased over time (baseline, 137.6, $n = 28$; 12-18 M, 118.0, $n = 13$). Mean BMI and HbA_{1c} remained stable over time.

Conclusions: Osilodrostat led to improvements in QoL in patients with Cushing's syndrome, as demonstrated by CushingQoL and PGIC scores. SBP, BMI and HbA_{1c} improved or remained stable over time in most patients. However, some data were limited by small patient numbers.

Abstract citation ID: lvag096.1340

EP1076 - ECE_2982 - LATS1 and LATS2 are dispensable for pituitary gonadotrope function

Natalia Jakuc[1], Luisina Ongaro[2], Xiang Zhou[2], Ulrich Boehm[3], Daniel Bernard[2], Alexandre Boyer[1], Derek Boerboom[1] and Gustavo Zamberlam[1]

[1]Centre de Recherche en Reproduction et Fertilité (CRRF), Faculté de Médecine Vétérinaire (FMV), Université de Montréal (UdeM), Saint-Hyacinthe, Canada; [2]Department of Pharmacology & Therapeutics, McGill University, Montréal, Canada; [3]Department of Experimental Pharmacology, Center for Molecular Signaling, Saarland University School of Medicine, Homburg, Germany

The Hippo signaling pathway is a highly conserved kinase cascade that regulates vital biological and pathological processes in mammals. The pathway's transcriptional co-activators, Yes-associated protein 1 (YAP) and Transcriptional coactivator with PDZ-binding motif (TAZ), play a central role in mediating these functions, as they represent the final downstream effectors of Hippo signaling.

We recently demonstrated that conditional deletion of YAP and TAZ in murine pituitary gland gonadotrope cells results in increased circulating luteinizing hormone (LH) levels in both sexes. Increased testosterone levels, testicular weight, and sperm concentration

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

were observed in males, while females presented a hyperfertility phenotype characterized by higher ovulation rates and larger litter sizes. Although these findings advanced our understanding of Hippo signaling in gonadotrope cells, the upstream mechanisms regulating YAP and TAZ activity remain to be elucidated.

In the Hippo signaling pathway, the canonical upstream kinases that regulate YAP and TAZ are the large tumor suppressor homolog kinases 1 and 2 (LATS1 and LATS2). To directly assess the role of these kinases in gonadotrope cells, *Lats1* and *Lats2* were conditionally knocked-out in murine gonadotropes using the GnRH receptor–IRES-Cre (GRIC) driver and a ROSA mTmG fluorescent reporter.

Deletion was firstly successful validated by fluorescence-activated cell sorting (FACS)–isolated gonadotropes from 12-16-week-old mice, which showed significant reduction in expression levels of both genes. Serum, gonads, and pituitaries were then collected from 10-12-week-old male mice and 8-10-week-old females at diestrus. Unexpectedly, hormonal analyses indicated no differences between controls and knock-out mice in LH or FSH levels in either males or females. Consequently, no reproductive phenotypic anomalies were observed in either sex. Curiously, RT-PCR analyses of pituitaries showed that YAP/TAZ target genes were not altered following *Lats1* and *Lats2* deletion. Taken together, these results suggest that, unlike many other cell types, YAP and TAZ activity does not appear to be regulated by LATS1 and LATS2 in gonadotropes.

We are currently using bulk RNA sequencing on FACS-sorted gonadotropes from control and knock-out mice to determine if there are unappreciated roles for LATS1 and LATS2 in these cells.

Abstract citation ID: lvag096.1341

EP1077 - ECE_2070 - Novel insights on the role of putative neuronostatin receptor GPR107 in liver pathophysiology

Antonio García-Estrada[1,2,3], Betsaida Ojeda-Pérez[1,2,3], Amelie Lupp[4], Stefan Schulz[4,5], Raul M. Luque[1,2,6], Juan Luis López-Cánovas[1,2,3] and Manuel D. Gahete[1,2,6]

[1]Maimónides Biomedical Research Institute of Córdoba (IMIBIC), Córdoba, Spain; [2]Department of Cell Biology, Physiology and Immunology, University of Córdoba (UCO), Córdoba, Spain; [3]Reina Sofía University Hospital (HURS), Córdoba, Spain; [4]Institute of Pharmacology and Toxicology, Jena University Hospital (UKJ), Friedrich-Schiller-University (FSU) Jena, Jena, Germany; [5]7TM Antibodies GmbH, Jena, Germany; [6]Reina Sofía University Hospital (HURS), CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Córdoba, Spain

Our understanding of the somatostatin (SST) endocrine system, which is a well-established source of biomarkers and therapeutic targets in neuroendocrine and pituitary tumours, has been lately expanded through the discovery of neuronostatin (NST), a SST-alternative peptide; the identification of its putative receptor, GPR107; and the extensive research on their role in metabolic regulation and prostate and breast cancer. Liver cancer, particularly hepatocellular carcinoma (HCC), is increasingly associated to underlying metabolic disorders, namely metabolic dysfunction-associated steatotic liver disease (MASLD), which challenge current tumour management strategies. In this study, we investigated the NST-GPR107 system in the MASLD-HCC progression to characterise its potential contribution and exploitability in these diseases.

GPR107 expression was evaluated in 2 internal chronic liver disease (CLD)-HCC retrospective cohorts (R1 [$n = 93$], R2 [$n = 102$]), 7 MASLD in silico cohorts ($n = [45\text{-}109]$/cohort), 6 HCC in silico cohorts ($n = [65\text{-}369]$/cohorts) and 4 human liver cell lines (THLE-2, HepG2, Hep3B, SNU-387). NST expression was assayed using ELISA in an additional internal MASLD-CLD-HCC plasma cohort ($n = 88$). In a subset of R1 ($n = 25$), immunohistochemistry (IHC) for GPR107 was performed. Gene set enrichment analysis (GSEA) were employed to link GPR107 expression with hallmark gene sets, metabolic pathways (KEGG, Reactome) and biological processes (GO). In cell lines, the impact of NST application and GPR107 silencing and overexpression was assessed through functional assays (proliferation, wound healing, colony and hepatosphere formation).

The expression of NST and GPR107 was progressively increased in the MASLD-HCC progression, wherein GPR107 was associated with key HCC aggressiveness features (lower portal hypertension and survival, higher microvascular invasion, recurrence and expression of proliferative biomarkers). IHC demonstrated GPR107 cytosolic and membranous presence in HCC cells, where the proliferative tumour borders showed the highest staining. GSEA directly linked GPR107 expression with global expression of cell cycle genes in HCC samples. Accordingly, GPR107 overexpression enhanced, while GPR107 silencing blunted, cancer traits, such as cell proliferation, in HCC cell lines. Moreover, NST showed antiproliferative effects on liver cancer cells, with no effect on healthy hepatocytes (THLE-2). NST addition counteracted the protumoral effects of GPR107 overexpression, whereas the combination of NST and GPR107 silencing enhanced the antitumoral effects.

Altogether, these results support the direct association between GPR107 expression and HCC in a metabolic context through cell cycle modulation, which could be exploited for diagnosis, staging and potential treatment in the rapidly evolving field of liver diseases.

Abstract citation ID: lvag096.1342

EP1078 - ECE_2325 - Hypophysitis with mixed histiocytosis

Mubina Hodzic[1,2], Amira Jagodić- Ejubovic[3] and Davorka Dautbegovic Stevanovic[1]

[1]Department of Internal Disease, Division of Endocrinology and Diabetology, Cantonal hospital, Zenica, Bosnia and Herzegovina; [2]Department for Internal Diseases, Zenica Cantonal Hospital, Zenica, Bosnia and Herzegovina; [3]Department of Internal Disease, Division of Rheumatology, Cantonal Hospital, Zenica, Bosnia and Herzegovina

A 44- year- old man was hospitalized in 2017. due to symptoms of diabetes insipidus, four months after tympanoplastic surgery of the right ear. Pituitary MRI showed absence of the posterior pituitary bright spot and pituitary stalk thickening. Desmopressin was initiated. One year later, the patient developed erectile dysfunction, low libido, decreased leg hair growth. The laboratory tests revealed low gonadotropins, low testosterone levels, while other anterior pituitary hormones(TSH, ACTH) were preserved. Pituitary MRI demonstrated a 3-mm pituitary microadenoma and persistent pituitary stalk thickening raising suspicion of hypophysitis. Testosterone cypionate replacement therapy, along with desmopressin was prescribed. Subsequently, the patient was rehospitalized for pulse corticosteroid therapy, without improvement in symptoms. In 2025. he reported chronic pain in the legs and arms and unintentional weight loss lasting for two years. He occasionally experienced subfebrile temperature and chills. Inflammatory markers were elevated. The patient

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

recognised similar symptoms in individual with diabetes insipidus and Erdheim-Chester disease through a social media patient support group. A repeat pituitary MRI performed in 2023. Again demonstrated pituitary stalk thickening, without evidence of microadenoma, and an inhomogeneous adenohypophysis. A biopsy of the left knee confirmed mixed histiocytosis(Erdheim-Chester disease and Langerhans cells histiocytosis) with BRAF V 600 mutation, PET/ CT imaging revealed increased metabolic activity in the long bones and lymph nodes of neck and axillary regions. He was hospitalized in Department of Hematology. Targeted therapy with dabrafenib was recommended. Follow-up PET/CT scan after three months showed regression of metabolic activity, accompanied by clinical improvement and decrease in inflamatory markers. Follow-up pituitary MRI showed no dynamic changes. Levothyroxine was initated last month, with a normal cortisol profile.

Keywords hypophysitis, hystiocytosis, diabetes insipidus, Erdheimer Chester disease, dabrafenib

Abstract citation ID: lvag096.1343

EP1079 - ECE_3679 - Sphenoid fibrous dysplasia presenting with hypopituitarism

Ozge Sahin Kimyon[1], Hayriye Gulsah Ozkan[2], Selin Celik[1], Buruc Erkan[3], Sema Ciftci[1] and Hamide Piskinpasa[1]

[1]Department of Endocrinology and Metabolism, University of Health Sciences, Bakırkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Türkiye; [2]Radiology, University of Health Sciences, Bakırkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Türkiye; [3]Department of Neurosurgery, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Türkiye

Introduction: Fibrous dysplasia (FD) is a benign developmental bone disorder characterized by replacement of normal bone with structurally weaker fibro-osseous tissue. It is classified into three clinical forms: monostotic, polyostotic, and McCune–Albright syndrome–associated FD. Craniofacial involvement occurs in approximately 10%-25% of patients with the monostotic form and in up to 50% of those with the polyostotic form. The clinical spectrum is broad, ranging from asymptomatic lesions detected incidentally to symptomatic presentations, including pain, compression-related neurological deficits, and/or facial asymmetry. Here, we present a rare case of sphenoid sinus FD presenting with hypopituitarism.

Case Presentation: A 79-year-old woman was referred to our outpatient clinic for follow-up of a sellar mass lesion. Ten years earlier, she had been evaluated at another center for hyponatremia and was diagnosed with panhypopituitarism and a sellar mass, for which surgical intervention had been recommended. The patient declined surgery and had since been treated with levothyroxine, hydrocortisone. Medical history revealed menopause at the age of 52 years. At presentation, she reported mild headache without additional symptoms. Laboratory evaluation revealed TSH 0.94 mIU/L, free T4 0.96 ng/dL, FSH 4.87 IU/L, estradiol 5 ng/L, prolactin65 µg/L, sodium 138 mmol/L, and potassium4.9 mmol/L. Pituitary magnetic resonance imaging demonstrated a $30 \times 25 \times 20$ mm lesion filling the sellar region, with intermediate signal intensity on T2-weighted images, heterogeneous contrast enhancement, and mild compression of the optic chiasm. Clear differentiation between the lesion and the sphenoid sinus could not be achieved. Paranasal sinus computed tomography performed for differential diagnosis suggested FD as the most likely diagnosis. Bilateral visual field examination was normal. Whole-body bone scintigraphy revealed increased tracer uptake at the sphenoid bone, supporting the diagnosis. The case was discussed at a multidisciplinary pituitary council. Due to optic nerve compression and headache, surgical intervention was recommended; however, the patient again declined surgery. Bisphosphonate therapy was therefore planned.

Discussion: Isolated sphenoid sinus FD is extremely rare. Surgical treatment may be considered in symptomatic patients or those with cosmetic deformities. Although bisphosphonates are effective in controlling pain in adults with polyostotic disease, their role in monostotic FD remains unclear, and they have not been shown to reduce fracture risk or disease progression. Our patient had been followed for years with a presumed sellar mass causing hypopituitarism. Sellar lesions should be carefully evaluated for sphenoid bone involvement, and FD should be included in the differential diagnosis. Diagnosis relies on combined clinical, radiological, and histological assessment.

Abstract citation ID: lvag096.1344

EP1080 - ECE_1001 - Comparison of the predictive power of morphological and therapeutic stratification predictors of monohormonal somatotroph pituitary tumors in patients with acromegaly

Evgeny Pronin[1], Mikhail Antsiferov[1,2], Vyacheslav Pronin[1,2], Alexey Petraikin[3], Anastasia Lapshina[4], Tatiana Alekseeva[1], Lilia Selivanova[4] and Safi Tamaeva[5]

[1]Moscow Health Department, Endocrinological Dispensary, Moscow, Russia; [2]Ministry of Health of Russia, Russian Medical Academy of Continuing Professional Education, Moscow, Russia; [3]Moscow Health Department, Scientific and Practical Clinical Center for Diagnostics and Telemedicine Technologies, Moscow, Russia; [4]Ministry of Health of Russia, National Medical Research Centre for Endocrinology, Moscow, Russia; [5]Ministry of Health of Russia, National Medical Research Center of Surgery named after A. Vishnevsky, Moscow, Russia

Given the heterogeneity of somatotroph tumors (STs), it is important to study diverse predictors of morphological identification and sensitivity to drug therapy (DT) with first-generation somatostatin receptor ligands (fg-SRLs).

Aim: Comparative analysis of the prognostic significance of predictors of STs pathomorphological status and the prospects for using fg-SRLs in patients with acromegaly.

Materials and Methods: A retrospective analysis of the long-term efficacy of fg-SRLs was conducted in 634 patients with acromegaly (197 men) receiving prolonged forms of lanreotide (120 mg/28-56 days) or octreotide (20-30 mg/28 days) as primary or secondary DT. The IGF-1 index, reflecting the ratio of IGF-1 to the upper limit of normal (IGF-1/ULN), was used for the initial and dynamic assessment of somatotroph function. The criterion for drug control was an IGF-1 index value ≤ 1. The age at diagnosis was 47.9 ± 13.8 years, the baseline IGF-1 index value was 2.7 ± 1.2, the duration of DT was 77.8 ± 52.7 months, and the IGF-1 index value at the last visit was 1.2 ± 0.7. Pharmacotherapeutic testing (PharmT) which consisted of assessing the percentage decrease in IGF-1 levels (%ΔIGF-1) 3 and 6 months after the start

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

of treatment with fg-SRLs was also performed. Treatment outcomes were compared with baseline clinical examination data, PharmT results ($n = 496$), cytological and immunohistochemical analysis data ($n = 104$), as well as quantitative indicators of relative tumor signal intensity (RTSI) on T2- and T1-weighted MRI with an additional calculation of the T2-T1 coefficient ($n = 106$).

Results: Among the markers of morphological stratification of STs, the most informative are: age at diagnosis (AUC 0.686), tumor volume and maximum diameter (0.664 and 0.665), expression of the 2nd subtype of somatostatin receptors (SSTR2; 0.816), the difference and ratio of SSTR2 and SSTR5 (0.826 and 0.808), proportion of cells with antibodies to GH (0.932) and with fibrous bodies (FB; 0.962), tumor cell composition (0.935), RTSI on T2-, T1- and (T2-T1)-weighted MRI (WI; 0.878, 0.822 and 0.918). Predictors of fg-SRLs efficacy include: volume and maximum diameter of STs (0.640 and 0.649), baseline IGF-1 index value (0.637), absolute and relative expression of SSTR2 (0.673, 0.688 and 0.713), proportion of cells with FB (0.698), tumor cell composition (0.742), results of RTSI on T2- and (T2-T1)-WI (0.684 and 0.636) and PharmT (%ΔIGF-1 after 3-6 months—0.840-0.849).

Conclusions: Priority predictors of the morphofunctional status of STs and the long-term effectiveness of fg-SRLs simplifying the differential diagnosis of the relevant histotype and facilitating the management of acromegaly treatment have been identified.

Abstract citation ID: lvag096.1345

EP1081 - ECE_1342 - Neurophysin-I dynamics upon different pituitary provocation tests in healthy participants

Andi Nikaj[1], Cihan Atila[1], Deborah Rudin[2], Dino Luethi[2], Clara Sailer[3], Bettina Winzeler[4], Sandrine A. Urwyler[1], Julie Celine Refardt[5], Matthias Liechti[2] and Mirjam Christ-Crain[1]

[1]Department of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland; [2]Division of Clinical Pharmacology and Toxicology, Department of Pharmaceutical Sciences, University of Basel, Basel, Switzerland; [3]Division of Endocrinology, Diabetes and Hypertension, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States; [4]Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich, Zürich, Switzerland; [5]Department of Internal Medicine, Section of Endocrinology, Erasmus Medical Center, Rotterdam, The Netherlands

Background: Oxytocin (OXT) is known for its role in regulating social behaviour, such as emotion recognition and bonding. The evidence for clinically relevant OXT deficiency is constantly increasing, but measurement of OXT is challenging. In contrast, neurophysin-I (NP-I), the carrier protein of OXT, co-released equimolarly, is a stable surrogate biomarker for OXT. This study evaluated OXT and NP-I levels upon four different pituitary provocation tests.

Design: Secondary analysis of four interventional diagnostic trials at the University Hospital Basel, Switzerland.

Methods: Sixty-six participants underwent a pituitary provocation test, 11 the hypertonic saline test, 20 the arginine infusion test, 25 the oral macimorelin test, and 10 the glucagon injection test. Plasma NP-I and OXT were measured at baseline and once plasma sodium level reached ≥150 mmol/L for the hypertonic saline, after 60 min for the arginine infusion, after 60 min, 120 min, and 180 min for the glucagon injection, and after 45 min for the oral macimorelin test. Primary outcome was change from baseline to maximally stimulated NP-I levels.

Results: Median (IQR) NP-I levels increased minimally in response to hypertonic saline (baseline: 55 pM, stimulated: 59 pM, relative median change of −8% [−16, +9]) and significantly to glucagon injection (baseline: 82 pM, stimulated: 94 pM, relative median change of +18% [+7, +28]). Median OXT levels showed similar trends in response to hypertonic saline (baseline: 0.36, stimulated: 0.48, relative median change of +22% [−15, +96]) and to glucagon injection (baseline: 82.7 pg/mL [62.3, 94.3], stimulated: 93.4 pg/mL [87.2, 121], relative median change of +25% [+6, +59]). There were no increases in NP-I plasma levels nor OXT levels upon arginine infusion and oral macimorelin, same for OXT levels.

Conclusions: NP-I showed minimal responses to pituitary provocation tests, paralleling OXT dynamics. These findings highlight NP-I's potential as a reliable and technically robust surrogate biomarker for OXT activity, warranting further evaluation in clinical and experimental settings.

Abstract citation ID: lvag096.1346

EP1082 - ECE_3435 - A pituitary abscess caused by Moraxella osloensis

Danai Georgakopoulou[1], Andreas Manakis[2], Charikleia Paschalidi[1], Christos Gkolemis[2], Labrini Papanastasiou[1], Athina Markou[1] and Athanasios Fountas[1]

[1]Department of Endocrinology and Diabetes Center, General Hospital of Athens "G. Gennimatas", Athens, Greece; [2]Department of Neurosurgery, General Hospital of Athens "G. Gennimatas", Athens, Greece

Background: Pituitary abscess (PA) is an uncommon, potentially life-threatening, condition which is often indistinguishable from other sellar lesions prior to surgery. In this report, we describe the clinical course of a PA due to Moraxella osloensis.

Case Report: A 31-year-old Greek woman underwent a pituitary MRI due to a 6-month history of secondary amenorrhea and hyperprolactinemia (78.6 ng/mL, normal range 2.8-29.2) which revealed an 8 mm micro-adenoma. Two months later, she presented with severe headache and vomiting. A follow-up MRI showed a cystic lesion with high T2 signal intensity, peripheral contrast enhancement and increased size (13 mm) compared to the previous MRI. CSF analysis revealed merely elevated WBC (80 μL, 85% lymphocytes). The patient was diagnosed with pituitary apoplexy and treatment with high-dose dexamethasone led to significant clinical improvement. She was discharged five days after dexamethasone initiation while being completely asymptomatic. However, few days later, she presented to the emergency department with severe headache, fever (38.5 °C), neck stiffness and bilateral visual field deficits with papilledema. A repeat MRI revealed further size increase of the pituitary cystic lesion (20 mm), optic chiasm compression and leptomeningeal enhancement. Hormonal investigation revealed anterior hypopituitarism with no evidence of diabetes insipidus. CSF analysis showed elevated WBC and protein levels (1858 μL, 98% PMNs, protein 320 mg/dL) as well as hypoglycorachia (glucose 36 mg/dL) indicating purulent meningitis.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Blood cultures were positive for Moraxella osloensis and iv antibiotic treatment with ceftriaxone and metronidazole was initiated. Despite antibiotics, the patient developed right abducens nerve palsy and transient left arm weakness. Transsphenoidal pituitary surgery was performed and a macroscopically purulent fluid collection was removed. Patient's symptoms gradually improved over the first postoperative days and she was discharged after receiving iv antibiotics for a period of 6 weeks. At the 6-month post-operative follow-up no recurrent lesion was depicted.

Conclusions: To our knowledge, this is the first reported PA case associated with Moraxella osloensis, extending the spectrum of central nervous system infections caused by this rarely invasive respiratory commensal. Whether this is a case of secondary PA in which dexamethasone treatment masked its clinical manifestations or a case of a pituitary adenoma apoplexy further complicated by an infection leading to an abscess stills remains a puzzle.

Abstract citation ID: lvag096.1347

EP1083 - ECE_3451 - Management of Cushing syndrome of different etiologies—a single center real life experience: data from ERCUSYN Krakow database

Mari Minasyan[1], Aleksandra Gamrat-Żmuda[2,3], Wiktoria Suchy[2], Katarzyna Majka[4], Alicja Hubalewska-Dydejczyk[1], Elena Valassi[5,6] and Aleksandra Gilis-Januszewska[1]

[1]Chair and Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [2]Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [3]Doctoral School of Medical and Health Sciences, Jagiellonian University Medical College, Krakow, Poland; [4]Students' Scientific Circle of Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [5]Barcelona, Spain; [6]Universitat Internacional de Catalunya (UIC), Barcelone, Spain

Introduction: Cushing's syndrome (CS) is characterized by chronic exposure to cortisol excess. Regardless of etiology, surgery remains a first line option. Pharmacological antihypercortisolemic therapy is used: as a preoperative management, as a main therapy in patients without option for radical therapy, after unsuccessful surgery or or when the source of CS cannot be identified.

Materials and Methods: A retrospective analysis of data regarding management of CS patients from the ERCUSYN Krakow database The study included 214 patients: 53% with pituitary-dependent CS (PIT-CS), 25% with adrenal CS (ADR-CS), and 22% with ectopic CS (ECT-CS). The median age was 54 years (Q1:38, Q4:65), and 77% of patients were women.

Results: Surgery: Surgery was a main therapeutic option for most patients with PIT-CS(97/114) and ADR-CS(43/47). Among ECT-CS, 15/53 underwent surgery. In PIT-CS the rate of successful surgery to date was 72% with identical relapse rates for microadenomas and macroadenomas (11%). The success rate of reoperation was lower (47%) than in cases of initial operation. In ADR-CS, adrenalectomy was successful for 100% of patients with unilateral adenoma and 18% with bilateral adenomas. Among operated ECT-CS patients (15/53) the success rate was 47% (7/15). Relapses (N:5/15) occurred in medullary thyroid cancer (N:2), atypical lung cancer (N:2) and nasal papilloma (N:1). 3/15 patients did notachieve remission after surgery (pancreatic neuroendocrine tumor N:2, breast cancer N:1). Medical therapy: In PIT-CS: antihypercortisolemic therapy was used preoperatively in 39 patients, due to relapse or non-radical surgery among 20 patients and as a main therapy without radical treatment among 4 patients. The most commonly used medication was ketoconazole (N:27), followed by metyrapone (N:18), osilodrostat (N:18), pasireotide (N:7), relacorilant in clinical trial (N:3), cabergoline (N:1) and etomidate (N:1). In ADR-CS: antihypercortisolemic therapy was used preoperatively among 8 patients and in one patient due to non-radical surgery. The most commonly used medication was ketoconazole (N:4), followed by metyrapone (N:3) and osilodrostat (N:2). In ECT-CS: antihypercortisolemic therapy was used preoperatively among 11 patients,as a main therapy without radical treatment among 13 patients, due to unidentified ectopic source among 5 patients and due to CS relapse or non-radical surgery among 3 patients. The most commonly used medication was metyrapone (N:16), followed by osilodrostat (N:13), ketoconazole (N:13), octreotide (N:2), mitotane (N:2) and relacorilant in clinical trial (N:1).

Conclusions: Presented study showed complexity of care required for optimal control of CS patients. Surgery was a main therapeutic option for most of the patients with PIT-CS and ADR-CS. Antihypercortisolemic medications served a principal role for most of the patients with ECT-CS.

Abstract citation ID: lvag096.1348

EP1084 - ECE_1413 - CAM 5.2 as a predictive marker of surgical outcomes in acromegaly patients undergoing endoscopic transnasal transsphenoidal surgery

Vaishali Kaur[1], Rahul Gupta[2], Diya Roy[3], Ashutosh Rai[4], Apinderpreet Singh[5], Chirag Kumar[6], Rajesh Chhabra[7], Debajyoti Chatterjee[3], Sanja Medenica[8] and Pinaki Dutta[1]

[1]Endocrinology, Postgraduate Institute of Medical Education and Research Chandigarh, Chandigarh, India; [2]Endocrinology, All India Institute of Medical Science Hospital, Bhopal, India; [3]Histopathology, Postgraduate Institute of Medical Education and Research Chandigarh, Chandigarh, India; [4]Biochemistry, Panjab University, Chandigarh, India; [5]Neurosurgery, Postgraduate Institute of Medical Education and Research Chandigarh, Chandigarh, India; [6]Radiodiagnosis, Postgraduate Institute of Medical Education and Research Chandigarh, Chandigarh, India; [7]Neurosurgery, New Opd Pgimer, Chandigarh, India; [8]Endocrinology, Podgorica, Montenegro

Background: The study aimed to characterize clinico-radiological differences and their impact on post-surgical outcomes in histological subtypes—densely granulated (DGSA) and sparsely granulated (SGSA) somatotroph adenomas (SA).

Methods: A single-centre ambispective study in individuals with SA from 2015 to 2024, where preoperative clinical, hormonal, and magnetic resonance imaging parameters were collected, and biochemical and radiological disease control were assessed postoperatively.

Results: Of 116 SA, 45(38.8%) and 71(61.2%) were DGSA and SGSA, respectively. The median (IQR) age at presentation was 35.0 (29.0-44.0) years, 56.9% were females, 92.2% had macroadenoma, and the mean tumour diameter was 24.9 ± 10.3 mm. The median (IQR) pre-operative nadir GH on OGTT was 31.1 (16.7-50.0) ng/mL, and IGF-1 was 3.7 ± 1.5 times the upper limit of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

normal. As compared to DGSA, SGSA presented earlier (40.0 vs 33.5 years; $P = .009$), had larger tumor size (2239.4 mm^3 vs 5221.6 mm^3; $P = <.005$), were more invasive (33.3% vs 54.1%; $P = .038$), proliferative (ki-67 Index 1.0% vs 3.0%; $P < .001$), and had higher SSTR5 expression (H score 30.0 vs 80.0; $P = .006$). The post-surgical radiological (19.4% vs 22.8%; $P = .707$) and biochemical (17.2% vs 32.2%; $P = .727$) disease control rates were similar in both groups.

Conclusions: In comparison to DGSA, SGSA presents a decade earlier, are larger in size, more invasive, exhibits higher proliferation, and SSTR5 expression. However, this does not impact post-surgical biochemical and radiological disease control.

Keywords somatotroph adenoma, sparsely granulated somatotroph adenoma, densely granulated somatotroph adenoma, acromegaly

Abstract citation ID: lvag096.1349

EP1085 - ECE_2400 - Demographics aspects of pituitary endocrine tumors according to gender in the city of Oran

Khadra Faraoun

Faculté de Médecine d'Oran, Endocrinology Larribere, Medecine, Sidi Chami, Algeria

Introduction/Objective: Endocrine pituitary tumors, or PitNets, develop from pituitary endocrine structures. Our objective is to evaluate the demographic characteristics of PitNets in Oran according to gender.

Subjects and Methods: Our study is observational, multicenter, prospective, and retrospective. Data entry and analysis were performed using EPI Info version 6 from the CDC (USA) and SPSS 20.

Results: We collected 475 pituitary tumors with 368 secreting pituitary neoplasms (77.5%). The male-to-female ratio was 0.54, $P < .0001$, with a predominance of female involvement (64.6%). The sex ratios were: prolactinomas 0.25, non-functional tumors 1.01, somatotropic tumors 1.36, corticotropic tumors 0.27, and thyrotropic tumors 0.5. The mean age in both sexes was 36.8 ± 14.3 years (range 7-78), with a mean age of 41.2 ± 15.5 years in men and 34.5 ± 13.0 years in women ($P < .001$). Pituitary adenomas were more frequent in individuals between 20 and 40 years of age and much less common at the extremes of age. The modal class is 30-39 years old. The predominance is female between 20 and 40 years old and male between 60 and 70 years old, the difference is not significant. The ages of diagnosis by Tumor are respectively for the two sexes (M, F): Prolactinomas 38.0 ± 12.1(16-76) vs 32.4 ± 11.4(16-78) $P = .004$, Non-functional adenomas 45.2 ± 18.0(7-76) vs 38.9 ± 15.7(10-74)NS, Somatotropic Tm 40.9 ± 15.1(15-67) vs 39.5 ± 14.5 (14-71)NS, Corticotropic Tm 32.7 ± 14.4(8-54) vs 34.5 ± 11.7(16-60)NS, Thyrotropic Tm 22.0 vs 32.8 ± 15.7(23-51)NS. In the mixed somato-lactotropic adenomas listed ($n = 5$), the condition predominates in the male sex, the ratio is 4 men to one woman.

Conclusions: As described in the literature, prolactinomas and corticotropic tumors are predominantly female. In contrast, somatotropic tumors were more frequent in men, although the difference was not statistically significant. The incidence of non-functional adenomas (NFAs) was equivalent in both sexes. Diagnosis in women was made at a younger age than in men across all pituitary tumors. Apart from prolactinomas, there was no significant difference in the age at diagnosis between women and men.

Abstract citation ID: lvag096.1350

EP1086 - ECE_1685 - The possible role of black blood magnetic resonance imaging sequences in pituitary tumor diagnosis

Pierluigi Mazzeo[1], Giacomo Voltan[1], Giulia Bovo[1], Filippo Ceccato[1], Renzo Manara[2] and Mattia Barbot[1]

[1]*Department of Medicine - DIMED, Endocrinology Unit, Padova University Hospital, Padova, Italy;* [2]*Department of Neuroscience, Neuroradiology Unit, University of Padova, University-Hospital of Padova, Padova, Italy*

Background: In the diagnosis of pituitary tumors, especially in Cushing's disease (CD), conventional MRI could be inconclusive, forcing clinicians to perform invasive tests like Inferior Petrosal-Sinus Sampling (IPSS) and exploring surgery. The black-blood (BB) MRI sequences are widely used in the diagnostic workup of several conditions including brain tumors, because the suppression of fast-flowing blood signal improves the identification of surrounding tissues, helping to differentiate tumoral lesions from vascular structures that could look similar on standard imaging. However, the role of BB in the diagnosis of pituitary adenomas has not been fully assessed.

Aim of the Study: to evaluate the potential utility of BB-MRI sequences in the diagnostic workup of pituitary adenomas.

Patients: from January 2023, 3T MRI with BB sequences was performed in 20 patients whose MRI findings remained inconclusive despite evaluation by an expert pituitary neuroradiologist within a dedicated multidisciplinary pituitary disease meeting. Among them, 4 patients with CD had undetectable lesion, 11 cases had doubtful findings and 5 patients were reported to have two lesions. The final clinical diagnoses were CD ($n = 14$), acromegaly ($n = 2$), prolactinoma ($n = 2$), NFPA ($n = 1$) and suspected pituitary metastasis ($n = 1$).

Results: BB-MRI sequences provide further diagnostic information in 16/20 cases and in 7 cases the final report was completely revised. Among patients with suspected double lesions, the diagnosis was confirmed in 2 cases, while in 2 patients only one lesion was reported, and they underwent transsphenoidal surgery (TSS) with histological confirmation of corticotroph PitNET; instead, in the remaining patient no lesion was described and IPSS was scheduled. In the group with doubtful lesions, the diagnosis was confirmed in 7 patients, 3 of whom underwent TSS. In 2 patients (a prolactinoma and a suspected NFPA), respectively the lesions were re-classified as Rathke's cleft cyst and partial volume artifact, while in the other 2 cases MRI remained inconclusive. In the group with negative MRI, a microadenoma was identified, with histological confirmation of corticotroph PitNET after TSS. However, MRI persisted negative in one patient and in 2 cases were still considered doubtful (one patient continued medical treatment, while one person underwent TSS with negative histology).

Conclusions: BB-MRI sequencing is a simple and non-invasive tool which could be helpful in the diagnostic workup of unclear pituitary lesions. However, given the small sample size and potential bias in patient selection, further studies are needed to better define its clinical impact.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1351

EP1088 - ECE_2431 - Surgical outcomes of nonfunctioning pituitary neuroendocrine tumors based on transcription factor expression

Jun Sugata, Shingo Fujio, Ryutaro Makino, Tomoko Hanada and Ryosuke Hanaya
Kagoshima, Japan

Background: Transcription factor immunostaining for pathological diagnosis is now recommended in the WHO classification over traditional anterior pituitary hormone staining for nonfunctioning pituitary neuroendocrine tumors (NF-PitNETs). This study retrospectively evaluated surgical outcomes of NF-PitNETs treated at our institution, reclassifying tumor specimens according to transcription factor expression patterns.

Methods: Two hundred one treatment-naïve patients with NF-PitNETs resected between 2012 and 2023 were analyzed. Tissue microarrays were constructed from formalin-fixed paraffin-embedded or frozen specimens for immunohistochemical analysis of SF1, TPIT, and PIT1.

Results: Median age was 64 years; 56.7% were male. Preoperatively, the median tumor volume was 5.1 cm^3, 62.2% of tumors were Knosp grade 0-2, 53.9% had severe growth hormone deficiency, and the median IGF-1 level was −1.74 SD. Gross total resection was achieved in 61.7%. During postoperative follow-up, regrowth of residual tumor occurred in 18.9%, and de novo recurrence was observed in 1.5%. Transcription factor analysis revealed SF1-only positivity in 70.2%, TPIT-only in 19.4%, PIT1-only in 3.0%, dual SF1/PIT1 positivity in 2.0%, and triple negativity in 5.5%. Compared with the SF1 group, the TPIT group demonstrated significantly higher female predominance (92.3% vs 30.5%, $P < .001$), lower preoperative severe GHD prevalence (25% vs 59.6%, $P = .03$), higher preoperative IGF-1 SD (−0.90 vs −1.83, $P < .001$), and higher reoperation rate (12.8% vs 0.7%, $P = .019$). Tumor volume, Knosp grade, and surgical complication rates did not differ significantly among groups.

Conclusions: Refined pathological subtyping based on transcription factor immunostaining may enable improved prognostic stratification and better surgical outcomes in NF-PitNETs.

Abstract citation ID: lvag096.1352

EP1090 - ECE_2862 - Clinical characteristics and therapeutic efficacy analysis of prolactinoma in children and adolescents

Huaiying Wang and Huiwen Tan
Department of Endocrinology and Metabolism, West China Hospital, Chengdu, Sichuan Province, China

Objective: This retrospective cohort study aimed to characterize clinical features and treatment outcomes of pediatric and adolescent prolactinoma patients (≤20 years) treated between 2019 and 2026, providing evidence-based guidance for clinical management.

Methods: We analyzed demographic, clinical, tumor, and treatment data from 69 patients, including gender differences in presentation and outcomes.

Results: The cohort included 55 females (79.7%) and 14 males (20.3%), with a median age of 17.0 years. Median tumor diameter was 1.5 cm, with 63.3% macroprolactinomas and 8.3% giant tumors; median baseline prolactin (PRL) was 320.85 ng/mL. Males had significantly larger tumors (2.9 cm vs 1.3 cm, $P < .001$) and higher PRL levels (573.7 vs 313.0 ng/mL, $P = .013$) than females. Most females (86.7%) presented with menstrual disorders, whereas males primarily had headache (44.4%) and visual field defects (33.3%). Galactorrhea occurred in 17.5% of patients. Dopamine agonists (DAs) were first-line therapy for 61 patients, with 19.7% developing resistance. Thirteen patients underwent surgery, achieving 46.2% long-term remission; tumor size was independently associated with worse surgical outcomes ($P = .047$).

Conclusions: Pediatric prolactinoma shows marked gender disparities: males exhibit larger tumors, higher PRL, and neurological symptoms, while females present with endocrine dysfunction. DAs remain first-line therapy, and surgery is reserved for selected cases, with tumor size predicting surgical efficacy. Early, personalized treatment optimizes outcomes.

Keywords prolactinoma, children, adolescent, dopamine agonists, surgery

Abstract citation ID: lvag096.1353

EP1091 - ECE_3001 - Pituitary apoplexy over the last 10 years: a retrospective study at a tertiary care centre

Smritimayee Panda[1], Subhash Yadav[1], Awadhesh Jaiswal[2] and Preeti Dabadghao[2]
[1]*Endocrinology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India;* [2]*Medical Genetics, Sanjay Gandhi Postgraduate Institute of Medical Science, Lucknow, India*

Background: Pituitary apoplexy is an emergency condition requiring prompt diagnosis and management. It commonly occurs in the presence of a pituitary adenoma. Symptoms include severe headache, visual impairment, vomiting, cranial nerve palsy, and altered sensorium. We are describing 10 years of clinical data and outcomes for patients with pituitary apoplexy managed in our hospital.

Aim: To analyze the 10-year clinical profile and outcome of pituitary apoplexy in a tertiary care hospital

Methodology: Retrospective data on patients with pituitary apoplexy admitted to SGPGIMS (from January 2014 to December 2023) were obtained from electronic medical records. Relevant clinico-radiological, hormonal parameters, management, and outcome details were analysed.

Results: Forty-six patients with symptomatic pituitary apoplexy presented to our hospital from January 2014 to December 2023. Among them, 25 (54%) were male. Forty-four (96%) patients had pituitary adenoma, and only 7 (16%) were functional. One patient had a tubercular granuloma, and one had septic shock leading to apoplexy. The most common presenting symptom was headache, accompanied by visual disturbance, in 43 (94%) patients. Eleven patients (24%) had cranial nerve palsy. Forty (87%) had hypocortisolism, 33 (72%) had hypothyroidism, 27 (59%) had hypogonadism, and 6 (13%) had diabetes insipidus. Seventeen (37%) patients required surgery within 2 weeks of presentation, 13 (28%) underwent surgery later, and 16 (35%) didn't require surgery. Patients who had deterioration in sensorium or vision were taken for immediate surgery. Two patients died within 2 weeks of presentation, and 44 (95%) patients

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

survived the acute event. At 6-month follow-up, 44 patients survived, and none had recovery of the anterior pituitary hormonal axis.

Conclusions: In conclusion, the study indicates that there is no notable difference in neurohormonal outcomes between patients who underwent surgery and those managed conservatively.

Abstract citation ID: lvag096.1354

EP1092 - ECE_3505 - Adult follow-up of patients with pituitary stalk interruption syndrome: a tertiary single-center experience

Zeynep Elüstü Belten[1], Ozge Sahin Kimyon[1], Bahar Atasoy[2], Hamide Piskinpasa[1], İlkay Çakir[1], Meral Mert[1] and Sema Ciftci[1]

[1]Endocrinology and Metabolism, Sağlık Bilimleri Üniversitesi Bakırköy Doktor Sadi Konuk Eğitim Ve Araştırma Hastanesi, Bakırköy, Türkiye; [2]Radiology, Sağlık Bilimleri Üniversitesi Bakırköy Doktor Sadi Konuk Eğitim Ve Araştırma Hastanesi, Bakırköy, Türkiye

Objective: Pituitary stalk interruption syndrome(PSIS) is a rare congenital anomaly characterized by absence or interruption of the pituitary stalk, hypoplasia of the anterior pituitary, and ectopic localization of the posterior pituitary, and is commonly associated with multiple pituitary hormone deficiencies. This study aimed to characterize the clinical, hormonal, and radiological features of patients with PSIS followed at a tertiary referral center.

Methods: Fourteen patients diagnosed with PSIS and followed at our center were retrospectively evaluated. Data regarding birth and family history, perinatal complications, clinical presentation, hormonal status, laboratory findings, MRI characteristics, and treatment modalities were collected and analyzed.

Results: The study included 14 patients (8 males, 6 females) with a mean age of 28.7 years. Age at diagnosis ranged from 2 to 22 years. The mean follow-up duration was 67.1 months. Twelve patients were diagnosed during childhood and two during adulthood. A family history of PSIS was present in two patients, and parental consanguinity was reported in three. Perinatal complications were documented in eight patients. Short stature was the most common presenting complaint; other presentations included constipation, amenorrhea, delayed puberty, and seizures. Dysmorphic facial features were observed in two patients, and several patients had additional structural abnormalities of the central nervous system. Growth hormone (GH) therapy was administered to all patients except three, and all but one female patient diagnosed in adulthood achieved their target height. Hormonal evaluation revealed combined GH deficiency, secondary adrenal insufficiency, central hypothyroidism, and hypogonadotropic hypogonadism in 13 patients. One patient had isolated GH deficiency accompanied by hypogonadotropic hypogonadism. None of the patients exhibited clinical diabetes insipidus, while mild hyperprolactinemia was detected in six patients. MRI demonstrated a mean pituitary height of 2.52 mm. The pituitary stalk was interrupted in two patients, thin in one, and not visualized in eleven. The posterior pituitary was ectopically located at the median eminence in thirteen patients and was not identified in one. Metabolic evaluation revealed hepatosteatosis and hyperlipidemia in ten patients each. Bone mineral density was lower than expected for age in five patients. Four patients expressed fertility expectations, and one achieved a successful pregnancy resulting in a healthy child.

Conclusions: Although PSIS is most frequently diagnosed during childhood, diagnosis may be delayed until adulthood. Timely initiation of appropriate hormone replacement therapy facilitates achievement of target height. Given that adequate hormone replacement dosing and regular monitoring are crucial for preventing complications, long-term follow-up under the supervision of adult endocrinologists is essential.

Abstract citation ID: lvag096.1355

EP1093 - ECE_3508 - Are the patients with prolactinomas truly resistant to dopamine agonists or treated with too low doses?– single-center observational study

Maria Aleksandra Komisarz-Calik[1,2], Anna Bogusławska[1], Aleksandra Gamrat-Żmuda[1,2], Mari Minasyan[1], Beata Piwońska-Solska[1], Jacek Kunicki[3], Grzegorz Zielinski[4], Agata Faron-Górecka[5], Alicja Hubalewska-Dydejczyk[1] and Aleksandra Gilis-Januszewska[1]

[1]Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland; [2]Doctoral School of Medical and Health Sciences, Jagiellonian University Medical College, Kraków, Poland; [3]Maria Sklodowska-Curie National Research Institute of Oncology, Warszawa, Poland; [4]Department of Neurosurgery, Military Institute of Medicine, Warsaw, Poland; [5]Maj Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland

Objective: Cabergoline (CAB) is the first-line therapy for prolactinomas; however, a substantial proportion of patients fail to achieve normoprolactinemia or adequate tumor shrinkage. If not reimbursed, CAB remains an expensive medication, especially in high doses. The aim of this study was to assess treatment outcomes in patients with prolactinoma treated with CAB, evaluating whether low CAB doses may contribute to the high prevalence of apparent resistance.

Methods: 125 patients with prolactinoma treated with CAB were evaluated; 85 patients with a median follow-up of 52 months were included in further analyses. Clinical, biochemical, and radiological parameters were assessed at baseline, 6, and 12 months. Resistance was defined as failure to normalize serum prolactin (PRL) concentration or to achieve ≥30% reduction in maximal tumor diameter after at least 6 months of standard CAB therapy. Responders were patients who achieved both normoprolactinemia and ≥30% tumor diameter reduction after ≥6 months of CAB treatment, irrespective of the administered dose. Patients not meeting criteria for either response or resistance were classified as partial responders.

Results: Among 125 patients (73 males, 52 females), only 34 (27.2%) received CAB doses ≥2.0 mg/week at any time during follow-up. In the subgroup of 85 included patients, the maximal CAB dose during the first 6 months ranged from 0.25 to 4.0 mg/week (1.0 mg/week, IQR 0.75-2.0), and during 12 months from 0.25 to 4.5 mg/week (1.0 mg/week, IQR 0.75-2.0). At 6 months, 29.4% of patients were resistant, 7.1% responders, 63.5% partial responders; at 12 months, 31.8% were resistant, 10.6% responders, and 57.6% partial responders. Patients classified as resistant received significantly higher CAB doses than non-resistant patients at 6 and 12 months, yet these doses remained relatively low compared with guideline-recommended maximal doses. Higher

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

doses of CAB at 6 and 12 months correlated with higher reduction in tumor volume at 6 (rho = 0.443; rho = 0.384; $P < .001$) and 12 months (rho = 0.416; rho = 0.364, $P < .001$), respectively. Male patients received higher CAB doses than females at both follow-up visits (12 months: 1.5 mg/week (IQR = 1.0-2.5 mg/week) vs 1.0 mg/week (IQR = 1.0-1.5 mg/week), $P = .002$), respectively.

Conclusions: A high proportion of patients were classified as resistant and partial responders to CAB. This appears to be largely driven by the widespread use of low CAB doses. The lack of reimbursement and high cost of CAB likely limited dose escalation, contributing to apparent resistance rather than true pharmacological unresponsiveness.

Abstract citation ID: lvag096.1356

EP1094 - ECE_3951 - Clinical course of non-functioning pituitary adenomas: insights from a retrospective single-center study

Alessandro Bavaresco, Filippo Ceccato, Pierluigi Mazzeo, Alberto Madinelli, Giulia Bovo, Irene Tizianel and Mattia Barbot
Endocrinology Unit, Padua, Italy

Background: Non-functioning pituitary adenomas (NFPAs) represent the most common subtype of pituitary macroadenomas and common finding among microadenomas. NFPAs show in a wide range of clinical behaviours, from clinically silent to compressive symptoms or hypopituitarism. Despite advances in surgery and radiotherapy techniques, optimal management of NFPAs remains debated, particularly finding reliable predictors of growth or recurrence.

Objective: This study aimed to evaluate the clinical, radiological, and histopathological features of NFPAs and to analyze their long-term natural history in patients managed conservatively or treated surgically, with or without adjuvant therapies. Prognostic factors associated with tumor progression and clinical outcomes were also investigated.

Methods: A retrospective single-centre study was conducted on 170 patients diagnosed with NFPA, all of whom underwent long-term clinical and radiological follow-up. Both patients under active surveillance and those who underwent transsphenoidal surgery, with or without adjuvant treatments, were included.

Results: Radiological progression occurred in 27.8% of patients in active surveillance. Probability of growth at 5 years was higher in macroadenomas (45.7%) compared with microadenomas (22.5%) ($P = .030$). Larger tumor volume was a significant predictor of progression ($P = .004$), like visual field defects ($P = .008$). Tumor progression was also linked to a higher incidence of new-onset hypopituitarism ($P = .035$). In the surgical cohort, the presence of any residual tumor significantly raised the risk of progression ($P = .019$), while visual improvement was linked to a reduction of more than 40% in tumor volume ($P = .010$). No significant correlation was found between proliferative markers (Ki-67, p53, mitotic count) and progression. Tumor shrinkage after reoperation was significantly lower compared with initial surgery ($P = .017$). Stereotactic radiosurgery achieved disease stability in 88% of treated patients, while temozolomide resulted in stabilization in two of three cases. Male patients presented with larger tumors and more frequent visual and endocrine impairment, but no sex-related differences in progression rates were observed.

Conclusions: Active surveillance is a safe approach for asymptomatic patients, while surgery remains the treatment of choice in symptomatic tumors or those showing growth. Surgery provides prompt and effective visual improvement and local tumor control; however, postoperative hypopituitarism occurs in approximately one-third of cases. Complete surgical resection is the most reliable predictor of long-term tumor control, while proliferative markers appear to have limited prognostic value.

Abstract citation ID: lvag096.1357

EP1095 - ECE_1623 - Continuous glucose monitoring in idiopathic postprandial syndrome: benefit or burden?

Sanda Cho, Tahir Omer, Rawia Adoma, Rachel Si Jing Tan and William Braithwaite
Diabetes and Endocrinology, Bedford Hospital, Bedford, United Kingdom

Background: Idiopathic postprandial syndrome (IPS) is characterised by postprandial symptoms suggestive of hypoglycaemia occurring despite normal plasma glucose levels. The condition is uncommon, diagnostically challenging, and frequently associated with health anxiety and symptom fixation. With increasing availability of continuous glucose monitoring (CGM) devices outside clinical settings, there is growing concern that their use in individuals without diabetes may contribute to misinterpretation of glucose data and unnecessary medical intervention.

Case Presentation: A 48-year-old schoolteacher presented with recurrent hypoglycaemia-like symptoms including tremor, dizziness, diaphoresis, muscle twitching, and anxiety, predominantly in the postprandial period. She also reported cyclical exacerbation of symptoms around ovulation. The patient had independently obtained a CGM device, which reportedly demonstrated recurrent glucose readings below 2.0 mmol/L coinciding with symptoms. On this basis, true hypoglycaemia was initially suspected. Comprehensive evaluation was undertaken. Biochemical investigations including thyroid function, serum cortisol, liver and renal function, anterior pituitary hormone profile, HbA1c, and 24-hour urinary catecholamines, metanephrines, and 5-hydroxyindoleacetic acid were unremarkable. Cross-sectional abdominal imaging demonstrated normal pancreatic and adrenal anatomy. Crucially, both a supervised 72-hour fast and a mixed-meal test failed to demonstrate fasting or postprandial hypoglycaemia, supporting a diagnosis of idiopathic postprandial syndrome. Despite objective evidence excluding hypoglycaemia, the patient remained convinced her symptoms were glucose-mediated, a belief reinforced by CGM readings. Dietary modification was advised, and treatment with acarbose resulted in modest symptomatic improvement. Persistent distress and preoccupation with CGM data prompted referral for specialist neuroendocrine review.

Discussion: This case highlights the potential unintended consequences of CGM use in individuals without diabetes. While CGM can be a useful tool to exclude hypoglycaemia, its reduced accuracy in the hypoglycaemic range and lack of validation in non-diabetic populations may lead to false low readings. In susceptible individuals, this can reinforce maladaptive illness beliefs,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

contribute to functional endocrine disorders, and drive extensive and unnecessary investigations. Careful clinical correlation and biochemical confirmation remain essential. Management of IPS should focus on patient education, reassurance, and dietary strategies, with limited pharmacological options such as alpha-glucosidase inhibitors. Clinicians should be mindful of the psychological impact of CGM data and the risk of harm from over-monitoring.

Abstract citation ID: lvag096.1358

EP1096 - ECE_1365 - Oral urea for SIADH in chronic critical illness: preserving nutrition without hemodynamic compromise

Ane Azketa[1], Pol Candela[1], Mercè Serra[1], Marina Sisó[1], Miquel Blasco[2,3], Sara Torrejón[1], Pere Leyes[1,2] and Adriana Pané[1,2,4]

[1]Endocrinology and Nutrition Department, Hospital Clínic, Barcelona, Spain; [2]Facultat de Medicina i Ciències de la Salut, Universitat de Barcelona (UB), Barcelona, Spain; [3]Nephrology and Kidney Transplantation Department, Hospital Clínic, Barcelona, Spain; [4]Centro de Investigación Biomédica en Red de la Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III (ISCIII), Madrid, Spain

Background: Hyponatremia is the most frequent electrolyte disorder in critically ill patients and carries significant prognostic impact. In the setting of chronic critical illness, syndrome of inappropriate antidiuretic hormone secretion (SIADH) often becomes persistent due to sustained non-osmotic stimuli such as systemic inflammation, prolonged mechanical ventilation, and postoperative cardiac dysfunction. Conventional treatment strategies—including fluid restriction, sodium supplementation, and vasopressin receptor antagonists—may be ineffective or unsafe, particularly when high nutritional requirements and hemodynamic fragility coexist.

Case Presentation: We report the case of a 59-year-old man with multiple metabolic comorbidities admitted for native-valve infective endocarditis due to *Staphylococcus capitis*, complicated by a left ventricular outflow tract pseudoaneurysm. He underwent highly complex cardiac surgery with aortic valve replacement, pseudoaneurysm repair, venoarterial extracorporeal membrane oxygenation support, and delayed chest closure. The postoperative course was marked by severe biventricular dysfunction, pulmonary hypertension, prolonged mechanical ventilation, and a prolonged ICU stay (>4 months), evolving into chronic critical illness. During ICU stay, the patient developed hypoosmolar euvolemic hyponatremia (nadir serum sodium 122 mEq/L) consistent with SIADH. The clinical relevance of SIADH became evident during the transition from prolonged parenteral nutrition to enteral nutrition. Caloric targets were set at 1700-2000 kcal/day (25-30 kcal/kg/day, ideal body weight 68 kg). Severe diarrhea related to postatrophic malabsorption required progression from standard to oligomeric and finally elemental enteral formulas (0.86 kcal/mL), resulting in a high obligatory fluid load that made fluid restriction unfeasible. Recent cardiac surgery and ventricular dysfunction limited sodium supplementation (>2 g/day) and discouraged the use of vasopressin receptor antagonists.

Intervention and Results: Oral urea was initiated at 15 g/day via gastrostomy as a water-sparing osmotic strategy. This approach enabled effective free-water excretion without compromising nutritional delivery or hemodynamic stability. Serum sodium increased gradually (1.5-2 mEq/L/day), reaching 130 mEq/L within 72 hours and normalizing to 140 mEq/L at discharge, without neurological complications or cardiac decompensation. Importantly, oral urea allowed maintenance of elemental nutrition until gastrointestinal recovery permitted transition to a higher-caloric-density peptide-based formula with reduced volume requirements.

Conclusions: This case highlights oral urea as an effective, safe, and underutilized therapeutic option for SIADH in chronic critically ill patients, particularly when nutritional requirements and fluid restriction are in conflict. A nutrition-centered approach is essential for successful electrolyte management and functional recovery in this population.

Abstract citation ID: lvag096.1359

EP1098 - ECE_3144 - Ectopic dissemination of adamantinomatous craniopharyngioma following surgical drainage?

Francisca Leitão H., Vera Teixeira, Diogo Pinto, Denil Tribovane, Miguel Marques, Daniel Duarte, Marta Almeida, Henrique Vara Luiz, Maria Carlos Cordeiro, Ana Cristina Rios and Rosa Couto

Unidade Local de Saúde de Almada-Seixal, Almada, Portugal

Introduction: Craniopharyngioma are rare epithelial tumors derived from remnants of Rathke's pouch, with an annual incidence of 0.5-2 cases per million. Despite their benign histology, craniopharyngiomas may cause symptoms through compression of adjacent structures. Two histological variants are recognized: adamantinomatous and papillary. The standard treatment is surgical resection, with or without adjuvant radiotherapy. However, craniopharyngiomas have a high recurrence rate. While local recurrence is common, dissemination along the surgical tract or through cerebrospinal fluid (CSF) pathways are exceedingly rare, with only isolated cases reported, often following intraoperative cyst rupture or drainage procedures.

Case Report: We report a case of a currently 28-year-old male diagnosed with a sellar/suprasellar craniopharyngioma at 22 months of life after presenting with headaches. He underwent craniotomy surgery at that time, achieving gross total resection, and histological examination confirmed adamantinomatous craniopharyngioma, grade 1 (WHO2021). At 4 years of age, the patient had a tumor recurrence requiring a second craniotomy surgical resection, followed by adjuvant radiotherapy at 5 years of age, with subsequent remission. Eight years later, at 13 years-old, he presented with somnolence, vomiting, and morning headaches. Sellar MRI revealed a marked cystic recurrence associated with mild supratentorial hydrocephalus. A left pterional craniotomy was performed, achieving partial resection of the calcified component and drainage of a multiseptated cyst within the prechiasmatic and left optocarotid cisterns, followed by placement of an intratumoral catheter connected to a subgaleal Ommaya reservoir. Postoperative MRI revealed new cisternal lesions (prepontine, pontocerebellar, and retroclival), consistent with tumor seeding. The patient was closely followed and at 19 years-old, due to lesion progression he underwent a

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

suboccipital craniotomy with resection of lesions in the basal cisterns. Intraoperatively, removal of the catheter was attempted but was not feasible due to dense adhesions. Histopathology analysis confirmed adamantinomatous craniopharyngioma with nuclear beta-catenin positivity (CTNNB1 mutated). Further progression involving the cystic and ectopic cisternal components required Gamma Knife radiosurgery via a suboccipital approach at 25 years-old. Currently, residual tumor persists in both sellar and deep cisternal regions and is under regular follow-up. The patient developed panhypopituitarism and remains under hormone replacement therapy with levothyroxine, hydrocortisone, testosterone, and desmopressin.

Conclusions: This case illustrates the therapeutic challenges of adamantinomatous craniopharyngioma, a tumor prone to recurrence despite multiple surgical and adjuvant treatment modalities. The occurrence of tumor dissemination following Ommaya reservoir placement supports the possibility of viable tumor cell migration after surgical manipulation. Therefore, careful imaging surveillance and multidisciplinary management are essential.

Abstract citation ID: lvag096.1360

EP1099 - ECE_3546 - Multiadenomatous hypophysitis: a case report

Chayma Besrour[1], Wiem Helali[2], Hiba Bettaieb[3], Manel Boudokhane[3], Rim Bourguiba[2] and Syrine Bellakhel[2]
[1]*Endocrinology, Internal Security Forces Hospital Marsa, Tunis, Tunisia;* [2]*Internal Medecine, Internal Security Forces Hospital Marsa, Tunis, Tunisia;* [3]*Rhumatology, Internal Security Forces Hospital Marsa, Tunis, Tunisia*

Introduction: Hypophysitis is a rare autoimmune disease, corresponding to a chronic inflammation of the pituitary gland, the pathogenesis of which is complex and still poorly understood. It more frequently affects women. In rare cases, it can be caused by immunosuppressive treatment.

Case Report: Herein we report the case of a 35 years old patient with a medical history of an acute myelomonocytic leukemia treated with an immunosupressor “Cyclophosphamide” and an induced bilateral optic neuropathy as a side effect of the treatment. Laboratory investigations showed a low cortisol level confirmed twice at 139 nmol and 140 nmol (140-360 nmol/L) with an ACTH level 50.79 ng/mL (Upper normal limit 63.3 ng/mL). The exploration of the other pituitary axes did not show any abnormalities (FT4 8.67 pmol/L [7-14], TSH 4.42 U/L[0.34-4], Prolactin 9.47 ng/mL <20). The Pituitary MRI revealed Three small lesions suggestive of microadenomas. One anteromedial lesion 3.4 × 2.5 mm, one right Para median lesion 3.4 × 2 mm and one right posterolateral lesion 1.6 × 2 mm The diagnosis of corticotropic insufficiency secondary to hypophysitis was made and the patient was put on hydrocortisone

Discussion: Multiadenomatous hypophysitis is a rare condition where multiple pituitary adenomas, benign tumors of the pituitary gland, coexist. Cyclophosphamide, an immunosuppressive agent used to treat several conditions, can also cause side effects, including autoimmune complications such as hypophysitis and ocular complications such as optic neuropathy. These two complications are very rare, and their coexistence is even rarer. Careful monitoring of patients receiving immunotherapy is essential. Regular screening of pituitary function (ACTH, cortisol, TSH, free T4) before each immunotherapy cycle can help detect hypophysitis early. Patient education about the signs and symptoms of hypophysitis is also crucial to enable prompt and effective management.

Abstract citation ID: lvag096.1361

EP1100 - ECE_3550 - Partial empty sella as a delayed sequela of childhood meningitis: a case report

Müge Keskin[1], Fatma Yörük Durmaz[1], Nefise Özen[2], Arzu Or Koca[1] and Mustafa Cesur[3]
[1]*Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Endocrinology and Metabolism, University of Health Sciences, Ankara, Türkiye;* [2]*Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Internal Medicine, University of Health Sciences, Ankara, Türkiye;* [3]*Department of Endocrinology and Metabolic Diseases, Ankara Güven Hospital, Ankara, Türkiye*

Background: Empty sella is a radiological condition characterized by herniation of cerebrospinal fluid (CSF) into the sella turcica, leading to compression and flattening of the pituitary gland. It may be primary or secondary, the latter most commonly occurring after pituitary surgery, radiotherapy, apoplexy, or central nervous system infections. Childhood meningitis is an established but often underrecognized cause of secondary empty sella, with pituitary structural and functional consequences that may manifest years or decades after the acute infection. We report a case of partial empty sella detected during the evaluation of low insulin-like growth factor-1 (IGF-1), highlighting the potential long-term impact of childhood meningitis on pituitary integrity.

Case Presentation: A 51-year-old woman presented with progressive fatigue lasting three months. Her medical history was notable for bacterial meningitis during infancy. She had no history of pituitary surgery, cranial radiotherapy, head trauma, or postpartum hemorrhage, and no family history of pituitary disease. Physical examination was unremarkable except for low-normal blood pressure (100/50 mmHg), with no visual field defects or clinical signs of overt hypopituitarism. Laboratory evaluation revealed low age-adjusted IGF-1 levels (65-78 ng/mL; reference range 90-250 ng/mL), with a basal growth hormone level <1 ng/mL. Other pituitary axes were preserved, including TSH 1.8 mIU/L, free T4 1.1 ng/dL, prolactin 12 ng/mL, morning cortisol 14.6 µg/dL, and ACTH 28 pg/mL. Gonadotropins were appropriate for menopausal status (LH 32 IU/L, FSH 58 IU/L, estradiol 18 pg/mL). Serum sodium, glucose, and potassium levels were within normal ranges. Pituitary magnetic resonance imaging demonstrated CSF filling of the sella with flattening of the pituitary gland to a height of approximately 3 mm, consistent with partial empty sella.

Conclusions: Childhood meningitis may lead to delayed secondary partial empty sella in adulthood, occasionally presenting with subtle or subclinical endocrine abnormalities. Post-inflammatory alterations in CSF dynamics may contribute to progressive pituitary compression. Targeted hormonal evaluation and sellar imaging should be considered in symptomatic patients or those with unexplained biochemical abnormalities to prevent missed pituitary dysfunction.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1362

EP1101 - ECE_3743 - Persistent obstructive sleep apnea despite ENT management: when endocrinology makes the diagnosis

Alma Badnjevic-Cengic, Mubina Hodzic and Amila Čerim-Aldobašić
Department of Internal Medicine with Hemodialysis Cantonal hospital Zenica, Department of Endocrinology and Diabetes, Cantonal Hospital Zenica, Zenica, Bosnia and Herzegovina

Background: Obstructive sleep apnea (OSA) is commonly attributed to upper airway anatomical abnormalities and is primarily managed within ENT practice. However, endocrine disorders, particularly acromegaly, may represent an underlying and frequently overlooked cause. OSA may precede the classical phenotypic features of acromegaly for several years, leading to delayed diagnosis and increased morbidity.

Case presentation: A 46-year-old male was admitted to the Department of Endocrinology at Cantonal Hospital Zenica for evaluation of suspected acromegaly accompanied by clinical signs of secondary hypogonadism. The patient reported a four-year history of subjective sleep apnea episodes and dysphonia. OSA had previously been confirmed by polysomnography, and treatment with a positive airway pressure device had been initiated. Physical examination revealed coarse facial features with pronounced mandibular enlargement, enlarged tonsils and uvula, and arterial hypertension. Laboratory investigations demonstrated markedly elevated insulin-like growth factor 1 (IGF-1) at 931 ng/mL and growth hormone (GH) level of 9.36 mIU/L. Total testosterone was reduced (3.88 ng/mL), FSH 5.9 mIU/mL, LH 1.9 mIU/mL, consistent with secondary hypogonadism. Thyroid function tests were within reference ranges (TSH 1.22 mIU/mL, FT4 1.02 ng/dL), while prolactin was mildly elevated (530 mIU/L). Basal insulin was increased (29 mU/L), with normal fasting plasma glucose (5.3 mmol/L). Morning ACTH (8.7 pg/mL) and cortisol (161 nmol/L) levels indicated preserved hypothalamic–pituitary–adrenal axis function. Echocardiography excluded cardiac hypertrophy, while scrotal ultrasound revealed a left-sided spermatocele. Pituitary magnetic resonance imaging demonstrated an enlarged pituitary gland with a left-sided expansile lesion extending ventrolaterally into the sphenoid bone, associated with widening and deepening of the sella turcica. The lesion measured $11 \times 11 \times 13$ mm and was isointense with pituitary parenchyma, consistent with a pituitary adenoma. The patient initially underwent tonsillectomy, followed one month later by transsphenoidal surgery of the pituitary lesion. Histopathological examination confirmed adenohypophyseal hyperplasia. Postoperatively, the patient reported complete resolution of symptoms, without further need for ENT-directed treatment. Ongoing management includes low-dose levothyroxine and testosterone replacement therapy.

Conclusions: This case emphasizes that persistent OSA may represent an early manifestation of acromegaly and highlights the critical role of endocrinological assessment in patients with refractory OSA. Early multidisciplinary intervention enables timely diagnosis, targeted therapy, and significant clinical improvement.

Keywords acromegaly, obstructive sleep apnea, pituitary adenoma

Abstract citation ID: lvag096.1363

EP1102 - ECE_2948 - The inflammasome machinery is dysregulated and represents a therapeutic vulnerability in pituitary tumours causing Cushing's disease

Álvaro Flores-Martínez[1,2], Miguel E. G-Garcia[1,2], Laura Arroyo-Millán[1,2], Aura D. Herrera-Martínez[1,2,3], Paloma Moreno-Moreno[1,3], Antonio C. Fuentes-Fayos[1,2], Antonio Jesús Martínez-Fuentes[1,2,4], Eva Venegas Moreno[5], David Cano Gonzales[5], Alfonso Soto[5] and Raul M. Luque[1,2,4]
[1]Maimónides Biomedical Research Institute (IMIBIC), Reina Sofia University Hospital (HURS), Córdoba 14004, Spain; [2]Department of Cell Biology, Physiology and Immunology, University of Cordoba, Córdoba 14004, Spain; [3]Service of Endocrinology and Nutrition, Reina Sofía University Hospital (HURS), Córdoba 14004, Spain; [4]CIBER Pathophysiology of Obesity and Nutrition (CIBERobn), Córdoba 14004, Spain; [5]Unidad de Gestión de Endocrinología y Nutrición, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Sevilla, Spain

Introduction: Corticotroph pituitary tumours (ACTHomas) are the leading cause of Cushing's disease and remain clinically challenging due to their heterogeneous behavior and the limited medical options for refractory or aggressive cases. Growing evidence suggests that endocrine tumour phenotypes are strongly influenced by inflammatory cues; however, a comprehensive, mechanism-oriented characterization of the inflammasome dysregulation in human ACTHomas is still lacking. In this context, the inflammasome represents a key stress- and damage-responsive multiprotein machinery whose activation has been implicated in immune evasion, regulated cell-death programmes and tumour microenvironment (TME) remodelling. This study was performed to systematically characterize the inflammasome transcriptomic landscape in ACTHomas versus non-tumour pituitary tissues, to identify clinically relevant discriminant factors, and to functionally validate their therapeutic tractability in ACTHoma models. Specifically, a clinically well-characterized multicentric cohort and a microfluidic-based qPCR profiling was used/performed to quantify a curated panel of inflammasome-related genes encompassing priming, core, and effector components in ACTHomas ($n = 81$) versus non-tumour pituitary tissues ($n = 15$), followed by integrative bioinformatic analyses to prioritize key candidates. Candidate validation and functional interrogation were conducted through genetic modulation *in vitro* in the AtT-20 corticotroph cell line and in primary cultures derived from human ACTHomas, coupled with functional *in vitro* assays of proliferation and aggressiveness-related phenotypes. Our results revealed that ACTHomas exhibited a marked and coordinated deregulation of the inflammasome machinery compared with controls, which was independently reproduced in external validation cohorts. Top-ranked factors, robustly discriminated ACTHomas from non-tumour pituitaries, consistently clustering samples by disease status. Importantly, *in vitro* modulation of these top-ranked factors significantly impacted proliferation and aggressiveness-associated readouts in AtT-20 cells and in patient-derived ACTHoma primary cultures. Moreover, pharmacological blockade of the inflammasome machinery using anakinra (an IL1R1 antagonist) attenuated inflammasome-driven functional hallmarks of aggressiveness *in vitro*, supporting the druggability of this pathway in corticotroph tumours. Altogether, our data demonstrated a clinically relevant

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

inflammasome-associated molecular dysregulation in ACTHomas and identify specific components as discriminant biomarkers and actionable therapeutic targets, providing a strong rationale for repurposing inflammasome inhibition as a precision-oriented therapeutic strategy in Cushing's disease.

Fundings: Junta de Andalucia (PI-0117-2025, DGP_PIDI_2024_00134), ISCIII (CD24-00240), FSEEN.

Abstract citation ID: lvag096.1364

EP1103 - ECE_3892 - Differences in membranous SSTR2 expression between densely and sparsely granulated somatotroph PitNETs: a single-center retrospective study of 416 patients

Beata Rak-Makowska[1,2], Maria Maksymowicz[3], Grzegorz Zielinski[4], Agnieszka Piekielko-Witkowska[1] and Dominika Nowis[2,5]

[1]Department of Biochemistry and Molecular Biology, Centre of Postgraduate Medical Education, Centre of Translational Research, Warsaw, Poland; [2]Laboratory of Experimental Medicine, Medical University of Warsaw, Warsaw, Poland; [3]Department of Cancer Pathomorphology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [4]Department of Neurosurgery, Military Institute of Medicine - National Research Institute, Warsaw, Poland; [5]Department of Immunology, Medical University of Warsaw, Warsaw, Poland

Purpose: Somatostatin receptor type 2 (SSTR2) plays a key role in the response of somatotroph pituitary neuroendocrine tumors (PitNETs) to somatostatin analogues (SSA). Densely granulated (DG) and sparsely granulated (SG) somatotroph PitNETs differ in their clinical behavior, proliferative activity (Ki-67 labeling index), and invasiveness. Our aim was to compare SSTR2 expression pattern and clinicopathological characteristics between DG and SG somatotroph PitNETs in a large retrospective cohort.

Methods: We performed a retrospective analysis of 416 patients with somatotroph PitNETs treated at a tertiary referral center. Tumors were classified as densely granulated (DG, $n = 256$) or sparsely granulated (SG, $n = 160$) based on histopathological criteria and electron microscopy (EM). Immunohistochemical analyses included SSTR2 expression, Ki-67 labeling index, and alpha subunit staining. Tumor invasiveness was assessed using Knosp's grading system as described previously in the literature.

Results: Mean age in the DG group was 50.21 years (SD ± 12.85; median 52) and 45.45 years in the SG group (SD ± 12.55; median 44), respectively ($P = .0002$***). Women accounted for majority in both groups but with a higher proportion of males in the DG group (144 females, 112 males) compared with the SG group (115 females, 45 males; $P = .0014$**). DG somatotroph PitNETs showed significantly lower invasiveness compared with SG tumors, with Knosp's grades 2-4 observed less frequently in the DG group ($P < .0001$****). Higher Ki-67 labeling index was significantly more common in SG tumors ($P < .0001$****), indicating increased proliferative activity. Positive immunostaining for the alpha subunit was also more frequent in DG PitNETs ($P < .0001$****).

The distribution of SSTR2 immunostaining patterns differed significantly between DG and SG somatotroph PitNETs, with DG tumors showing more frequent combined membranous and cytoplasmic expression, while sparsely granulated tumors more often demonstrated cytoplasmic-only or absent SSTR2 staining ($P = .001$**). Furthermore, when we analyzed membrane-only and combined (membranous and cytoplasmic) versus cytoplasmic- only or absent, DG somatotroph PitNETs demonstrated functional (membrane only or combined) SSTR2 expression significantly more frequently than SG tumors.

Conclusions: DG and SG somatotroph PitNETs exhibit distinct clinicopathological profiles. SG tumors are characterized by younger age at diagnosis, female predominance, higher invasiveness, increased proliferative activity, and less frequently membranous SSTR2 expression. These findings support the biological heterogeneity of somatotroph PitNETs. Our results in this large cohort confirm prior literature on the importance of membranous SSTR2 expression for DG phenotype.

Funding: Grant from the National Science Center, Poland SONATINA UMO-2025/56/C/NZ4/00016 received by first author (B.R.M).

Abstract citation ID: lvag096.1365

EP1104 - ECE_1643 - Postoperative body composition outcomes in 104 patients with acromegaly: a single-center retrospective cohort study

Ryutaro Makino[1,2], Shingo Fujio[1,2], Jun Sugata[1,2], Shigeru Kawade[2,3], Katsutaro Morino[2,3] and Ryosuke Hanaya[1]

[1]Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan; [2]Pituitary Disorders Center, Kagoshima University Hospital, Kagoshima, Japan; [3]Department of Diabetes and Endocrine Medicine, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan

Background: Surgery for acromegaly improves quality of life and prognosis by normalizing GH and IGF-1 levels. However, abrupt hormonal shifts can induce changes in body composition. This study investigated longitudinal body composition changes and their clinical associations.

Methods: We retrospectively analyzed 104 acromegaly patients who underwent pituitary surgery between 2006 and 2024. Body composition data from preoperative to 3 years postoperative, including weight, body mass index (BMI), percent body fat (PBF), body fat mass (BFM), fat-free mass (FFM), total body water (TBW), and muscle mass (MM), were evaluated using bioelectrical impedance analysis.

Results: The mean age was 52.6 years, and 65.4% were female. Preoperative averages were: weight 65.4 kg, BMI 24.4, PBF 24.6%, BFM 16.1 kg, FFM 49.0 kg, TBW 36.1 kg, and MM 46.3 kg. Within one postoperative week, weight decreased by 2.9 kg, mainly from reduced TBW. By one year, BFM increased by 2.6 kg and weight returned to baseline; however, females showed greater 1-3-year declines in FFM and MM than males. At 12 weeks, IGF-1 normalized in 85.6%, and 50% achieved OGTT nadir GH < 0.4. IGF-1 normalization correlated with reduced FFM and improved glucose tolerance, whereas OGTT showed no clear associations. In patients with delayed postoperative hyponatremia (DPH), preoperative body weight and BMI were lower than in non-DPH cases. While body fat–related

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

indices were comparable between the groups, FFM, MM, and TBW were significantly lower.

Conclusions: After surgery for acromegaly, marked short-term reductions in TBW and longer-term increases in BFM with decreases in FFM were observed. Changes in FFM were particularly associated with sex and IGF-1 levels. Predicting postoperative body composition based on patient background and clinical factors may help optimize individualized strategies to prevent frailty and declines in quality of life.

Abstract citation ID: lvag096.1366

EP1105 - ECE_1819 - Impact of preoperative growth hormone levels on acromegaly-related complications

Daniela-Georgiana Amzar[1], Mihaela Maria Vlad[1], Melania Balas[1], Ioana Golu[1], Stoian Dana[1], Oriana Pelineagră[1] and Laura Cotoi[2]
[1]*Endocrinology, Spitalul Clinic Județean de Urgență Timișoara, Timișoara, Romania;* [2]*Endocrinology, Centre Hospitalier de Luxembourg, Luxembourg, Luxembourg*

Introduction: Acromegaly is a rare, insidious disease caused by excessive production of growth hormone (GH) and is associated with multiple complications. The prevalence of associated complications and mortality are related to the duration of exposure to elevated GH levels, making early diagnosis essential. The presence of multiple complications in these patients contributes to increased mortality/morbidity and decreased quality of life.

Methods: The study cohort comprised 22 patients with acromegaly (female-to-male ratio, 15:7), aged 24 to 71 years (50.00 ± 5.32). The patients were diagnosed and subsequently followed in the Endocrinology Department of our institution between 2000 and the present, in accordance with internationlly accepted diagnostic criteria.

Results: The diagnosis was delayed, 90.9% of the patients had pituitary macroadenoma (preoperative adenoma dimension 25.43 ± 12.50 mm) and 95% exhibited at least one acromegaly-related complication. The mean preoperative GH and insulin-like growth factor-1 (IGF-1) levels were 21.54 ± 25.51 ng/ml and 666.57 ± 346.10 ng/ml, respectively. The mean estimated disease duration was in the study group was 9.82 ± 5.32 years. Most patients underwent transfenoidal adenomectomy, with only one patient not receiving surgical tratment. Postoperatively, six patients had no tumour remnant, and the mean tumour remnant in the other 16 patients was 10.81 ± 6.81 mm. Eighteen patients required additional therapy with somatostatin analogues, 2 patients required GH receptor antagonist association and supplemental radiotherapy was recommended in 4 of them. Acromegaly-related complications were frequent in our cohort with 68.2% presenting left ventricular hyperthropy, 54.5% sleep apnoea, 13.6% atherosclerotic disease, 40.9% splenomegaly, 31.8% type II diabetes, 59.1% impaired glucose tolerance and 72.7% obesity. Visual field defects were present in 8 out of 9 patients who underwent ophthalmological examination. Pearson correlation analysis revealed no statistically significant association between the presence of acromegaly-related complications and preoperative GH and IGF-1 levels or total disease duration.

The normalisation of hormonal parameters in the following years was accompanied by an improvement of the clinical picture and complications, with an improvement of the quality of life.

Conclusions: Early diagnosis and timely assessment of complications play a critical role in improving quality of life and in reducing disease-related complications, morbidity and mortality.

Abstract citation ID: lvag096.1367

EP1106 - ECE_1674 - Genotype-phenotype correlation of ophthalmic, renal/genitourinary, neurological and neurodevelopmental manifestations in published cases of Bardet-Biedl syndrome

Mauro Longoni[1], Patrick Sleiman[1], Paul Park[1], Gian Sepulveda[2], Taylor Sells[2] and Gauri Malthankar[1]
[1]*Rhythm Pharmaceuticals, Inc., Boston, United States;* [2]*Coefficient Health, New York, United States*

Introduction: Bardet-Biedl syndrome (BBS) is a rare autosomal recessive ciliopathy that is diagnosed clinically based on Beales criteria, originally published in 1999. Among clinically diagnosed cases, 80%-90% are confirmed by genetic testing covering 26 associated genes. Genotype-phenotype correlations are limited, often based on cases or small studies.

Methods: A systematic literature search, covering January 1998-March 2025, was conducted to evaluate ophthalmic, renal/genitourinary, and neurological/neurodevelopmental manifestations in BBS using Human Phenotype Ontology terminology. Demographics, age of onset, body mass index (BMI), and gene variants were captured for each reported case. After deduplication, data were analysed at child and parent ontology levels, reporting frequencies, median age of onset, and interquartile ranges for each manifestation by the most frequently reported gene cohorts *BBS1*, *BBS10*, *BBS2*, and *BBS12*.

Results: From 415 screened publications, 261 were included, reporting individual patient data for 1776 patients (44.8% male, 36.6% female, and 18.6% unspecified) with over 500 manifestations. Genetic testing was performed in 86.2% of cases; 93.2% of those had variants reported. Among these, 24.0% had ≥1 variant in *BBS1*, 18.8% in *BBS10*, 12.5% in *BBS2*, and 8.3% in *BBS12*. Rod-cone dystrophy was most prevalent in *BBS2* (92.9%) and least in *BBS12* (69.8%). Night blindness was most common in *BBS1* (93.2%) and *BBS10* (95.4%) and least in *BBS12* (57.7%). Median age of onset of rod-cone dystrophy overall was 13-14 years, except in *BBS1* (21.5 years). Renal abnormalities ranged from 36.3% (*BBS1*) to 53.4% (*BBS10*), with renal cysts more frequent in *BBS12* (45.5%) than in other cohorts (23.1%-33.9%). Chronic kidney disease was highest in *BBS10* (17.7%) and *BBS2* (13.3%). Genitourinary abnormalities were most common in *BBS2* (70.8%) and *BBS12* (66.7%). In *BBS10,* neurodevelopmental delay was highest (69.9%), but intellectual disability less often reported (35.7%). Compared with Beales criteria, chronic kidney disease, renal cysts, and neurodevelopmental delay appear more common in published cases, while others (ataxia, speech deficit, micropenis) are less frequent.

Conclusions: Analysis of genetic and phenotypic data in 1776 published cases confirm the heterogeneity of major features of BBS, presenting a diagnostic challenge. These data confirm that clinical presentation, prevalence and age of onset of manifestations vary widely and differ by gene, highlighting the value of increased genotype-phenotype knowledge for patient counselling and management. As genetic testing becomes standard,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

further analysis may help define the minimal constellation of clinical manifestations needed for a molecular BBS diagnosis and refine diagnostic criteria.

Abstract citation ID: lvag096.1368

EP1107 - ECE_1775 - Scientific output and impact of rare endocrine disease registries: a quantitative exploratory analysis

Karen Tordjman[1,2], Merav Serebro[1], Etty Osher[1,2] and Yona Greenman[1,2]
[1]Metabolism and Hypertension, Institute of Endocrinology, Tel Aviv-Yafo, Israel; [2]Grey Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv-Yafo, Israel

Background: Registries for rare endocrine diseases aim to pool otherwise scarce clinical data to further knowledge about these conditions and to support research, guideline development, and clinical trials. Although many such registries have been created over the past decades, their scientific output and translational impact have rarely been examined in a systematic and quantitative way.

Objective: To assess the scientific output and guideline impact of registries devoted to rare endocrine conditions and to explore registry characteristics associated with greater impact.

Methods: An exploratory search identified 152 initiatives described as rare endocrine disease registries. Registries were included if they met a predefined operational definition, had at least 8 years of documented activity, enrolled between 700 and 7000 patients, and had produced registry-derived publications. Scientific output was assessed using a composite Registry Impact Index (RII), integrating annualized publication output, citation impact, production of highly cited papers, and contribution to clinical guidelines. Associations between RII and registry characteristics were explored using Spearman correlations, with sensitivity analyses using alternative weighting schemes.

Results: Fourteen registries met all inclusion criteria. The time from registry inception to first publication was substantial (median 5 years, range 3-13). Publication trajectories differed between registries, with some showing sustained output over time, while others appeared to plateau despite longer duration. This may relate to limited patient accrual, the coexistence of parallel registries, and practical difficulties in maintaining funding and long-term investigator involvement. Among 116 true original registry-derived studies, most relied on retrospective cross-sectional designs, while purely prospective longitudinal studies accounted for only 7% (8/116). Contribution to clinical guidelines was limited: only 10 studies (8.6%) reached a guideline output role score indicating a substantive contribution. Guideline contribution was strongly associated with publication output (true original studies per year, Spearman $\rho = 0.71$, $P = .004$) and with annual citation rates ($\rho = 0.69$, $P = .006$). The median RII was −0.27 (IQR −0.61 to 0.75; range −1.13 to 1.90), reflecting marked heterogeneity in scientific output. Registry size, disease rarity, governance model, industry involvement, geographic scope, maturity, and data platform adaptability were not independently associated with RII.

Conclusions: Scientific output among rare endocrine disease registries is heterogeneous and characterized by long publication latency, limited prospective research, and modest integration into clinical guidelines. While exploratory and requiring replication, these findings point to missed opportunities to make better use of registries for prospective studies, clinical trials, and knowledge generation.

Abstract citation ID: lvag096.1369

EP1108 - ECE_2149 - Nicotinamide phosphoribosyltransferase (NAMPT) inhibition—a novel metabolically-guided personalised therapy for neuroendocrine neoplasia

Katharina Wang[1], Julia Hamati[1], Umberto MacCio[2], Julian Maurer[1], Lea Peischer[1], Astrid Reul[3], Elena Kuzmenko[3], Petra Zimmermann[4], Maximilian Hungbauer[4,5], Diana Vetter[6], José Oberholzer[6], Thomas Knoesel[5,7], Mercedes Robledo[8,9], Katharina Schilbach[10], Christine Spitzweg[1,5], Matthias Auer[1], Ulrike Disko[1], Christian Lottspeich[1], Felix Beuschlein[1,3,11], Constanze Hantel[3], Martin Reincke[1], Nicole Reisch[1], Ashley B. Grossman[12,13], Karel Pacak[14,15], Kathrin Zitzmann[1], Christoph Auernhammer[1,5] and Svenja Noelting[1,3]
[1]Department of Medicine IV, LMU University Hospital, LMU Munich, Munich, Germany; [2]Department of Pathology and Molecular Pathology, University Hospital Zurich, Zurich, Switzerland; [3]Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich, Zurich, Switzerland; [4]Department of General, Visceral and Transplantation Surgery, LMU University Hospital, LMU Munich, Munich, Germany; [5]Interdisciplinary Centre of Neuroendocrine Tumours of the GastroEnteroPancreatic System (GEPNET-KUM, ENETS Centre of Excellence), LMU University Hospital, Munich, Germany; [6]Department of Visceral and Transplantation Surgery, University Hospital Zurich, Zurich, Switzerland; [7]Faculty of Medicine, LMU University Hospital, Institute of Pathology, Munich, Germany; [8]Hereditary Endocrine Cancer Group, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; [9]Centro de Investigación Biomédica en Red de Enfermedades Raras, Madrid, Spain; [10]Munich, Germany; [11]The LOOP Zurich- Medical Research Centre, Zurich, Switzerland; [12]Green Templeton College, University of Oxford, Oxford, United Kingdom; [13]Royal Free Hospital, NET Unit, ENETS Centre of Excellence, London, United Kingdom; [14]AKESO, Centre of Adrenal Endocrine Tumours, Prague, Czech Republic; [15]Palacky University, Olomouc, Czech Republic

Background: Tumour cells often display increased reliance on the salvage pathway for nicotinamide adenine dinucleotide (NAD^+) production, highlighting the rate-limiting enzyme of this pathway, nicotinamide phosphoribosyltransferase (NAMPT), as a potential target for anti-cancer therapy.

This study aimed to explore NAMPT inhibition as a novel therapeutic strategy for gastro-enteropancreatic (GEP) neuroendocrine tumours (NETs) and phaeochromocytomas/paragangliomas (PPGLs).

Methods: We investigated the effects of the NAMPT inhibitor GNE-617, and co-administration of niacin (vitamin B3), in GEP-NET/pulmonary NET and PPGL cell lines and fresh patient-derived GEP-NET/PPGL primary cultures ($n = 49$, including 1 neuroendocrine carcinoma [NEC] primary culture and 2 corresponding normal tissue primary cultures). We also extended our findings to pancreatic, thyroid and breast cancer cell lines. Additionally, we correlated cell viability data with NAPRT1 protein expression levels.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: We found strong significant anti-tumour effects of the NAMPT inhibitor GNE-617 in NAPRT1-deficient GEP-NET/pulmonary NET, PPGL, pancreatic, thyroid and breast cancer cell lines, and also in the GEP-NET/GEP-NEC and PPGL primary cultures. Niacin co-administration consistently rescued the NAPRT1-expressing cell lines from the anti-tumour effects of NAMPT inhibition, while having no effect in the NAPRT1-deficient cell lines. Niacin was also able to rescue 82% (22/27) of GEP-NET/GEP-NEC primary cultures and 50% (8/16) of PPGL primary cultures from the effects of NAMPT inhibition. In contrast, importantly, in 15% (4/27) of GEP-NET/GEP-NEC primary cultures and in 13% (2/16) of PPGL primary cultures, NAMPT inhibition led to strong anti-tumour effects (mean cell viability ≤60%) without tumour cell-rescue by niacin. Additionally, niacin rescued the normal tissue primary cultures from the effects of GNE-617, but not a corresponding small intestinal NET primary culture—suggesting NAPRT1-deficiency of the tumour but functional NAPRT1-expression in normal tissue.

Conclusions: Our results suggest that NAPRT1 expression could serve as a critical biomarker for predicting GEP-NET and PPGL tumour response to NAMPT inhibition, as well as potentially guide recommendations for niacin supplementation in patients with GEP-NETs or PPGLs. The pre-selection of patients based on this biomarker could enable precision targeted NAMPT inhibitor therapy of NAPRT1-deficient tumours, while preserving NAPRT1-expressing normal tissue with niacin co-administration.

Abstract citation ID: lvag096.1370

EP1109 - ECE_2744 - Neurofilament light chain and glial fibrillary acidic protein in chronic SIAD-induced hyponatremia

Clara Consoli[1,2], Cihan Atila[1,2], Jens Kuhle[3,4], Aleksandra Maleska[3,4], Julie Celine Refardt[1,2,5] and Mirjam Christ-Crain[1,2]

[1]*Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland;* [2]*Clinical Research, University Hospital Basel, Basel, Switzerland;* [3]*Basel, Switzerland;* [4]*Neurology, University Hospital Basel, Basel, Switzerland;* [5]*Endocrinology, Erasmus Medical Centre, Rotterdam, The Netherlands*

Background: Hyponatremia is the most common electrolyte disorder, most commonly due to the syndrome of inappropriate antidiuresis (SIAD). Chronic hyponatremia itself is associated with neurocognitive impairment, and its rapid correction can result in osmotic demyelination (ODS), which may be considered the end stage of a cascade of osmotic brain stress. Recently, we showed that acute hyponatremia and its correction are associated with increases in neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP), biomarkers of neuroaxonal and astrocytic injury. However, data on chronic hyponatremia and its correction are lacking. Here, we investigated whether chronic hyponatremia and cautious correction are associated with changes in NfL and GFAP.

Methods: Analysis of a randomized, double-blind, placebo-controlled trial conducted at University Hospital Basel, Switzerland, investigating the SGLT2 inhibitor empagliflozin as a treatment option for chronic hyponatremia due to SIAD. Participants received a 4-week treatment with empagliflozin or placebo in randomized order (crossover design). NfL and GFAP were measured at baseline and at the end of treatment (4 weeks), and results were presented as age- and BMI-adjusted Z-scores relative to a large healthy control population. Plasma sodium was assessed at baseline and 7 days post-treatment. We fitted a linear mixed-effects model to assess whether changes in plasma sodium during the first week of each treatment phase were associated with plasma NfL or GFAP levels at week 4.

Findings: In total, 11 out-patients (age: 72 years [62-77]) were included. Among patients, in the active treatment phase, baseline plasma sodium was 130 mmol/L [126-134], increasing by 4 mmol/L [1-5] within seven days. Plasma NfL-Z-score numerically increased from 0.2 [−0.6-0.9] at baseline to 0.4 [−1.0-1.2] within 4 weeks. Plasma GFAP slightly decreased from a baseline Z-score of −0.1 units [−0.8 to 0.2] to −0.3 units [−0.5 to 0.9] within 4 weeks. In a linear mixed-effects model, fitted with treatment group (empagliflozin vs placebo), sodium change, and their interaction, adjusting for baseline NfL-Z-scores, there was no significant association between the degree of sodium correction within 7 days with NfL-Z-scores measured at week 4 ($\beta = -.02$, 95% CI: −0.16 to 0.12, $P = .79$).

Conclusions: In patients with chronic hyponatremia, a cautious increase in plasma sodium was not associated with changes in NfL-Z-scores. These findings support the notion that slow correction of sodium levels in chronic hyponatremia is not associated with osmotic brain stress or neuronal injury.

Abstract citation ID: lvag096.1371

EP1111 - ECE_3011 - Evaluating endocrinopathies in patients with midline anomalies: a retrospective, single-center study

Mustafa Berkay Tastekin[1], Selin Tekin[2], Suleyman Nahit Sendur[2], Selcuk Dagdelen[2] and Tomris Erbaş[2]

[1]*Internal MEdicine, Hacettepe University School of Medicine, Ankara, Türkiye;* [2]*Department of Internal Medicine, Division of Endocrinology & Metabolism, Hacettepe University School of Medicine, Ankara, Türkiye*

Background: Midline anomalies are migration defects occurring while during development. They involve various systems and demonstrate a wide range of clinical variations. Moreover, it has been shown in many studies to cause various endocrinopathies, especially hypopituitarism. There are few studies due to low clinical awareness. We aimed to contribute to the literature on the management of endocrinopathy in patients with midline anomalies by retrospectively reviewing real-life data from our center.

Methods: Between January 2000 and 2025, patients with diagnoses of various midline defects or information regarding midline defects in their medical history were examined in the electronic registration system. Finally, we evaluated nine patients with holoprosencephaly (HOL), cleft lip and palate (CLAP) and absence of corpus Callosum (ACC).

Results: Seven patients (77.8%) were male. The median age at diagnosis was 1 (1-8) years and the median age at the time of study was 25 (19.5-37.5). The median follow-up period was 15.2 (12.6-21.0) years. Five patients (55.6%) had multiple pituitary hormone deficiency (MPHD). The most common pituitary hormone deficiency was hypogonadism, which occurs in seven

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

patients (77.8%). GH deficiency was detected in four patients (44.5%). Hypothyroidism and AVP deficiency were observed in three patients each (33.4%). The least common pituitary hormone deficiency was secondary adrenal insufficiency and hyperprolactinemia seen in only one patient. Furthermore, this patient was the only one with panhypopituitarism in our study. A total of seven patients (77.8%) had cleft palate and lip anomalies, with or without cranial anomalies. Two patients had no midline anomalies other than cleft palate and lip. Seven patients who underwent bone mineral density, five (71.4%) of them had measurements consistent with osteoporosis.

Conclusions: When patients present with a history of cleft lip and palate and mental retardation, clinicians might not initially consider endocrinopathy as the primary medical concern. In our study, we demonstrated the association between midline anomalies and hypopituitarism in adult patients presenting to the clinic. Our findings emphasize that clinicians should remain alert to hypothalamo-pituitary endocrinopathies in patients presenting with midline anomalies and neurological deficits.

Abstract citation ID: lvag096.1372

EP1113 - ECE_3454 - Inferior petrosal sinus sampling

Tereza Foglarová[1], Tomáš Padrta[2], Václav Hána[2], Jan Kaván[2], Adela Krausova[2], Michal Krsek[2], Tomas Brutvan[2], Jan Jiskra[2], Jana Jezková[2], David Netuka[3], Vaclav Masopust[3], Petr Vacek[3] and Martin Májovský[3]
[1]*3rd Department of Medicine, 1st Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic;* [2]*General University Hospital in Prague, Prague, Czech Republic;* [3]*Military University Hospital Prague, Prague, Czech Republic*

Background: Inferior petrosal sinus sampling (IPSS) is the most sensitive method for differentiating a pituitary from an ectopic source of adrenocorticotropic hormone (ACTH). It is recommended in patients with ACTH-dependent Cushing's syndrome and either a negative pituitary MRI or a pituitary adenoma <6 mm. The procedure consists of bilateral catheterization of the inferior petrosal sinuses via femoral venous access. After confirmation of correct positioning of both microcatheters near the sella turcica, corticotropin-releasing hormone (CRH) or desmopressin is administered to stimulate ACTH secretion. Blood samples are collected at predefined time intervals to measure ACTH levels and to assess the central-to-peripheral ACTH gradient. A basal gradient ≥2, or a stimulated gradient ≥3 after CRH/desmopressin administration, is consistent with a pituitary source of ACTH secretion.

Methods: Between 2022 and 2024, 20 patients with ACTH-dependent Cushing's syndrome were diagnosed at the General University Hospital in Prague. Inferior petrosal sinus sampling was performed in 15 of these patients. In 8/15 patients, pituitary MRI was negative; in the remaining patients, a suspected pituitary adenoma measuring 3-8 mm in maximal diameter was identified. One patient with a 20-mm pituitary adenoma also had a thyroid tumor detected on FDG - PET/CT. In 5/20 patients with a suspected pituitary adenoma measuring 5-19 mm, CRH/desmopressin stimulation tests were performed without IPSS.

Results: In all 20 patients, IPSS (15 patients) or CRH/desmopressin testing alone (5 patients) indicated a pituitary source of ACTH. In one patient, catheterization of the inferior petrosal sinuses was not feasible due to anatomical reasons, and only a CRH stimulation test was performed. In 2/15 patients, a basal ACTH gradient >2 was not present, and a diagnostic gradient (>3) was observed only after CRH/desmopressin stimulation. No complications related to the catheterization procedure were observed. Pituitary ACTH secretion was subsequently confirmed in all patients either by histological verification following neurosurgical resection or by postoperative resolution of hypercortisolism.

Conclusions: Inferior petrosal sinus sampling is a sensitive and safe method for differentiating ACTH-dependent hypercortisolism. In more than half of patients with a negative pituitary MRI, it confirms the indication for neurosurgical intervention.

Abstract citation ID: lvag096.1373

EP1115 - ECE_3673 - CD8$^+$ T-cell infiltration in PIT1-positive pituitary neuroendocrine tumors

Valeria Nicoleta Nastase[1,2,3], Iulia Florentina Burcea[4,5], Dumitriu Roxana Ioana[4,5], Amalia Raluca Ceausu[1,3], Flavia Zara[1,3,6], Catalina Poiana[4,5] and Marius Raica[1,3]
[1]*Victor Babes University of Medicine and Pharmacy, Timisoara, Romania;* [2]*Pius Branzeu University County Hospital, Timisoara, Romania;* [3]*Angiogenesis Research Centre, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania;* [4]*"C. I. Parhon" National Institute of Endocrinology, Bucharest, Romania;* [5]*Endocrinology Department, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania;* [6]*Emergency Clinical Municipal Hospital, Timisoara, Romania*

Introduction: Although pituitary neuroendocrine tumors (PitNETs) are generally benign, recent studies have identified aggressive variants that respond poorly to conventional therapies. Consequently, investigation of the tumor microenvironment has become mandatory for understanding pituitary tumorigenesis and developing new targeted treatments. A key component of this microenvironment is the immune cell population, which primarily includes: tumor-associated macrophages, dendritic cells, and tumor-infiltrating lymphocytes (TILs). CD8$^+$ cytotoxic T lymphocytes act as main effectors of antitumor immunity by targeting and destroying neoplastic cells.

Aim: To evaluate the distribution of CD8$^+$ TILs in a subset of PIT-1-positive PitNETs.

Materials and Methods: Twenty-eight PIT-1-positive PitNETs were included in the present study. An integrated diagnosis was performed by correlating clinical, radiological, histopathological and immunohistochemical (IHC) findings. IHC analysis included anterior pituitary hormones and transcription factors (PIT1, TPIT, SF1). CD8 marker was used to identify T lymphocytes, showing membranous staining. Positive cells were counted in five representative intratumoral high-power fields (×40), and the mean value was calculated.

Results: Histopathological analysis using routine hematoxylin–eosin staining revealed the following tumor growth patterns: diffuse ($n = 21$), papillary ($n = 5$), trabecular ($n = 1$), and alveolar ($n = 1$).

Immunohistochemical assessment of anterior pituitary hormones and lineage-specific transcription factors identified twelve somatotroph (GH$^+$/PIT1$^+$), eleven mammosomatotroph (GH$^+$/PRL$^+$/PIT1$^+$), and five plurihormonal PIT1-positive tumors (GH$^+$/PRL$^+$/TSH$^+$/PIT1$^+$).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

The number of CD8+ TILs varied among the three PIT1-positive tumor subtypes. In somatotroph tumors, the mean number of CD8+ cells per high-power field (HPF) was 2.43, with a median of 2.1. In mammosomatotroph tumors, the mean count was 1.91 cells/HPF and the median was 2.2. Plurihormonal PIT1-positive tumors showed the highest lymphocytic density, with a mean of 5.44 cells/HPF and a median of 2.8. Nine tumors showed no CD8+ TILs (three somatotroph, five mammosomatotroph, and one plurihormonal PIT1-positive case). The highest number of T lymphocytes, with a mean of 12 cells/HPF, was identified in a plurihormonal PIT1-positive tumor.

Conclusions: Although lymphocytic infiltration in pituitary neuroendocrine tumors may have therapeutic implications—the potential use of immunotherapy in aggressive cases—its distribution among different tumor subtypes remains incompletely characterized. T lymphocytes represent a central component of tumor immunology, acting as key effectors in the recognition and elimination of neoplastic cells.

Our results suggest subtype-dependent variation in CD8+ TILs density within PIT1-positive PitNETs, supporting the hypothesis that immune-endocrine interactions may shape tumor behavior and may hold therapeutic relevance.

Abstract citation ID: lvag096.1374

EP1116 - ECE_2417 - Pituitary apoplexy masquerading as infectious meningitis and complicated with salt-wasting syndrome in a man with pituitary macroadenoma - a case report and review of the literature

John Valsamidis[1], Chrysanthi-Tzenin Omar[1], Panagiotis Mpatzakis[1], Anastasios Poutachidis[1], Christina Tzoulakitze[1], Maria Sarigianni[1], Vasileios Kotsis[1], Maria Kosmidou[1] and Panagiotis Anagnostis[1,2]

[1]3rd Department of Internal Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Aristotle University of Thessaloniki, Thessaloniki, Greece

Pituitary apoplexy is a rare complication of pituitary macroadenomas, usually manifesting with acute headache, loss of consciousness, and visual disturbances. Herein, we report a case of pituitary apoplexy presenting with clinical and laboratory features mimicking bacterial meningitis. In particular, a 39-year old man was admitted to our department due to acute headache, fever, meningeal signs, and altered mental status. Initial clinical examination and laboratory investigation was compatible with inflammatory meningeal reaction, indicative of central nervous system (CNS) infection. Consequently, the patient was initially treated empirically with antibiotics. Magnetic resonance imaging (MRI) of the brain revealed a pituitary macroadenoma with areas of hemorrhage and necrosis, bilateral extrasellar extension to cavernous sinuses and suppression of optic chiasm, resulting in right temporal hemianopia and left loss of visual acuity. Endocrinological work-up showed panhypopituitarism, including also central diabetes insipidus. Therefore, hormone replacement therapy (HRT), including intravenous hydrocortisone, per os L-thyroxine and sublingual desmopressin, was initiated, leading to gradual improvement of his clinical status. However, due to persistent hyponatremia and severe natriuresis, with low aldosterone concentrations, a "cerebral salt-wasting syndrome (CSWS)" was suspected and, subsequently, the patient was started on fludrocortisone, which resulted in restoration serum and urinary sodium levels. Subsequent MRIs of the pituitary gland showed stabilization and a slight decrease in the size of macroadenoma. The patient was discharged under HRT, including also testosterone enanthate. In conclusion, pituitary apoplexy may rarely be complicated as CSWS and may mimic acute meningitis.

Abstract citation ID: lvag096.1375

EP1117 - ECE_2933 - Transient vasopressin deficiency following inhaled glucocorticoid–induced adrenal insufficiency: a case report

Stefano Testa[1], Vittoria Favero[1,2], Brian Randazzo[1], Elena Magni[3], Roberta Civiletti[3], Lisa Pancini[3], Natalie Prinzi[2] and Iacopo Chiodini[1,2]

[1]Department of Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [2]Endocrinology Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [3]TB Reference Centre and Lab, ASST Grande Ospedale Metropolitano Niguarda, Villa Marelli Institute, Milan, Italy

Introduction: Glucocorticoid-induced adrenal insufficiency (GIAI) is a common yet under-recognized consequence of prolonged glucocorticoid therapy. Although uncommon during inhaled glucocorticoid treatment, GIAI has been reported in selected clinical settings, particularly in the presence of CYP3A4-interacting drugs. In such patients, increased glucocorticoid receptor sensitivity has been hypothesized, potentially predisposing to both hypothalamic–pituitary–adrenal axis suppression and immunosuppression even at relatively low glucocorticoid doses, facilitating opportunistic infections.

Vasopressin deficiency (AVP-D) may result from various causes, including iatrogenic, neoplastic, autoimmune, infiltrative, inflammatory or infectious disorders affecting the hypothalamic–neurohypophyseal system.

Case report: We report a 56-year-old woman with severe asthma and pulmonary aspergillosis, managed with itraconazole (known CYP3A4 inhibitor) in addition to her ongoing fluticasone/vilanterol therapy. Few weeks after antifungal therapy, she developed clinical features of Cushing syndrome: cushingoid facies, easy bruising, hirsutism, proximal muscle weakness and myalgia.

Following itraconazole discontinuation, adrenal function testing revealed GIAI (cortisol 2.48 μg/dL; ACTH 13 pg/mL), associated with symptoms compatible with glucocorticoid withdrawal syndrome. Hydrocortisone was initiated (30 mg/day) with planned gradual tapering. However, due to early recurrence of cushingoid features, rapid dose reduction was required, followed by clinical improvement.

Three months later, the patient reported new-onset intense thirst and polyuria, up to 4 L/day for two weeks. Initial investigations showed: copeptin 2.3 pmol/L, sodium 143 mmol/L, preserved renal function, urine specific gravity 1.016, serum osmolality 299 mOsm/kg, urine osmolality 99 mOsm/kg. Over the subsequent month, polyuria worsened (approximately 7 L/day), prompting initiation of low-dose desmopressin and hospital admission.

At admission, laboratory findings were consistent with AVP-D. However, a rapid spontaneous improvement in symptoms and fluid balance occurred within days. Therefore, desmopressin

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

was progressively reduced and withdrawn. By day 6, biochemical parameters confirmed the improvement in the hydroelectrolytic profile (serum osmolality 290 mOsm/kg, urine osmolality 465 mOsm/kg). Anterior pituitary function was preserved, except for the pre-existing GIAI.

Pituitary MRI demonstrated a poorly defined 4-mm lesion adjacent to the neurohypophysis, hypointense on T2-weighted sequences, with reduced contrast enhancement and pituitary stalk thickening, suggestive of an inflammatory/infectious focus.

Conclusions: This case highlights the complex interplay between prolonged glucocorticoid therapy, opportunistic infections, and AVP-D. In a patient with possible increased steroid sensitivity, rapid steroid tapering in the presence of an inflammatory/infectious neurohypophyseal lesion may have contributed to hypothalamic–neurohypophyseal dysregulation, precipitating a transient functional AVP-D. Awareness of uncommon causes of AVP-D and their interactions with the hypothalamic–pituitary–adrenal axis is crucial to optimize management and follow-up.

Abstract citation ID: lvag096.1376

EP1119 - ECE_3610 - Giant haemorrhagic prolactinoma presenting with temporal lobe epilepsy

Hannah Brown[1], Waseem Majeed[1,2], Adhithya Sankar[3], Adam Robinson[1] and Tara Kearney[1,2]
[1]*Department of Diabetes, Endocrinology and Obesity Medicine, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Salford M6 8HD, United Kingdom;* [2]*Faculty of Biology, Medicine and Health, The University of Manchester, Manchester M13 9PL, United Kingdom;* [3]*Department of Diabetes, Endocrinology and Obesity Medicine, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Salford, United Kingdom*

Introduction: Giant prolactinomas are rare secretory pituitary adenomas, defined by a diameter >40 mm and markedly elevated serum prolactin levels. While visual field defects and hypopituitarism are classic complications, neurological sequelae from involvement of adjacent cerebral structures are less commonly reported. This case highlights an unusual neurological presentation of focal seizures in patient with treated giant prolactinoma, illustrating the long-term consequences not only from tumour extension, but from regression.

Case presentation: A 44-year-old male with a history of treated systemic tuberculosis initially presented with headaches and low libido. MRI of the head identified an extensive skull base tumour (57 mm × 86 mm) with suprasellar and right-sided temporal lobe extension, including a haemorrhagic component. Biochemistry confirmed markedly elevated serum prolactin of 176 000 mIU/L and hypogonadotropic hypogonadism (LH 1.5 U/L, FSH 1.7 U/L, testosterone 2.4 nmol/L), with intact thyroid, adrenal and growth hormone axes. A diagnosis of giant invasive prolactinoma was made and he was commenced on dopamine agonist (DA) with cabergoline and testosterone replacement. Subsequent dynamic MRI of the pituitary demonstrated significant tumour shrinkage, indicating tumour responsiveness to DA.

After 6 months of DA therapy, the patient presented to the emergency department with an acute episode of confusion and memory loss consistent with a focal seizure. Initial investigations, including blood tests and a CT head, were unremarkable. A retrospective review of imaging from diagnosis showed progressive haemosiderin deposition and residual gliosis in the temporal lobe, with tumour regression. This chronic scarring likely caused cortical irritation, triggering a focal seizure. No alternative metabolic or infective cause was identified, and the patient was referred for neurology review.

Discussion/conclusions: Giant prolactinomas are rare (2%-4% of prolactinomas) and can exhibit aggressive behaviours with skull base invasion, making differentiation from malignant brain tumours difficult. Furthermore, inflammatory conditions such as pituitary tuberculosis can mimic a suprasellar mass with elevated prolactin, a pertinent differential in patients with a history of systemic TB. The key to management is early biochemical identification of significantly elevated prolactin, confirming the diagnosis and allowing for medical therapy. Though DA remains the first line therapy; a subset of patient may need early multimodal therapy. Tumour shrinkage with DA can lead to chronic gliotic changes which may confer a long-term seizure risk. This case emphasises that acute neurological symptoms can emerge later in the treatment course, necessitating long-term vigilance and multidisciplinary follow-up.

Abstract citation ID: lvag096.1377

EP1120 - ECE_3897 - Manic episode as a severe neuropsychiatric manifestation of Cushing's disease

Adriana Duarte[1], Mariana Coelho[1], Ana Margarida Sobral[1], Bárbara Jesus[1], Leonor Rodrigues[2], Alice Monsanto[1], Mariana Lavrador[1], Daniela Guelho[1] and Leonor Gomes[1]
[1]*Coimbra's Local Health Unit, Endocrinology, Diabetes and Metabolism, Coimbra, Portugal;* [2]*Local Health Unit of Aveiro, Aveiro, Portugal*

Introduction: Neuropsychiatric manifestations are frequent and debilitating complications of Cushing's syndrome, affecting up to 80% of patients. However, manic episodes and psychosis occur in approximately 30% and may represent the initial presentation. Preoperative medical treatment has shown efficacy in normalizing cortisol levels and improving neuropsychiatric symptoms in severe hypercortisolism.

Case-report: A 38-year-old woman with no relevant past medical history was referred to the Endocrinology outpatient clinic with a 6-month history of progressive insomnia, 9-kg weight gain (+15%), hirsutism, and new-onset facial acne. Physical examination revealed hirsutism on the upper limbs and scapular region, acne on the chin and frontal region, and a buffalo hump without other stigmata of hypercortisolism. Laboratory investigation confirmed endogenous hypercortisolism: 1-mg dexamethasone suppression test cortisol 13.1 μg/dL; 24-h urinary free cortisol (UFC) 669 μg/24 h (4.3-176; urine volume 1900 mL); late-night salivary cortisol 1.2 μg/dL; morning cortisol 22 μg/dL; ACTH 63 pg/mL; and 11 PM serum cortisol 21 μg/dL. She also presented dyslipidemia and HbA1c of 6.1%. Pituitary MRI revealed a 5-mm right-sided inferior microadenoma. Inferior petrosal sinus sampling confirmed right-sided lateralization, concordant with MRI findings (central-to-peripheral gradient >3 after stimulation). She was started on metformin 700 mg twice daily, atorvastatin 40 mg, trazodone 150 mg and edoxaban 60 mg once daily, and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

referred for neurosurgery with intent of short-term surgical intervention. Three months later, she presented to the psychiatric emergency department with worsening insomnia, behavioral changes with psychomotor agitation, and disorganized speech with persecutory ideation. Examination showed motor restlessness, disinhibition, tachypsychia, and marked emotional lability, with no insight. She had no prior psychiatric history. A manic episode in the context of uncontrolled hypercortisolism was assumed, and she was admitted with Endocrinology support. Treatment with antipsychotics and metyrapone 250 mg twice daily was initiated, later adjusted to a total daily dose of 750 mg. At discharge, biochemical normalization was achieved: UFC 122 μg/24 h(urine volume 2300 mL), 11 PM cortisol 12 μg/dL, 8 AM cortisol 14 μg/dL, and late-night salivary cortisol 0.23 μg/dL. No liver enzyme abnormalities were observed, and complete remission of the manic episode occurred. The patient remains clinically stable and has transsphenoidal surgery scheduled.

Conclusions: This case highlights the importance of recognizing severe neuropsychiatric manifestations of Cushing's disease, including manic episodes, which may occur without prior psychiatric history. Metyrapone was effective and safe for rapid control of hypercortisolism, achieving biochemical normalization and remission of psychiatric symptoms. Preoperative medical treatment with steroidogenesis inhibitors is a key strategy in patients with severe hypercortisolism or complications delaying surgery, allowing stabilization and optimization for definitive management.

Abstract citation ID: lvag096.1378

EP1121 - ECE_1058 - Structural and functional parameters of the left heart in patients with acromegaly: changes at 1 year follow up

Ivana Ságová[1,2], Tomáš Bolek[2], Milan Dragula[2], Martin Péč[2], Jakub Jurica[2], Marián Mokáň[2] and Matej Samoš[2]
[1]Department of Endocrinology, National Institute of Endocrinology and Diabetology, Ľubochňa, Slovakia; [2]Prague, Czech Republic

Background: The aim of this study was to assess changes in the morphology and function of the left heart using two-dimensional transthoracic echocardiography (TTE) in newly diagnosed patients with acromegaly (AP) 1 year after the initiation of treatment (transsphenoidal surgery and/or somatostatin analogues) and to explore the effects of disease activity and body composition parameters on changes of the left heart.

Patients and Methods: This prospective study included 34 AP and 34 age-, sex-, and body mass index–matched healthy controls (CON). Physical and laboratory examinations, DXA and TTE were performed at baseline and 1 year after initiation of acromegaly treatment.

Results: At baseline, AP exhibited an increased left atrial volume index (LAVI) and diastolic dysfunction of the left ventricle (LV). The left ventricular mass index (LVMI) was significantly higher in AP compared with CON (124 vs 86 g/m^2, $P < .001$), while LV size and systolic function did not differ between groups. One year after treatment initiation, serum IGF-1 and GH levels decreased significantly ($P < .001$), and biochemical disease control was achieved in 73.5% of patients. In AP, both LAVI and LVMI decreased significantly ($P < .05$), and LV diastolic function improved without changes in systolic function. Multiple regression analysis identified changes in body surface area ($\beta = -.444$, $P < .001$) and lean body mass ($\beta = -.298$, $P = .027$) as independent predictors of LVMI reverse remodeling after the treatment.

Conclusions: This study demonstrates that effective treatment of acromegaly leads to a reversal of left heart remodeling and improvement in left ventricular diastolic function within one year of therapy initiation in previously untreated AP.

Keywords acromegaly, body composition, growth hormone, insulin-like growth factor 1, 2D echocardiography

Abstract citation ID: lvag096.1379

EP1122 - ECE_1713 - ATRX mutation and HER-2/neu receptor positivity in a cohort of clinically silent corticotropic PitNETs

Matej Bronec[1], Mikulas Kosak[1], Jana Jezkova[1], Monika Manethova[2], Quang Bui[2], Vaclav Masopust[3], David Netuka[3], Martin Májovský[3], Michal Krsek[4], Vaclav Hana[4], Václav Hána[4], Eva Traboulsi[5] and Jiří Soukup[5]
[1]Prague, Czech Republic; [2]First Faculty of Medicine, Charles University and General University Hospital, Institute of Pathology, Prague, Czech Republic; [3]Department of Neurosurgery and Neurooncology, First Faculty of Medicine, Charles University and Military University Hospital, Prague, Czech Republic; [4]Third Department of Internal Medicine, First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic; [5]Department of Pathology, Military University Hospital, Prague, Czech Republic

Introduction: Clinically silent ACTH-positive PitNETs are considered to be locally aggressive. ATRX is a tumor suppressor gene whose somatic mutations have been identified across a range of typically aggressive neoplasms. Loss of ATRX protein expression by immunohistochemistry (IHC) is routinely used as a surrogate for mutational status. ATRX alterations have been reported in aggressive pituitary neuroendocrine tumors (PitNETs) and pituitary carcinomas.

The HER2/neu receptor is overexpressed in multiple tumor types; beyond breast cancer, overexpression has been reported in subsets of gastric, endometrial, and salivary gland cancers. HER2/neu positivity has also been observed in aggressive prolactinomas and has been associated with increased hormonal activity and accelerated tumor growth. In some tumor types, HER2/neu expression has therapeutic implications because targeted therapies are available. To date, ATRX status and HER2/neu expression have not been systematically evaluated in silent corticotroph (Tpit-lineage) PitNETs.

Patients and Methods: We performed a retrospective review of patients who underwent pituitary surgery at our center from January 2020 through December 2024. Inclusion criteria were Tpit-lineage PitNETs without clinical or biochemical evidence of Cushing's syndrome. IHC for ATRX and HER2/neu was performed on all cases; additional IHC for Tpit and ACTH was performed selectively. Clinical and histopathological data were extracted from medical records.

Results: The study cohort comprised 30 patients (50% female) aged 27-85 years (mean 53 years). Ki-67 index was ≤1% in 18 patients, 1%-3% in 7 patients, and ≥3% in 5 patients (range 0.6%-10%). Four tumors expressed Tpit but lacked ACTH expression; one tumor was classified as a Crooke cell tumor.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Radiologically, cavernous sinus invasion (Knosp grade ≥1) was present in all but one case (Knosp grade 0). Knosp grade distribution: grade 1, 23.3% ($n = 7$); grade 2, 16.6% ($n = 5$); grade 3, 23.3% ($n = 7$); grade 4, 33.3% ($n = 10$). None of the samples demonstrated loss of ATRX expression by IHC. HER2/neu was not expressed in any case, aside from four tumors showing ultralow (borderline/minimal) staining scores.

Conclusions: In this series of silent corticotroph (Tpit-lineage) PitNETs, we found no immunohistochemical evidence of ATRX loss or clinically relevant HER2/neu overexpression. These findings contrast with prior reports that identified ATRX alterations in aggressive PitNETs and pituitary carcinomas and HER2/neu positivity in other subtypes of PitNETs.

Abstract citation ID: lvag096.1380

EP1123 - ECE_1878 - When acromegaly reveals a mixed gangliocytoma–somatotroph PitNET

Filipa Barros Alves[1], Tânia Fernandes[1], Marta Castro Tomé[1], Rosa Maria Príncipe[1,2], Jorge Pinheiro[3], Joana Oliveira[3], Josué Pereira[3] and Cláudia Nogueira[1,2]

[1]Local Health Unit of Matosinhos, Matosinhos, Portugal; [2]Faculty of Medicine, University of Porto, Porto, Portugal; [3]Local Health Unit of São João, Porto, Portugal

Introduction: Acromegaly is a rare endocrine disorder caused by chronic growth hormone (GH) excess, most frequently due to a pituitary neuroendocrine tumor (PitNET). Mixed pituitary adenoma and gangliocytoma tumors are rare and may be difficult to distinguish from conventional pituitary adenomas pre-operatively. The majority of gangliocytomas are associated with clinical manifestations of anterior pituitary hormone hypersecretion, particularly GH. Only a limited number of cases of these mixed tumors have been reported, and their clinical significance remains incompletely understood.

Case presentation: A 64-year-old woman with a history of dyslipidaemia, subclinical hypothyroidism previously treated with low-dose levothyroxine and depressive disorder was referred for endocrinological consultation after incidental detection of a sellar mass on cervical MRI performed during the investigation of salivary gland hypertrophy. She reported long-lasting headaches, hyperhidrosis and enlargement of the hands, without visual disturbances. Physical examination revealed coarse facial features and enlarged hands. Biochemical evaluation showed an IGF-1 of 419 ng/mL (normal range 40-225), FSH 21.98 mUI/mL, LH 5.54 mUI/mL, estradiol <13 pg/mL, morning cortisol of 12.8 ug/dL, prolactin 8.63 ng/mL, normal TSH 3.39 uUI/mL and free T4 1.01 ng/dL. Hypercalcaemia of 10.7 mg/dL with hypercalciuria (445 mg/24 h) and parathyroid hormone of 73.7 pg/mL (normal range 15.0-68.3) were also present. Pituitary MRI demonstrated a large pituitary macroadenoma (26 mm craniocaudal diameter) with suprasellar extension, cavernous sinus invasion and contact with the optic chiasm.

Management and Histopathology: The patient underwent transsphenoidal pituitary surgery. Histological examination revealed a biphasic neoplasm with an intermingled pattern, composed of adenohypophyseal cells and a neuronal component with dysmorphic ganglion cells. Immunohistochemistry showed synaptophysin expression in both components and chromogranin positivity in ganglion cells. Adenohypophyseal cells demonstrated diffuse Pit-1 expression, weak and diffuse GH positivity, and scattered prolactin expression, with no expression of TSH, ACTH, FSH or LH. The Ki-67 proliferation index was <1%. These findings were consistent with a mixed gangliocytoma–somatotroph PitNET of sparsely granulated type. Postoperative endocrinological follow-up is ongoing.

Conclusions: This case highlights a rare mixed pituitary tumor presenting as acromegaly and underscores the importance of detailed histopathological and immunohistochemical characterization. Given the limited number of reported cases, the clinical behaviour and prognostic implications of mixed gangliocytoma–somatotroph PitNETs remain incompletely understood, justifying careful long-term follow-up.

Abstract citation ID: lvag096.1381

EP1124 - ECE_2244 - Is it time to redefine the treatment algorithm for acromegaly?

Cristina Guillen[1], Ruth Sanchez-Ortiga[1], Clara Navarro-Hoyas[1], Elena García[1], Jorge Navarro[2], Johana Sottile[2], Javier Abarca Olivas[1], María Eugenia Torregrosa-Quesada[1], Joaquin Serrano[1], Francisca María Peiró-Marqués[1] and Antonio Pico[1]

[1]Hospital General Universitario Dr. Balmis, Alicante, Spain; [2]Instituto de Investigación Biomédica de Alicante (ISABIAL), Alicante, Spain

Introduction: The latest consensus on acromegaly emphasizes the importance of early biochemical control. Although information exists regarding presurgical treatment with somatostatin analogs,the results are heterogeneous. Regardin pegvisomant, there is no prior evidence of its use before surgery. Pegvisomant would be ideal in this period given that it is independent of tumor biology, with rapid effectiveness (4-6 weeks) without requiring dose titration. Preoperative biochemical optimization could mitigate anesthetic risks and improve surgical outcomes, but optimal strategies remain undefined.

Objective: To evaluate the efficacy and safety of preoperative treatment with pegvisomant to achieve rapid biochemical control and metabolic optimization prior to transsphenoidal surgery in patients with acromegaly.

Methods: Prospective cohort study that included 10 treatment-naïve patients with acromegaly who received preoperative therapy with pegvisomant (mean dose 20 mg/day, mean duration 90.4 days) followed by transsphenoidal surgery. The evolution of IGF-1 concentrations, metabolic profile (fasting glucose, HbA1c), quality of life (AcroQoL), tumor immunohistochemistry (SSTR2/5 expression, granularity), perioperative complications, and biochemical remission rates were evaluated.

Results: Preoperative treatment with pegvisomant achieved a significant reduction in IGF-1 from 617.2 ± 203.4 ng/mL at baseline to 373.8 ± 175.9 ng/mL pre-surgery (39% reduction, $P < .001$). Following surgery, IGF-1 concentrations reached a nadir of 177.2 ng/mL at the last visit (total reduction of 71% from baseline). Ninety percent of patients (9/10) achieved biochemical control (IGF-1 < 1.3 × ULN) at final follow-up. Using this therapeutic algorithm and guided by personalized medicine, control was achieved in record time (less than three months after surgery). Metabolic parameters improved substantially: fasting glucose decreased from 146.2 mg/dL to 96.2 mg/dL ($P = .0044$) and HbA1c from 6.84% to 6.00% ($P = .0196$). Quality of life improved significantly as assessed by AcroQoL ($P = .0016$). No serious adverse events or major perioperative complications were recorded.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: Short-term treatment with pegvisomant in the presurgical period rapidly achieves biochemical control and metabolic optimization in patients with acromegaly, potentially reducing perioperative anesthetic and surgical risks. This approach demonstrates to be a safe and effective strategy that optimizes presurgical biochemical control, improves metabolic profile and quality of life, and potentially increases surgical remission rates. These findings suggest the need to redefine the current therapeutic algorithm for acromegaly.

Abstract citation ID: lvag096.1382

EP1125 - ECE_2255 - Predictive value of copeptin for the diagnosis of arginine-vasopressin deficiency in the early postoperative period following pituitary surgery

Paola Parra-Ramírez[1,2,3], Patricia Martín Rojas-Marcos[1], Carlos Pérez López[4], Pablo García Feijoo[4], María Luisa González Casaus[5], Abraham García López[5], María Carmen Hernández Lucas[6], Arturo Lisbona Catalán[1] and Maria Cristina Alvarez Escola[1]

[1]Endocrinology & Nutrition Department, Hospital Universitario La Paz, Madrid, Spain; [2]La Paz University Hospital, Madrid, Spain; [3]Hospital Universitario La Paz, Madrid, Spain; [4]Neurosurgery Department, Hospital Universitario La Paz, Madrid, Spain; [5]Laboratory Medicine, Hospital Universitario La Paz, Madrid, Spain; [6]Anesthesiology Department, Hospital Universitario La Paz, Madrid, Spain

Introduction: Arginine-vasopressin (AVP) deficiency, is a frequent complication following sellar area surgery, with a prevalence ranging from 1% to 67%, depending on the medical center. Traditional diagnosis relies on monitoring polyuria and biochemical parameters such as natremia and urinary osmolarity; however, this approach is time-consuming and requires frequent blood tests, making it a common cause of prolonged hospital stays. Copeptin, the C-terminal fragment of pro-vasopressin, has emerged as a reliable surrogate biomarker for AVP. It exhibits greater in vitro stability and is secreted equimolarly with AVP in response to physiological stress and osmotic stimuli.

Methods and Objectives: This prospective study, conducted at Hospital Universitario La Paz (HULP), Madrid, evaluated patients undergoing sellar and parasellar surgery over an-18-month period. The primary objective was to analyze the evolution of copeptin in the early postoperative phase to establish discriminative cut-off points that facilitate the rapid diagnosis or exclusion of AVP deficiency. Measurements were taken at six time points: pre-surgery, 1 hour after extubation, and at 1, 2, 7 days, and 5 weeks postoperatively. Optimal cut-off values were determined using ROC curve analysis.

Results: Among the patients studied, 13% developed permanent AVP deficiency and 12% developed transient deficiency. Surgical stress significantly stimulates copeptin release in patients with intact neurohypophyseal function. Patients without deficiency showed markedly higher copeptin levels one hour post-extubation (median 19.18 pmol/L) compared to those who developed the deficiency (median 4.28 pmol/L). To safely "rule out" the condition, cut-off points were identified as >3.34 pmol/L at one hour after extubation and >2.3 pmol/L between the first and second postoperative days. In general, values below 2.5-3.5 pmol/L were associated with the development of deficiency. Additionally, it was identified that the risk is higher in patients with non-adenomatous tumors (such as craniopharyngiomas or meningiomas) and those with a pre-surgical ACTH deficiency.

Conclusions: Copeptin is established as an early and reliable marker to guide postoperative management. Its implementation would reduce the number of laboratory tests required after discharge, optimize the use of desmopressin, and help predict the risk of developing postoperative SIADH, thereby improving efficiency in high-complexity surgical centers

Abstract citation ID: lvag096.1383

EP1126 - ECE_2724 - Prevalence and characteristics of secondary adrenal insufficiency in patients with euvolemic hyponatremia

Michelle Müller[1,2], Lea Galvagno[1,2], Laura Potasso[1,2], Julie Celine Refardt[1,2,3] and Mirjam Christ-Crain[1,2]

[1]Department of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland; [2]Department of Clinical Research, University Hospital Basel, Basel, Switzerland; [3]Department of Internal Medicine, Section of Endocrinology, Erasmus Medical Centre, Rotterdam, Rotterdam, The Netherlands

Background: Secondary adrenal insufficiency is a rare cause of hyponatremia. However, it represents an important differential diagnosis to the syndrome of inappropriate antidiuresis (SIAD), the most common cause of euvolemic hyponatremia. Differentiation between adrenal insufficiency and SIAD is crucial, as treatment strategies differ substantially and rapid initiation of corticosteroid therapy is critical in patients with secondary adrenal insufficiency. The aim of this study is to improve the understanding of clinical characteristics of patients with secondary adrenal insufficiency.

Method: This is a descriptive secondary analysis based on a randomized, controlled, parallel-group, multicentred trial, which included patients with moderate to severe hyponatremia (serum sodium <130 mmol/L). All clinically euvolemic hyponatraemic patients were included in the analysis. Baseline characteristics as well as the applied therapeutic algorithms and treatment responses, were assessed.

Results: Among the 1074 euvolemic hyponatremic patients, the predominant etiologies were SIAD ($n = 857$, 80%), primary polydipsia ($n = 155$, 14%), secondary adrenal insufficiency ($n = 32$, 3%), and thiazide diuretic-associated hyponatremia ($n = 5$, 0.5%). Cortisol was measured in 45.7% of all euvolemic patients during hospitalization. In patients with newly diagnosed secondary adrenal insufficiency ($n = 20$), the median cortisol level at study inclusion was 77 nmol/L (IQR 33.5-120.5). After the first recorded low sodium level, the median time to correct diagnosis and to first administration of corticosteroids was 2 days (IQR 1-3 and 1-3, respectively). In all 32 patients with secondary adrenal insufficiency, mean plasma sodium concentration at study inclusion was 124 mmol/L (95% CI 123-126) and increased to 135 mmol/L (95% CI 134-136) at discharge. Sodium normalization was achieved in 66% of patients after a median of 3 days (IQR 1-3). At the 30-day follow-up, the recurrence rate of hyponatremia in patients with secondary adrenal insufficiency was 31.2%, the readmission rate was 15.6%, and mortality was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

9.4%. In comparison, patients with SIAD had a recurrence rate of 29.2%, a readmission rate of 15.8%, and mortality rate of 4.0%.

Conclusions: In our cohort, secondary adrenal insufficiency was a rare cause of chronic euvolemic hyponatremia, however, cortisol was only measured in 45.7% of all euvolemic patients, thus prevalence might have been higher. Patients with secondary adrenal insufficiency initially presented with moderate hyponatremia (serum sodium <125 mmol/L) and experienced a prompt increase in serum sodium upon treatment with corticosteroids.

Abstract citation ID: lvag096.1384

EP1127 - ECE_2890 - The study of Indirect calorimetry as an additional marker for the challenging diagnosis of central hypothyroidism

Alice Casiraghi[1], Elisa Delle Donne[1], Alessandro Amodeo[1], Lidia Lewandowsky[1,2], Giulia Pocaterra[1], Marco Bonomi[1,3], Alberto Battezzati[1,2], Irene Campi[3], Luca Persani[1,3] and Biagio Cangiano[1,3]

[1]Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [2]Department of Food, Nutrition and Environmental Sciences, IRCCS Istituto Auxologico Italiano, Milan, Italy; [3]Endocrinology Department & Lab of Endocrine and Metabolic Research, IRCCS Istituto Auxologico Italiano, Milan, Italy

Introduction: Central hypothyroidism (CH) is a rare disorder characterized by low free T4 (FT4) levels and inappropriately normal or low TSH. In CH, adequate levothyroxine (LT4) therapy aims to maintain FT4 in the upper half of the reference range, as TSH is unreliable. Indirect calorimetry (IC) provides a measure of resting energy expenditure (REE), an indicator of metabolic status that is typically reduced in hypothyroidism. This study aimed to investigate the potential role of IC in assessing the adequacy of LT4 therapy in patients with CH.

Matherials and Methods: We performed indirect calorimetry (IC) in 34 patients with CH under different treatment conditions: adequate, suboptimal, or withdrawn levothyroxine therapy.

Results: Twenty-one patients underwent two assessments, one during adequate LT4 therapy and one during suboptimal or withdrawn therapy, whereas the remaining 13 patients were evaluated only under inadequate treatment conditions. REE was inversely correlated with total cholesterol levels ($P = .0032$) and with the FT3/FT4 ratio. The FT3/FT4 ratio was lower during adequate therapy compared with inadequate therapy ($P = .05$), although this difference was less evident when the analysis was restricted to the 21 patients with paired measurements. Among these patients, 52% showed an increase in REE under adequate therapy, 42% showed a decrease, and one patient showed no change. Mann–Whitney analysis demonstrated that a lower FT3/FT4 ratio predicted an improvement in REE after achieving therapeutic targets ($P = .01$). Multivariate regression analysis confirmed a trend toward a negative association between REE improvement and a lower FT3/FT4 ratio ($P = .06$).

Discussion: The significant association between REE and cholesterol levels suggests that indirect calorimetry is a valuable functional tool for assessing metabolic status in patients with central hypothyroidism. Patients with higher FT3/FT4 ratios exhibited a poorer metabolic response to LT4 dose optimization, possibly reflecting a compensatory adaptation to adverse metabolic conditions, such as metabolic syndrome. Further studies are warranted to determine whether the FT3/FT4 ratio represents a cause or a consequence of impaired metabolic efficiency in this population and to elucidate the underlying mechanisms.

Abstract citation ID: lvag096.1385

EP1129 - ECE_1352 - Anti-rabphilin-3A antibody–positive arginine vasopressin deficiency after COVID-19 infection and vaccination: evidence for autoimmune hypothalamic–neurohypophyseal inflammation

Yoshihisa Sugimura[1], Yuka Natsuki[2], Hiroki Takizawa[3], Hiromasa Goto[3], Naoko Iwata[1,4], Haruki Fujisawa[1], Yuki Nagata[5,6], Hirotaka Watada[3] and Atsushi Suzuki[1]

[1]Department of Endocrinology, Diabetes and Metabolism, Fujita Health University, Toyoake, Japan; [2]Department of Metabolism, Endocrinology and Molecular Medicine, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan; [3]Department of Metabolism & Endocrinology, Juntendo University Graduate School of Medicine, Tokyo, Japan; [4]Nagoya, Japan; [5]Department of Vascular Medicine, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan; [6]Vascular Science Center for Translational Research, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan

Background: Arginine vasopressin deficiency (AVP-D) has been increasingly reported after coronavirus disease 2019 (COVID-19) infection and SARS-CoV-2 vaccination. However, most published cases have been described as idiopathic or post-infectious, and the underlying etiology remains largely unresolved. Anti-rabphilin-3A antibodies have recently been identified as a highly sensitive and specific biomarker for lymphocytic infundibulo-neurohypophysitis (LINH), an autoimmune inflammatory disorder of the hypothalamic–neurohypophyseal system.

Aim: To present two anti-rabphilin-3A antibody–positive cases of COVID-19–associated AVP-D and to re-evaluate previously reported cases.

Case presentations: We describe two patients who developed new-onset AVP-D following COVID-19–related events. One patient developed abrupt polyuria and polydipsia approximately three weeks after SARS-CoV-2 infection, while the other developed progressive AVP-D several weeks after SARS-CoV-2 vaccination following prior infection. Endocrinological evaluation in both cases demonstrated hypotonic polyuria with inappropriately low plasma AVP levels, blunted AVP responses to hypertonic saline, and preserved responsiveness to desmopressin. Pituitary magnetic resonance imaging showed loss of the posterior pituitary bright spot with pituitary stalk thickening. During follow-up, pituitary stalk swelling markedly improved within one month in the post-infection case, whereas persistent stalk enlargement was observed for more than one year in the post-vaccination case. Serum anti-rabphilin-3A antibodies were detected in both patients, strongly supporting a diagnosis of LINH and allowing avoidance of invasive pituitary biopsy.

Review of the literature: A review of previously reported COVID-19–associated AVP-D cases suggests that pituitary stalk swelling is observed more frequently after vaccination than after infection, whereas immunological evaluation has rarely been performed in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

either setting. This pattern is consistent with our longitudinal imaging findings, indicating potential differences in disease course depending on the triggering event. No established diagnostic biomarkers have been applied in most cases, leaving the etiology undefined.

Additional evidence: We have also recently reported a pediatric case of post-COVID-19 AVP-D with positive anti-rabphilin-3A antibodies, supporting autoimmune involvement across age groups.

Conclusions: Our findings provide immunological evidence that a subset of COVID-19–associated AVP-D represents autoimmune hypothalamic–neurohypophyseal inflammation. Anti-rabphilin-3A antibody positivity may serve as a non-invasive biomarker indicating autoimmune involvement and could aid etiological classification and avoidance of invasive diagnostic procedures in patients with AVP-D occurring after COVID-19 infection or vaccination. Although all COVID-19–associated AVP-D cases experienced at our institutions to date have been antibody-positive, further case accumulation is required to evaluate diagnostic sensitivity and to clarify differences between antibody-positive and -negative AVP-D.

Abstract citation ID: lvag096.1386

EP1130 - ECE_1448 - Clinical evolution from disease presentation to progression in primary and secondary empty sella: a real-world comparative study

Francesca Paglia[1], Vanessa Caccin[1], Gianluca Margiotta[2], Nicolò Bacchi[1], Chiara Diazzi[3], Bruno Madeo[4], Maria Chiara Decaroli[1], Maria Laura Monzani[1], Sara De Vincentis[1] and Vincenzo Rochira[1]

[1]Endocrinology Unit, Department of Biomedical, Metabolic and Neurosciences, University of Modena and Reggio Emilia, Modena, Italy; [2]South-Western Piedmont Area, Local Health Authority (ASL) CN1, Cuneo, Italy; [3]Endocrinology Unit, Department of Specialized Medicine, University Hospital of Modena, Modena, Italy; [4]Modena, Italy

Background: Empty Sella (ES) describes a neuroradiological condition in which the pituitary gland appears flattened due to partial or complete occupation of the sella turcica by cerebrospinal fluid. ES is traditionally considered a stable condition, although long-term endocrine outcomes may differ substantially according to etiology. Comparative longitudinal data between Primary (PES) and Secondary ES (SES) remain limited.

Methods: We conducted a retrospective, longitudinal study including adult patients with ES evaluated at a tertiary endocrinology center between 2007 and 2025. ES was classified as PES or SES based on clinical history. Clinical and neuroradiological features, comorbidities, and pituitary hormonal assessments were collected at baseline and at last follow-up. Longitudinal changes in pituitary function were compared between groups.

Results: A total of 258 participants were included (64.3% women; median age 51.5 years). PES was more prevalent than SES (61.6% vs 38.4%). Over long-term follow-up (median 58.5 months), endocrine function trajectories diverged markedly between PES and SES. In the PES cohort, pituitary function did not change in 83.3% of patients, with a very low incidence of newly developed hormonal deficiencies (≤4% per axis). Recovery of pre-existing deficits was rare (<5%), confirming the generally non-progressive nature of PES with a stability of pituitary function.

In contrast, SES exhibited a significantly progressive change in pituitary function. Compared with PES, SES patients showed a significant increase over time in both anterior pituitary deficiencies ($P = .037$) and total pituitary deficiencies ($P = .027$). New-onset hormonal impairments occurred predominantly in SES, affecting the corticotropic (7.4%, $P = .01$), thyrotropic (11.6%, $P = .018$), and gonadotropic axes (5.3%, $P = .01$).

Arginine vasopressin deficiency appeared and partially resolved exclusively in SES, mirroring the persistence or fluctuation of polyuria and polydipsia in this subgroup. From a clinical standpoint, headache, asthenia, and visual disturbances remained largely unchanged in both groups. Notably, sexual dysfunction showed greater variability in SES, with both onset and partial recovery of reduced libido occurring more frequently than in PES ($P = .031$).

Conclusions: Long-term follow-up reveals two distinct endocrine phenotypes of ES. PES is characterized by durable hormonal stability, whereas SES carries a significant risk of progressive pituitary dysfunction over time. These findings support an etiology-driven management approach, advocating prolonged and closer endocrine surveillance in patients with SES, while suggesting that a more conservative follow-up strategy may be appropriate for the clinical management of PES.

Abstract citation ID: lvag096.1387

EP1131 - ECE_1778 - Pituitary hormone profiles and male hypogonadism in dialysis patients

Büşra Tunç Topuz[1], Ceren Tufan[1], İlhan Kılıç[2], Emre Saygili[1], Hayri Bostan[3], Ali Degirmenci[4] and Ersen Karakilic[1]

[1]Department of Endocrinology and Metabolism, Canakkale Onsekiz Mart University, Canakkale, Türkiye; [2]Department of Nephrology, Trakya University, Edirne, Türkiye; [3]Department of Endocrinology, Çanakkale Mehmet Akif Ersoy State Hospital, Canakkale, Türkiye; [4]Departmant of Nephrology, Çanakkale Mehmet Akif Ersoy State Hospital, Çanakkale, Türkiye

Objective: Chronic kidney disease affects approximately 10%-13% of the general population and may be associated with multiple endocrine abnormalities, particularly alterations in anterior pituitary hormones. However, data comparing pituitary hormone profiles in patients undergoing hemodialysis (HD) or peritoneal dialysis (PD) are limited. This study aimed to evaluate anterior pituitary hormone profiles in patients receiving active dialysis therapy.

Methods: This retrospective study included patients followed in dialysis units of tertiary and secondary care centers. Demographic and clinical characteristics and routine biochemical and hormonal parameters were obtained from electronic medical records. Statistical analyses included appropriate parametric and nonparametric tests, correlation analysis, and multivariable logistic regression. A P value <.05 was considered statistically significant.

Results: A total of 111 patients were included (median age: 66 years; 47.7% female). Age-adjusted IGF-1 levels were below the reference range in 21.8% of patients and were significantly lower in the HD group than in the PD group. Patients receiving PD had significantly higher serum prolactin, TSH, and cortisol levels, as well as higher estradiol levels in men and postmenopausal women. Serum calcium and albumin levels were lower, and hypertension prevalence was higher, in the PD group.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Among 58 male patients, 32 (55.2%) had total testosterone levels below 3 ng/mL, consistent with biochemical hypogonadism. In men, total testosterone levels were negatively correlated with prolactin (rho = −0.387; $P = .003$), FSH (rho = −0.357; $P = .006$), and LH (rho = −0.315; $P = .016$), and positively correlated with fT4 (rho = 0.392; $P = .002$). Increased body weight was also associated with lower testosterone levels (rho = −0.473; $P = .023$). In multivariable logistic regression analysis, higher serum prolactin levels were independently associated with biochemical hypogonadism in men (OR 1.25, 95% CI 1.09-1.43), whereas higher estradiol levels were inversely associated with low total testosterone (OR 0.94, 95% CI 0.89-0.98). Age and dialysis modality were not independently associated with hypogonadism(Nagelkerke $R^2 = 0.559$; classification accuracy: 82.8%).

Conclusions: Dialysis patients exhibit significant alterations in anterior pituitary hormone profiles, with differences according to dialysis modality. Reduced IGF-1 levels and biochemical hypogonadism are common, particularly in men. Higher prolactin increases, whereas higher estradiol decreases, the likelihood of low total testosterone. These findings highlight the importance of routine hormonal assessment in patients with end-stage kidney disease.

Abstract citation ID: lvag096.1388

EP1132 - ECE_1995 - Higher PANOMEN-3 grade predicts the need for additional interventions following surgery in patients with non-functioning pituitary macroadenomas

Efrat Markus[1,2], Yaron Rudman[2,3], Genady Drozdinsky[2,4], Ilan Shimon[2,3] and Shlomit Koren[1,2]
[1]*Shamir Medical Center, Endocrine and Diabetes Institute, Zerifin, Be'er Ya'akov, Israel;* [2]*Gray Faculty of Medical & Health Sciences, Tel Aviv University, Tel Aviv, Israel;* [3]*Beilinson Hospital, Rabin Medical Center, Institute of Endocrinology, Petah Tikva, Israel;* [4]*Rabin Medical Center, Infectious Diseases Unit, Beilinson Hospital, Petah Tikva, Israel*

Introduction: In 2024, the Pituitary Society proposed the Pituitary Adenoma Nomenclature 3 (PANOMEN-3) classification for assessing the prognosis of pituitary tumors. The rationale behind this new classification was to enable the prognostic assessment of tumors managed surgically and conservatively—a feature particularly relevant for patients with non-functioning pituitary adenomas (NFPAs), which are increasingly managed non-surgically.

Aim: To assess how PANOMEN-3 grade, both at diagnosis and postoperatively, relates to the likelihood and timing of additional treatment, and its potential utility in guiding intervention decisions in patients with non-functioning pituitary macroadenomas (macro-NFPAs).

Methods: This is a retrospective cohort study. We conducted a computerized search in Rabin and Shamir medical centers databases for the diagnosis of macro-NFPAs recorded between the years 1974-2024. Of 210 patients, 180 had at least one year of pituitary MRI follow-up and were included in the analysis. Clinical, biochemical, and imaging data were collected to assess the PANOMEN-3 grade at diagnosis and postoperatively.

Results: Our cohort included 180 patients (80 females, 44.4%; age at diagnosis, 61.0 ± 14.1 years), of whom 116 underwent transsphenoidal surgery (TSS). Median follow-up was 5 years [IQR 2-10]. After initial TSS, the proportion of patients requiring additional treatment (including repeat TSS and/or dopamine agonist therapy and/or radiotherapy) increased with higher PANOMEN-3 grade at diagnosis (Grade 1: 25.6%, Grade 2: 35.6%, Grade 3: 50%, $P = .093$) and postoperatively (Grade 0: 0%, Grade 1: 28.3%, Grade 2: 46.5%, Grade 3: 75%, $P < .01$). Median time from first TSS to additional treatment was shorter with increasing PANOMEN-3 grade. This trend was observed both at diagnosis (Grade 1: 54 months [IQR 16-88], Grade 2: 47 months [IQR 12-97], Grade 3: 5 months [IQR 3-24], $P = .041$) and postoperatively (Grade 1: 68 months [IQR 16-94], Grade 2: 24 months [IQR 12-53], Grade 3: 5 months [IQR 3-16], $P = .079$).

Conclusions: Our data indicate that higher PANOMEN-3 grade, both at diagnosis and postoperatively, was associated with an increased likelihood of requiring additional treatment after surgery and earlier. This highlights the potential of PANOMEN-3 grade to guide decisions regarding the intensity of intervention at diagnosis, and to predict the need for additional treatment in patients with macro-NFPA.

Abstract citation ID: lvag096.1389

EP1133 - ECE_2266 - Preoperative infection burden in Cushing's disease: association with urinary free cortisol levels

Rukiye Dilara Tekin Uzman, Aysel Unver Ozkahraman, Gizem Karatas Kiliccioglu, Mutlu Niyazoğlu and Esra Hatipoglu
Istanbul, Türkiye

Objective: To evaluate the frequency and spectrum of preoperative infections in Cushing's disease (CD) and assess their association with urinary free cortisol (UFC) levels.

Methods: This single-centre retrospective study included 60 CD patients who underwent transsphenoidal surgery between January 2019 and December 2023. Patients with ectopic ACTH syndrome, adrenal Cushing's syndrome, chronic immunosuppression, active malignancy, or incomplete UFC measurements were excluded. Physician-diagnosed infections requiring antimicrobial treatment within six months preoperatively were identified through medical records, ICD-10 codes, and prescriptions.

Preoperative assessments included basal serum cortisol and ACTH, 24-hour UFC, late-night salivary cortisol, glycaemic parameters, complete blood count, and inflammatory markers. Correlation analyses and receiver operating characteristic (ROC) curve analysis were performed.

Results: The cohort comprised 50 women (83.3%) and 10 men (16.7%); mean age 48.7 ± 11.4 years. Preoperative infections were common: 56.7% of patients experienced ≥2 antimicrobial-treated infections. Upper respiratory tract infections predominated (58.3%), followed by dermatophytosis (28.3%), bacterial dermatitis (21.7%), and urinary tract infections (20.0%).

Infection number correlated positively with UFC levels ($\rho = 0.4$, $P = .02$). ROC analysis demonstrated modest discriminatory performance of UFC for identifying infections requiring treatment (AUC = 0.69; 95% CI: 0.52-0.87), with a threshold of 107.5 µg/24 h yielding 70% sensitivity and 75% specificity.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Basal serum cortisol, late-night salivary cortisol, haematological indices, inflammatory markers, HbA1c, and fasting plasma glucose showed no significant associations with infection burden.

Conclusions: Among evaluated biochemical markers, UFC alone demonstrated a significant association with preoperative infection frequency in CD. UFC measurement may facilitate risk stratification for infection surveillance and timely intervention before definitive treatment.

Table 1 Number of infections during the pre-treatment period

Number of infections	Patients (*n*, %)
0	**8 (13.3)**
1	**18 (30.0)**
2	**14 (23.3)**
3	**8 (13.3)**
4	**3 (5.0)**
5	**7 (11.7)**
≥6	**2 (3.4)**
Total	**60 (100)**
Median [IQR]	**2 [1-3]**

Table 2 Types of infections during the pre-treatment period

Infection type	Patients (*n*, %)
Upper respiratory tract	**35 (58.3)**
Lower respiratory tract	**8 (13.3)**
Urinary tract	**12 (20.0)**
Dermatophytosis	**17 (28.3)**
Bacterial dermatitis	**13 (21.7)**
Bacterial conjunctivitis	**10 (16.7)**
Vaginitis[a]	**9 (18.0)**
Acute gastroenteritis	**3 (5.0)**
Otitis	**2 (3.3)**
Herpes simplex virus	**1 (1.7)**

[a]Percentage among female patients ($n = 50$).

Keywords Cushing's disease, urinary free cortisol, infection burden, pre-treatment period

Abstract citation ID: lvag096.1390

EP1134 - ECE_2943 - Body composition in acromegaly assessed by bioelectrical impedance analysis: differences between active and controlled disease

Signe Graungaard[1], Mai C. Arlien-Søborg[2], Niels Henrik Bruun[1], Erlend Gjersdal[1,3], Jens Otto Jørgensen[2] and Jakob Dal[1,4]

[1]Research data and Biostatistics, Aaborg Universityhospital, Aalborg, Denmark; [2]Endocrinolgy, Aarhus Universityhospital, Aarhus, Denmark; [3]Endocrinology, Aalborg University hospital, Aalborg, Denmark; [4]Steno Diabetes Center North Jutland, Aalborg, Denmark

Purpose: To evaluate the accuracy of bioimpedance analysis (BIA) compared to dual-energy x-ray absorptiometry (DXA) measurements of body composition in patients with active and controlled acromegaly.

Methods: BIA and DXA methods were applied to estimate body composition in patients with active acromegaly and again after disease control.

Results: 16 patients with active acromegaly were included and followed until after disease control. GH nadir decreased from 5.5 ± 5.7 µg/L to 0.2 ± 0.3 µg/L, and IGF-1 levels from 565 ± 189 ng/L to 191 ± 137 ng/L after treatment. Body weight remained stable (95.4 ± 30.0 kg and 95.5 ± 26.7 kg) throughout the study period although fat mass increased by 3.2 kg (from 34.1 ± 15.2 kg to 37.5 ± 14.6 kg) or 4.5 kg (31.5 ± 14.6 kg to 36.0 ± 16.0 kg) measured by DXA or BIA, respectively. Lean body mass measured by DXA decreased by 2.2 kg (61.6 ± 16.9 kg to 59.4 ± 14.5 kg), while fat free mass decreased by 4.2 kg (63.4 ± 19.0 kg to 59.2 ± 15.7 kg) and total body water (L) decreased by 3.1 kg (46.4 ± 13.9 kg to 43.3 ± 11.5 kg) estimated by BIA. Using Bland–Altman analysis the bias in estimates for lean mass was −1.7 kg (LOA: −10.0-6.6 kg) in active acromegaly and 0.2 kg (LOA: −10.1-10.5 kg) with hormonal control. For fat mass, bias was 2.6 kg (LOA: −3.8-9.0 kg) in active disease and 1.5 kg (LOA: −5.0-8.1 kg) in controlled disease.

Conclusions: We observed ahigh conformity between BIA predictions and DXA scan measurements in patients with acromegaly during both active disease and hormonal control which supports the utility of BIA in clinical practice. BIA estimates can add important clinical insights about hydration and fluid shifts that DXA alone does not provide, which are clinically relevant in acromegaly where fluid balance is altered by GH/IGF-I excess.

Abstract citation ID: lvag096.1391

EP1135 - ECE_3556 - Postoperative quality of life and sleep disorders following transsphenoidal resection of pituitary adenomas

Hamza El Hadi, Jona Streit, Eric Suero Molina, Walter Stummer, Jonel Trebicka and Elena Vorona

Münster University Hospital, Münster, Germany

Introduction: Despite recent advances in surgical techniques and endocrinological management, patients undergoing transsphenoidal resection of pituitary adenomas (PA) frequently report persistent impairment in quality of life (QoL) and sleep disturbances. The potential impact of postoperative hypopituitarism (HP) on these outcomes in these patients remains incompletely understood.

Methods: This cross-sectional study evaluated patient-reported outcomes related to health-related quality of life (HRQoL) and sleep quality in patients with a history of transsphenoidal PA resection. The primary aim was to assess the postoperative prevalence of impaired QoL and sleep disorders in relation to pituitary hormone deficiency. A secondary aim was to identify predictors of sleep disturbances.

Patients with a prior transsphenoidal PA resection who were undergoing follow-up at our Endocrinology Unit between March

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and December 2025 were enrolled. Patients were divided into two groups based on the presence or absence of HP, defined as one or more partial or complete deficiencies of adenohypophyseal or neurohypophyseal hormones diagnosed during postoperative follow-up. All hormone deficiencies were adequately replaced according to international clinical practice guidelines. HRQoL was assessed using the 36-Item Short Form Health Survey (SF-36), sleep quality using the Pittsburgh Sleep Quality Index (PSQI), and daytime sleepiness using the Epworth Sleepiness Scale (ESS).

Results: The study population included 100 patients: 53 with preserved postoperative pituitary function and 47 with HP. Median age was 54 years in patients without HP and 60 years in those with HP ($P > .05$). No significant between-group differences were observed in gender, BMI, sleep apnea, dyslipidemia, or cardiovascular disease.

Patients with hormonally inactive adenomas had higher prevalence of postoperative HP compared with those with hormonally active tumors (30% vs 18%, $P = .005$). Impaired QoL and sleep disturbances were common in both groups, with no significant differences questionnaire scores.

Correlation analyses showed that higher PSQI scores (indicating poorer sleep quality) were associated with higher ESS scores ($\rho = 0.23$, $P = .02$), lower vitality ($\rho = -0.36$, $P < .001$), and poorer mental health ($\rho = -0.37$, $P < .001$). In multivariable regression analysis, impaired mental health remained the only independent predictor of worse PSQI scores ($\beta = -.07$, 95% CI −0.11 to −0.02, $P = .005$).

Conclusions: Our findings provide additional evidence of a high prevalence of impaired QoL and sleep disturbances following transsphenoidal resection of PA. These disturbances appear largely independent of postoperative pituitary hormonal status, highlighting the central role of mental health in postoperative sleep quality and overall well-being.

Abstract citation ID: lvag096.1392

EP1136 - ECE_2877 - Patient experiences with the digital communication tool *InvolveMe* in outpatient management of pituitary adenomas

Elin Børøsund[1,2], Kari Abelsen[3], Anders Jørgensen[3,4], Line Cecilie Krabbe Schie[3] and Berit Seljelid[1,5]
[1]*Division of Medicine, Department of Digital Health Research, Oslo University Hospital, Oslo, Norway;* [2]*Faculty of Health and Social Sciences, Department of Nursing and Health Sciences, University of South-East Norway, Drammen, Norway;* [3]*Division of Medicine, Section of Specialized Endocrinology, Department of Endocrinology, Morbid Obesity and Preventive Medicine, Oslo University Hospital, Oslo, Norway;* [4]*Faculty of Medicine, Institute of Clinical Medicine, University of Oslo, Oslo, Norway;* [5]*Norwegian Center for Health Literacy and Coping, Department of Education and Competence Development, Oslo University Hospital, Oslo, Norway*

Background: Patients with pituitary adenomas (PA) often experience persistent symptoms following pituitary surgery, underscoring the importance of effective communication with healthcare providers. Digital tools offer the potential to enhance patient-provider communication by enabling patients to report issues they consider important to discuss during clinical encounters. *InvolveMe*, a digital communication tool, facilitates a systematic assessment of patients' symptoms, needs and preferences prior to consultations. This tool aims to assist patients in preparing for their appointment, support agenda-setting, and promote greater patient involvement in their care. *InvolveMe* is integrated into the Norwegian health platform and the hospital's electronic patient record system. However, the successful implementation of such novel follow-up approaches requires careful adaptation to the needs of users and alignment with existing clinical workflows.

Aim: To explore patients' experience of using the *InvolveMe* communication tool as part of outpatient consultations.

Method: Participants with PA were recruited from an outpatient clinic at a tertiary referral center between October and December 2025. Patients scheduled for postoperative outpatient follow-up appointments were invited to complete the *InvolveMe* tool via digital appointment letters. Data was collected on how many patients received the invitation and the number who completed the *InvolveMe* assessment. Furthermore, we collected information on reasons for non-use of *InvolveMe* and invited a subset of patients ($n = 5$) to participate in individual interviews to explore their experiences with using *InvolveMe* during outpatient consultations. The data were analyzed using a rapid analysis approach.

Results: Of 50 invited patients, 21 (42%) completed *InvolveMe*. Main reasons for not using *InvolveMe* included not noticing the invitation, perceiving no personal need, or lacking necessary digital skills. Analysis of the interviews with patients who used *InvolveMe* revealed four themes: (1) Being prepared for the upcoming consultation, (2) High expectations of its use during consultations, (3) A tool for addressing patient-prioritized topics, and (4) Suggestions for improving routines and *InvolveMe* functionalities. Patients described *InvolveMe* as a tool that facilitated reflection on important topics to discuss during consultations and that healthcare providers in most cases used the summary as part of consultations.

Conclusions: Patients valued the opportunity to use *InvolveMe* as part of their preparation for outpatient consultations. To enhance accessibility, further investigation is needed to understand barriers for use. Additionally, exploring the perspectives and experiences of healthcare providers in utilizing *InvolveMe* will be essential for optimizing its implementation into clinical practice.

Abstract citation ID: lvag096.1393

EP1137 - ECE_2413 - The importance of cell adhesion molecules CADM2/3 and miR-127 and miR432 for clinically non-functioning pituitary tumours

Beata Rak-Makowska[1,2], Sayka Barry[3], Maria Maksymowicz[4], Agnieszka Koppolou[5], Małgorzata Rydzanicz[5], Grzegorz Zielinski[6], Dawid Mehlich[2,7,8], Filip Garbicz[7,9], Neil Dorward[10], Anouk Borg[10], Hani J Marcus[10], Rafał Płoski[5], Paweł Włodarski[11], Agnieszka Piekielko-Witkowska[1], Marta Korbonits[3] and Dominika Nowis[2,9]
[1]*Centre of Translational Research, Department of Biochemistry and Molecular Biology, Centre of Postgraduate Medical Education, Warsaw, Poland;* [2]*Laboratory of Experimental Medicine, Medical University of Warsaw, Warsaw, Poland;* [3]*Barts and The London School of Medicine and Dentistry, Centre for Endocrinology, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom;* [4]*Department of Cancer Pathomorphology, Maria*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [5]Department of Medical Genetics, Medical University of Warsaw, Warsaw, Poland; [6]Department of Neurosurgery, Military Institute of Medicine - National Research Institute, Warsaw, Poland; [7]Department of Methodology, Medical University of Warsaw, Warsaw, Poland; [8]Polish Academy of Sciences, Laboratory of Molecular OncoSignalling, International Institute of Molecular Mechanisms and Machines, Warsaw, Poland; [9]Department of Immunology, Medical University of Warsaw, Warsaw, Poland; [10]Department of Neurosurgery, The National Hospital for Neurology and Neurosurgery, Queen Square, London, United Kingdom; [11]Department of Histology and Embryology, Medical University of Warsaw, Warsaw, Poland

Purpose: The exact molecular mechanisms driving non-functioning-PitNETs invasiveness are still unclear, and reliable molecular biomarkers remain unknown. Although, the role of microRNAs (miRs) as promising markers of invasiveness in other PitNETs is increasingly highlighted. Our study aimed to identify novel miRs and differentially regulated genes in invasive and noninvasive NF-PitNETs. We have validated our results in a large cohort of tumour and control normal normal pituitary samples.

Methods: RNA sequencing was conducted on 13 fresh-frozen human NF-PitNET samples (7 invasive and 6 noninvasive; gonadotrophs), while microRNA sequencing was performed on 12 of these samples. Validation was carried out using Fluidigm HD GEX arrays with TaqMan assays and quantitative PCR among NF-PitNETs ($n = 80$) and normal pituitary samples ($n = 10$). Confirmatory results included 23 selected mRNA genes (controls: *GAPDH* and *SNORD61*) and 38 miRs (including 35 miRs identified by microRNA sequencing, two reference genes, and three miRs previously reported in the literature).

Results: RNA sequencing revealed differential expression of 10 733 genes, of which 364 reached statistical significance (adjusted $P <$ .05) and were involved in 783 biological processes. Parallel miRNA-Seq identified 35 downregulated miRNAs mapping to 143 Gene Ontology (GO) processes. Gene Ontology and KEGG pathway analyses highlighted dysregulation of cell adhesion and adherens junction pathways, implicating their role in tumor invasiveness.

Validation in an expanded cohort demonstrated overexpression of cell adhesion molecules (*CADM2, CADM3*) important for cell-cell adhesion, aggregation as well as synapse organization and ephrin receptor B1 (*EPHB1*), whose major role includes targeted cell migration and adhesion. We also found downregulation compared to normal pituitary tissue of *CRIM1* (Cysteine Rich Transmembrane BMP Regulator 1) responsible for tissue development through interactions with members of the transforming growth factor beta family, together with downregulation of *BCL2L11* transcript (belonging to BCL-2 protein family) known to act as apoptotic activator.

MiR-127-5p showed a weak but statistically significant positive correlation with *BCL2L11* and *CRIM1* and a statistically significant negative correlation with *CADM2* and *CADM3*. Additionally, *miR-432-5p* was negatively correlated with *CADM2* expression in NF-PitNET tissues ($r = -0.4176$, $P = .0005$). MiRs may regulate post-transcriptionally genes expression, thus our findings may suggest possible mechanisms underlying NF-PitNETs development and/or progression.

Conclusions: Our study reveals novel genes and miRs in NF-PitNETs suggesting their potential regulatory role in cell adhesion, migration, and apoptosis therefore potentially contributing to their pathogenesis.

Fundings: Grants from the National Science Center, Poland PRELUDIUM UMO-2016/23/N/NZ5/02597 and SONATINA UMO-2025/56/C/NZ4/00016 received by first author (B.R.M).

Abstract citation ID: lvag096.1394

EP1138 - ECE_1835 - Muscle performance, body composition, and disease control in acromegaly: insights from an observational study

Rosa Pitino[1], Chiara Mele[1], Martina Romanisio[1], Sara Sturnia[1], Alice Ferrero[1], Gianluca Aimaretti[1], Paolo Marzullo[1], Flavia Prodam[1,2] and Marina Caputo[1,2]
[1]Endocrinology, Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy; [2]Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy

Aim: To evaluate muscle strength, body composition, and quality of life (QoL) in acromegalic patients compared with age-, sex-, and BMI-matched healthy controls.

Patients and Methods: In this observational study, 26 acromegalic patients followed at a tertiary referral center and age-, sex-, and BMI-matched controls were enrolled. Patients with uncontrolled metabolic diseases (ie, HbA1c > 8.5%), active malignancies, acute severe illness were excluded. For acromegalic patients, clinical characteristics, disease duration and activity, metabolic complications, and hormonal parameters were collected, including GH and IGF-1 levels at baseline and at last follow-up; ΔIGF-1 was calculated as the difference between baseline and last available follow-up measurement. Muscle strength, body composition, and QoL were assessed cross-sectionally at the last follow-up visit in both patients and controls. Muscle strength was evaluated using handgrip dynamometry, sit-to-stand test, and Medical Research Council (MRC) scale. Body composition was assessed by bioelectrical impedance analysis (BIA), including fat-free mass (FFM), muscle mass (MM), fat mass (FM), and abdominal fat mass (A-FM). EQ-5D and SARC-F questionnaires were used for QoL.

Results: Patients with acromegaly and controls were comparable for metabolic comorbidities, except for a higher prevalence of diabetes (53.8% vs 7.7%, $P = .003$) and cardiovascular disease (26.9% vs 0%, $P = .005$) in the acromegaly group. Controls showed a higher abdominal fat mass percentage (A-FM%) compared with patients with acromegaly (45.3% vs 24.9%, $P < .0001$). Disease control was associated with a more favorable body composition: ΔIGF-1 correlated inversely with FM% and A-FM% ($\rho = -0.45$, $P = .04$; $\rho = -0.67$, $P = .001$) and positively with MM% and FFM% ($\rho = 0.47$, $P = .03$; $\rho = 0.45$, $P = .04$). Despite this more favorable body composition, acromegalic patients showed reduced biceps and quadriceps strength on the MRC scale compared with controls ($P = .002$ and $P = .0001$, respectively). Notably, patients showing a greater reduction in IGF-1 from baseline to last follow-up exhibited higher handgrip strength (right: $\rho = 0.52$, $P = .03$; left: $\rho = 0.62$, $P = .006$), regardless of sex, age, BMI, and physical activity level.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

QoL, assessed by EQ-5D questionnaire, was lower in acromegalic patients than healthy controls (70 vs 80; $P = .002$), in line with the observed impairments in muscle strength and physical performance.

Conclusions: In acromegaly, biochemical disease control is associated with a more favorable body composition and with better muscle performance at follow-up. However, despite these metabolic advantages, patients exhibit muscle weakness and reduced QoL compared with healthy controls, highlighting the need for management strategies beyond biochemical control.

Abstract citation ID: lvag096.1395

EP1139 - ECE_3086 - Paradoxical GH response during OGTT in acromegaly predict disease phenotype

Penelope Giambò[1,2], Sabrina Chiloiro[1,2], Antonella Giampietro[1,2], Pier Paolo Mattogno[2,3], Liverana Lauretti[2,3], Laura De Marinis[1,2], Antonio Bianchi[1,2], Francesco Doglietto[2,3] and Alfredo Pontecorvi[1,2]

[1]Endocrinology and Metabolism, Dipartimento di Medicina e Chirurgia traslazionale, Fondazione Policlinico Universitario Agostino Gemelli, Roma, Italy; [2]Endocrinology and Metabolism, Dipartimento di Medicina e Chirurgia traslazionale, Agostino Gemelli University Policlinic, Roma, Italy; [3]Neurosurgery, Neuroscience, Sensory Organs, and the Chest, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy

Introduction: Acromegaly is a rare neuroendocrinological disease. According to the last consensus, the diagnosis is based on an IGF-I value >1.3 times the upper limit of normal for age. In cases of doubt, in order to confirm the diagnosis, the oral administration of 75 g of glucose and the dosages of GH at baseline and every 30 minutes until 2 hours can be practiced. Some acromegalic patients show a paradoxical response to this test, meaning that an elevation of GH levels can be observed rather than a more "physiological" decrease. However, a universally accepted definition of paradoxical response is missing. Furthermore, this phenomenon has been studied to investigate a possible correlation between the latter and the disease outcome.

Patient and Methods: To contribute to answering to this question, we conducted a retrospective and observational study including 41 patients, defining the paradoxical response as an OGTT ratio (ratio between the peak of GH value during OGTT and the baseline value) > 120% in the first 90 minutes.

Results: Ten patients showed a GH paradoxical response (GH-par) to OGTT at the diagnosis (24.4%), the remaining 31 patients showed a not-paradoxical GH response (GH-not-par). GH-par response occurred more frequently in smaller somatotroph tumors (GH-par: 16 millimetres IQR: 25 vs GH-not-par 18 millimetres IQR: 12 millimetres, $P = .006$), low proliferative somatotroph tumors (GH-par: 1% IQR: 2 vs GH-not-par 2% IQR: 2, $P = .05$) and in densely granulated somatotroph tumors (OR: 0.67 95% IC: 0.42-0.98).

The occurrence of GH paradoxical response did not differ among gender ($P = .46$), age ($P = .87$), BMI ($P = .8$), GH, IGF-I levels at diagnosis ($P = .39$ and $P = .27$), hyperinsulinism ($P = .37$), presence of type 2 diabetes at acromegaly diagnosis ($P = .32$), glycemia and insulinemia at diagnosis ($P = .48$ and $P = .21$), expression of somatostatin receptor (SSTR2A *P*-value: .54; SST5 *P*-value: .43), and disease outcome, such as post-surgery cure ($P = .53$), response to first generation SRL ($P = .67$), and to second generation SRL ($P = .72$), and did not predict the occurrence of acromegaly related complications, such as type 2 diabetes ($P = .62$), osteopenia/osteoporosis ($P = .61$), other neoplasia ($P = .31$), and arterial hypertension ($P = .61$).

Conclusions: In conclusion, in our study the paradoxical response to OGTT in acromegaly seems to predict a mild disease phenotype. Therefore, although the definition of paradoxical response, as well as its predictive and prognostic role, had changed in last years, the evaluation of GH levels during OGTT remain a useful diagnostic tool in patient with doubt diagnosis of acromegaly and in cases of challenging in interpretation of IGF-I values.

Abstract citation ID: lvag096.1396

EP1141 - ECE_2078 - Neuroactive steroids, cytokines and tau-proteins as potential biomarkers of normal pressure hydrocephalus

Lucie Kolatorova[1], Tereza Skodova[1], Jana Vitku[1], Petr Skalicky[2], Michala Vosátková[3], Josef Vcelak[4], Tomas Moravec[5], Adela Bubenikova[2] and Ondrej Bradac[2,5]

[1]Department of Steroids and Proteofactors, Institute of Endocrinology, Prague, Czech Republic; [2]Department of Neurosurgery, Motol University Hospital, Prague, Czech Republic; [3]Department of Clinical Biochemistry, Institute of Endocrinology, Prague, Czech Republic; [4]Department of Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic; [5]Department of Neurosurgery and Neurooncology, Military University Hospital, Prague, Czech Republic

Background: Normal pressure hydrocephalus (NPH) is a potentially reversible neurodegenerative disorder caused by impaired cerebrospinal fluid (CSF) absorption, leading to ventricular enlargement. It presents with gait disturbance, urinary incontinence, and cognitive impairment and is often misdiagnosed as other neurodegenerative diseases. As one of the few treatable causes of dementia, accurate diagnosis is crucial, and shunt implantation leads to clinical improvement in 70%-90% of patients. Within the NPH diagnostic framework, including the lumbar infusion test (LIT), CSF is an accessible source of biomarkers. While cytokines and tau proteins have been proposed as biomarkers, steroid metabolism—closely linked to osmotic dysregulation and neuroinflammation in NPH—remains understudied.

Aim: This study aims to identify CSF steroid biomarkers and validate the diagnostic potential of cytokines and tau proteins in NPH.

Methods: 17 neuroactive steroids (androgens, gestagens, corticoids, estrogens) were quantified by LC-MS/MS. Amyloid-β42, tau proteins (p-tau and t-tau) and cytokines were determined by immunoassay.

Results: The patient group included 116 subjects (43 female, 73 male) average 74 years old diagnosed with NPH. They underwent surgical shunt implantation and were observed 3 and 12 months after surgery. Control group were subjects ($n = 95$, 34 female, 61 male, average age 75 years) who underwent LIT and were classified as non-responders. In NPH, we observed significantly decreased CSF levels of tau-proteins, interleukin-10, MPC-1, TNF-α, and significantly increased estrone and aldosterone compared to control group both in men and women. In NPH before, 3 and 12 months after the surgery, we found significantly increased CSF amyloid-β42, p-tau, t-tau, MCP-1 and MIP-1β in both time intervals after surgery. In men, in contrast to women, there was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

significant increase in CSF androgens (androstenedione, testosterone and their 11-oxygenated metabolites), corticoids (cortisol, cortisone, corticosterone, 11-deoxycortisol), pregnenolone and 17-hydroxyprogesterone after 3 months; thereafter, a non-significant decrease of mentioned steroids was observed.

Conclusions: Within the known CSF biomarkers for NPH (tau-proteins, MCP-1, IL-10, TNF-α), we have found CSF aldosterone and estrone as possible biomarkers helpful in the NPH diagnosis. The association of high CSF estrone in NPH with low tau-protein is biologically plausible, given that estrogens are known to reduce tau-protein phosphorylation. The finding of elevated CSF aldosterone levels is consistent with its mineralocorticoid activity in line with the NPH pathophysiology. We also observed sex-specific differences in neurosteroid metabolism after shunt insertion, which may be relevant for personalized medicine.

Acknowledgement: Supported by NU23-04-00551 of Czech Ministry of Health.

Abstract citation ID: lvag096.1397

EP1142 - ECE_1271 - Clinically diagnosed MEN 1: diagnostic challenges and delayed recognition

Tamara Dojcinovic[1,2], Jelena Malinovic Pancic[1,2], Bojana Caric[1,2] and Aleksandra Markovic[1,2]
[1]*University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina;* [2]*Faculty of medicine University of Banja Luka, Banja Luka, Bosnia and Herzegovina*

Background: Multiple endocrine neoplasia type 1 (MEN1) or Wermer syndrome) is a rare autosomal dominant disorder caused by germline mutations in the tumor suppressor gene MEN1. Gold standard for diagnosis is genetic testing, however the diagnosis is often clinically made by the combined occurrence of two or more of the following classical endocrinopathies: primary hyperparathyroidism (PHPT), anterior pituitary tumors, and duodenopancreatic neuroendocrine tumors (DP-NETs). Due to limited access to genetic testing, diagnosis can be established based on presence of two or more of the classical endocrinopathies.

Case report: We present the case of a 58-year-old male who was referred to an endocrinologist following a new diagnosis of diabetes mellitus. During clinical evaluation, acromegalic features were noted, prompting inpatient endocrine assessment. Hormonal testing revealed elevated IGF-1 levels (992 ng/mL) and unsuppressed GH levels during oral glucose tolerance testing (OGTT), consistent with a somatotropinoma. Pituitary MRI confirmed the presence of a macroadenoma measuring 11 mm. Given the patient's history of recurrent kidney stones, parathyroid hormone (PTH) levels were assessed and found to be elevated (98 pg/mL), accompanied by mildly increased serum calcium levels, raising suspicion of primary hyperparathyroidism. MIBI scintigraphy was subsequently performed and confirmed the diagnosis, demonstrating an enlarged and hyperactive right lower parathyroid gland. On top of that, abdominal MRI revealed a cystic neoplasm in the pancreas and detailed gastroenterological evaluation was conducted. The patient underwent transsphenoidal pituitary surgery. The pathological examination showed a plurihormonal pituitary neuroendocrine tumor (PitNET). At the three-month reevaluation, disease remission had not been achieved, so somatoatatin analogue octreotid was introduced into the treatment. Parathyroidectomy is planned as the next step. Given the presence of multiple endocrine neoplasias, clinical diagnosis of MEN1 was established, and referral to a higher-level reference center for genetic testing is planned.

Conclusions: This case highlights the importance of detailed clinical history and thorough physical examination in endocrinological outpatient clinic. Every patient with acromegaly should undergo comprehensive endocrine evaluation to rule out syndromic causes, given the implications for diagnosis, treatment, and family screening.

Abstract citation ID: lvag096.1398

EP1143 - ECE_3783 - Rare coexistence of intracranial tumors: craniopharyngioma, PitNET, and vestibular schwannoma—a case report

Karolina Cylke-Falkowska[1,2], Wojciech Zgliczyński[1] and Maria Stelmachowska-Banaś[1]
[1]*Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland* [2]*Centre of Postgraduate Medical Education, Doctoral School of Translational Medicine, Warsaw, Poland*

Background: Collision tumor is a rare entity that poses a real diagnostic and treatment challenge. To date, only 22 patients presenting with both craniopharyngioma and PitNET have been reported so far. Six of these cases involved GH-secreting PitNETs.

Case presentation: 61-year-old woman was admitted to endocrinology department with signs and symptoms suggesting acromegaly (enlargement of hands and feet and coarsening of facial features, headaches, changes in voice tone, chronic constipation). Her only long-term medication was L-thyroxine due to primary hypothyroidism. Apart from elevated IGF-1 levels and failure of GH suppression during OGTT, her hormonal profile was otherwise unremarkable.

Pituitary MRI revealed a heterogeneous, solid–cystic lesion in the suprasellar area. The lesion was compressing the optic chiasm and extending to the floor of the third ventricle. Additionally, a solid lesion was present within the sella turcica, encasing the internal carotid artery and displacing the optic nerves. Based on these findings, a collision tumor consisting of an adamantinomatous craniopharyngioma and a pituitary macroadenoma was suspected. Additionally MRI revealed a cystic lesion in the left cerebellopontine angle, consistent with vestibular schwannoma.

Head CT scan present calcifications in the suprasellar tumor, which further confirmed the presence of an adamantinous craniopharyngioma. Four months later, the patient underwent transsphenoidal surgery to remove both tumours: a GH–secreting pituitary PitNET and WHO adamantinomateus craniopharyngioma.

The postoperative course was complicated by multiple anterior pituitary deficiencies, AVP deficiency and hyperprolactinemia. These complications were managed using hydrocortisone, L-thyroxine and desmopressin replacement therapy. Due to GH deficiency patient was started on hGH replacement therapy.

Conclusions: Although extremely rare, the coexistence of GH-secreting PitNET and craniopharyngioma is possible in one patient and simultaneous surgery to remove both tumors can lead from GH excess to its deficiency.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1399

EP1144 - ECE_1866 - ATRX protein expression in pituitary carcinomas

Dana Erickson[1], Diane Donegan[1] and Jorge Trejo-Lopez[2]
[1]Endocrinology, Mayo Clinic, Rochester, United States; [2]Pathology and Laboratory Medicine, Mayo Clinic, Rochester, United States

Introduction: Pituitary carcinomas (PC) are rare tumors as they represent around 0.2% of all pituitary neuroendocrine tumors (PA). Studies suggest inactivation of alpha thalassemia/mental retardation syndrome X-linked protein (ATRX) expression is associated with aggressive neuroendocrine tumors, limited data is available for PC.

Aim: To assess expression of ATRX in patients with PC and its association with clinical characteristics and outcome.

Methods: Patients with PC (1997-2025) were identified. Clinical information was extracted. ATRX expression was analyzed via immunostaining using mouse monoclonal antibody (D-5 sc-5584, Santa Cruz Biotechnology) when sufficient tissue blocks were available. Results were grouped as A) aberrant (loss of staining in neoplastic nuclei), B) wild -type (retention within nuclei) and C) heterogenous expression. Staining was performed either on tissue from sellar location of tumor or metastasis.

Results: Of 25 patients with PC, 9 (36%) had sufficient tissue for analysis. Median initial PA size was 2.3 cm (range 0-4.6). ATRX expression was aberrant in 5 (55%), retained in 3 (30%) and heterogeneous in 1 (11%). Although the median age in group A compared to group B was younger at PA (34 [range 30-59] vs 53 [range 49-67], $P = .14$) and PC (48 [range 44-65] vs 57 [range 56-67], $P = .07$) diagnosis, this was not statistically significant. The number of surgical resections for PA varied from 1-4, 1 prolactinoma was initially treated medically. Median time to development of metastases in group A vs B was 13 [range 4-20] vs 4 [range3-6] years, respectively. Group A included 3 corticotroph, 1 gonadotroph and 1 null cell tumor, group B only corticotroph tumors, and group C lactotroph tumor. ATRX analysis was performed on tissue a median 14 years from initial PA diagnosis in group A (4 from pituitary location, 1 from brain metastasis), 5 years for group B (3 from metastatic disease) and 32 years for Group C (metastasis to pons). Median follow-up from PA diagnosis to last follow-up/ death did not differ between group A and B (14 [range 4-44] vs 11 [range7-11], $P = .214$). One patient died in group A whereas all 3 died in group B and the patient in group C is alive.

Conclusions: ATRX expression was lost in 55% of PC analyzed. Although not statistically significant, patients with aberrant ATRX expression tended to be younger at the initial PA diagnosis with a shorter time to metastasis development. . Next steps include confirmation of findings by next generation sequencing gene analysis.

Abstract citation ID: lvag096.1400

EP1145 - ECE_2143 - Body phenotyping with bedside techniques in cushing disease: a case-control study

Andrés Jiménez Sánchez, Pablo Remón Ruiz, Eva Venegas Moreno, Elena Dios-Fuentes, Jaime Perea Cortés, David Cano González and Alfonso Soto
Unidad de Gestión Clínica de Endocrinología y Nutrición, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Sevilla, Spain

Introduction: Chronic glucocorticoid exposure in Cushing disease may lead to muscle wasting and central adiposity.

Objective: To compare the body composition of adult Cushing disease patients under active surveillance in our Pituitary Unit with healthy controls.

Materials and Methods: Design: case-control study.

Sampling: non-consecutive, from June 2023 to June 2024.

Matching protocol: exact for sex, and nearest neighbour with a generalized linear model and 0.5 caliper width for body mass index (BMI).

Body composition analysis devices: calibrated weight and stadiometer, 50 kHz bioelectrical impedance analysis (BIA) (Nutrilab, AKERN), 5-10 Hz linear probe ultrasound system (Mindray), and handgrip dynamometer (JAMAR Plus).

Ultrasonography protocol: measurements were taken at the distal third of the right thigh and midpoint between umbilicus and xiphoid process. Subcutaneous adipose tissue (SAT) was measured at both locations. Rectus femoris (RF) and whole quadricipital (Quad) muscle thickness (RF-MT; Quad-MT) were measured at thigh. Preperitoneal adipose tissue (PPAT) was measured at abdomen.

The mean of three trials for handgrip strength (HGS) was used.

Blood samples: IGF-1 was determined.

Data analysis: with RStudio. Numerical variables expressed as median (IQR). Groups (Cushing disease versus control) were compared using 95% confidence intervals (95% CI) computed after k = 2000 bootstrapping. A positive 95% CI means case > control, and a negative 95% CI means control > case. Statistical significance was defined as a 95% CI excluding zero.

Results: 78 matched participants (72 female) with a median BMI 28.5 (8.5) kg/m^2. Their characteristics are described in the following table:

Variable	Between-group difference	Lower 95% CI limit	Upper 95% CI limit
Age (years)	2.026	−4.273	8.499
Weight (kg)	0.933	−7.141	8.036
Height (m)	−0.046	−0.0804	−0.012
BMI (kg/m^2)	2.057	−0.849	4.706
Abdominal perimeter (cm)	7.064	−0.178	14.886
R	−24.469	−62.366	15.320
Xc	−7.174	−11.902	−3.417
Phase angle (°)	−0.487	−0.735	−0.255
Thigh SAT (mm)	0.335	−2.667	3.299
RF-MT (mm)	−1.507	−3.140	0.005
Quad-MT (mm)	−2.548	−5.598	0.372
Abdominal SAT (mm)	0.721	−3.945	5.219
PPAT (mm)	0.165	−0.878	1.067
HGS (kg)	−1.256	−4.047	1.433
IGF-1 (ng/mL)	−3.018	−26.106	23.613

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: At equal age, BMI, and IGF-1 levels, cases of Cushing disease had a lower capacitive reactance and raw phase angle in bioelectrical impedance analysis (BIA). Ultrasound revealed no differences in adiposity, though cases tended to have lower muscle thickness and strength.

Abstract citation ID: lvag096.1401

EP1146 - ECE_2526 - Long-term treatment with first-generation somatostatin receptor ligands in acromegaly: predictors of dose reduction and withdrawal

Chiara Palumbo[1], Sabrina Chiloiro[1], Antonella Giampietro[1], Pier Paolo Mattogno[2], Rosalinda Calandrelli[3], Tommaso Tartaglione[3], Liverana Lauretti[4], Marco Gessi[5], Simona Gaudino[3], Laura De Marinis[6], Antonio Bianchi[1], Francesco Doglietto[2] and Alfredo Pontecorvi[1]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, Department of Internal Medicine, Endocrinology and Diabetology, Università Cattolica del Sacro Cuore, Rome, Italy; [2]Department of Neurosurgery, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [3]Department of Radiological Sciences, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [4]Department of Neurosurgery, Università Cattolica del Sacro Cuore, Rome, Italy; [5]Neuropathology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [6]Department of Internal Medicine, Endocrinology and Diabetology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Introduction: In acromegaly, therapy with first-generation somatostatin receptor ligands (fgSRLs) plays a central role, especially in patients who do not achieve surgical remission. We have observed that long-term use of fgSRLs, may allow, in some patients, a progressive dose reduction and even a complete withdrawal, resulting in sustained disease remission.

Patients and Methods: A longitudinal, retrospective, observational study was performed on patients with acromegaly in therapy with fg-SRLs, with a 15 years follow-up. Dose reduction and withdrawal were correlated with gender, age at diagnosis, GH and IGF-I levels at diagnosis and after surgery, biochemical control, adenoma's size and its intensity on MRI, and finally, histopathological characteristics.

Results: Dose reduction and withdrawal was achieved in 9 patients out of 34 patients treated with fg-SRLs at our institution with a 15 years follow-up. In this group of patients, fg-SRL dose reduction and withdrawal did not differ among patient gender ($P = .5$), age at acromegaly diagnosis ($P = .204$), GH and IGF-I levels at diagnosis, after surgery and with the achievement of biochemical control at 6 and 12 months of treatment with conventional dose of fg-SRLs ($P = .64$ and $P = .46$). All patients with microGH secreting pituitary adenoma underwent fg-SRL dose reduction/withdrawal ($P < .003$), without difference in invasive and not-invasive macroadenoma ($P = .124$). Fg-SRL dose reduction/withdrawal was achieved more frequently in hypointense tumors in T2-weighted MRI sequencies ($P = .028$). The proliferative index, cytokeratin pattern and SSTR2A expression did not differ among patients underwent and not-underwent fg-SRL dose reduction/withdrawal. Treatment with high frequency fg-SRLs administrations did not correlate with the fg-SRL dose reduction/withdrawal ($P = .581$).

Discussion: Our study shows that the probability of reducing or withdrawing therapy with fgSRLs depends on tumor characteristics, particularly size and MRI intensity. These results support prognostic stratification of patients and, most importantly, underline the importance of a personalized therapeutic approach.

Abstract citation ID: lvag096.1402

EP1147 - ECE_2539 - Joint and bone quality deteriorate in acromegaly despite long-term disease control

Christian Rosendal[1], Frederik Klit[2], Annika Kvist[3], Peter Vestergaard[3] and Jakob Dal[1]

[1]Endocrinolgy, Aalborg Universityhospital, Aalborg, Denmark; [2]Research data and Biostatistics, Aaborg Universityhospital, Aalborg, Denmark; [3]Steno Diabetes Center North Jutland, Aalborg, Denmark

Context: Joint and bone disorders are frequent and disabling complications of acromegaly. HR-pQCT provides precise and integrated assessment of bone quality and joint abnormalities.

Objective: To evaluate bone and joint quality in patients with long-term controlled acromegaly.

Methods: Seventeen patients with acromegaly and age- and sex-matched healthy controls.

HR-pQCT of hand joints, tibia and radius; bone microindentation; vertebral fracture assessment; dual X-ray absorptiometry; circulating bone biomarkers; questionnaires.

Results: Patients with acromegaly (mean age: 61.8 years, mean disease duration: 13.1 years, mean IGF-I Z-score: 1.2) had wider joint spaces of the second (2.85 vs 2.68 mm, $P = .004$) and third (2.92 vs 2.80 mm, $P = .037$) metacarpophalangeal joints, the latter with a higher risk of osteophytes (50% vs 11.8%, $P = .017$). Vertebral deformities were more common (88% vs 47%, $P = .01$), more numerous (2.1 vs 0.7, $P < .001$), and associated with higher spinal deformity index values (2.6 vs 1.3, $P = .04$) in participants with acromegaly. HR-pQCT demonstrated lower trabecular bone mineral density in the radius (114.8 vs 150.3 mg/cm^3, $P = .008$) and tibia (129.3 vs 166.2 mg/cm^3, $P = .002$), as well as fewer (1.63 vs 2.11 mm^{-1}, $P = .001$) and thinner (0.056 vs 0.064 mm, $P = .005$) trabeculae. Bone and joint abnormalities increased with age in the acromegaly group.

Conclusions: Acromegaly is associated with impaired bone microarchitecture and structural joint alterations that deteriorate with increasing age despite long-term, biochemically controlled.

Abstract citation ID: lvag096.1403

EP1148 - ECE_2638 - Quality of life and mental health disorders in acromegalic patients

Mihaela Maria Vlad, Plotuna Iulia-Ștefania, Melania Balas, Ioana Golu and Daniela Amzar

2nd Internal Medicine, "Victor Babes" University of Medicine and Pharmacy, Timișoara, Romania

Introduction: Acromegaly is a rare pathology, caused in most cases by a growth hormone-secreting pituitary adenoma. Its low prevalence is one of the factors contributing to the late diagnosis of the disease. As a result, irreversible morphological changes occur, as well as numerous complications, including psychiatric ones.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Materials and Methods: The study group included 40 patients diagnosed with acromegaly at our hospital between January 1st, 2017, and April 30th, 2024. The group included 14 men (35%) and 26 women (65%), with a mean age at diagnosis of 43.8 ± 11.6 years. The mean duration of the disease was 85.9 ± 97.7 months (1-468). Psychiatric evaluation to determine the presence of psychiatric pathology was performed as part of the current evaluations for all patients in the study cohort. Patients completed the Romanian version of the AcroQol (Acromegaly Quality of Life Questionnaire), which was designed to measure health-related quality of life in patients diagnosed with acromegaly. In the study group, acromegaly was controlled in 32.5% of patients.

Results: Nine patients (22.5%) were diagnosed with psychiatric pathology (anxiety and/or depression), of whom 88.88% were women. Patients with psychiatric disorders were older (55.1 ± 15.7 years) compared to those without this complication (48.4 ± 9.2 years), but without a statistically significant difference. The average GH and IGF-1 levels in patients with psychiatric disorders were 17.5 ± 31.0 ng/ml and 409.6 ± 144.8 ng/ml, respectively, and in those without psychiatric pathology 18.40 ± 56.55 ng/ml and 380.7 ± 260.3 ng/ml, respectively, with no statistically significant differences. Biochemical parameters, disease duration, and disease control were similar between the two groups. Patients with psychiatric pathology tend to be more likely to be retired or unemployed and have a lower quality of life on the ACROQOL questionnaire: 43.4 ± 20.4 points compared to 65.8 ± 19.1 points in acromegaly patients without psychiatric pathology ($P = .003$). Among comorbidities, type 2 diabetes mellitus was more frequently diagnosed in the group of patients with psychiatric pathology.

Conclusions: The percentage of patients diagnosed with anxiety and/or depression is 22.5% in our group of acromegalic patients, with one in four cases presenting psychiatric pathology. Acromegalic patients with psychiatric pathology have a significantly lower quality of life and are more frequently diagnosed with type 2 diabetes mellitus.

Abstract citation ID: lvag096.1404

EP1149 - ECE_3732 - Comparison of low-dose (1 μg) versus standard high-dose (250 μg) ACTH stimulation tests for the assessment of the hypothalamic–pituitary–adrenal axis

Anastasia Patricia Stanescu-Smocot[1,2], Beatrice Cristea[2], Vlad Radulescu[1,2], Maria Tudorache[2], Viorica Nicuta[2] and Corin Badiu[1,2]

[1]*Endocrinology, Endocrinology IV, "C Davila" University of Medicine and Pharmacy, Bucharest, Romania;* [2]*Research Department, Endocrinology IV, C.I. Parhon National Institute of Endocrinology, București, Romania*

Introduction: Assessment of the hypothalamic–pituitary–adrenal (HPA) axis remains challenging, particularly in patients with suspected central adrenal insufficiency. The conventional high-dose ACTH stimulation test (250 μg) uses a supraphysiological dose, which may mask subtle degrees of adrenal dysfunction. In contrast, the low-dose ACTH test (1 μg) has been proposed to better reflect physiological adrenal responsiveness.

Aim: To compare the diagnostic performance of the low-dose (1 μg) versus high-dose (250 μg) ACTH stimulation tests in patients with suspected adrenal insufficiency and to evaluate recovery of the HPA axis according to etiology.

Patients and Methods: We conducted a retrospective observational study including **173 patients** evaluated between **2024-2025** for suspected adrenal insufficiency. Patients underwent assessment of the hypothalamic–pituitary–adrenal (HPA) axis using either a **low-dose (1 μg)** or **standard high-dose (250 μg)** ACTH stimulation test, according to clinical indication.

In a predefined subgroup of patients (***n* = 20**), **both low-dose and high-dose ACTH stimulation tests were performed in the same individual**, at **24 h interval**, allowing direct intra-individual comparison. Peak cortisol response was defined as the highest value obtained at **30 or 60 min.** after ACTH administration. A peak serum cortisol **≥18 μg/dl** was considered a normal response, values **12-18 μg/dl** were **borderline (partial) response,** and values **<12 μg/dl** were diagnostic of adrenal insufficiency. Recovery of the HPA axis was assessed during follow-up and categorized as **recovery within <3 months, within <1 year, after >1 year**, **>2 years**, or as **persistent adrenal insufficiency,** according to clinical, biochemical, and treatment-related data.

Results: Low-dose stimulation identified adrenal insufficiency in **24.3%** of patients, compared with **18.2%** diagnosed using the high-dose. In addition, **17.1%** patients demonstrated a borderline response on low-dose, consistent with partial or evolving adrenal insufficiency. In contrast, the high-dose classified **70.4%** cases as normal adrenal function, suggesting that supraphysiological ACTH stimulation may **overestimate adrenal reserve**.

Twenty patients underwent **both low-dose and high-dose stimulation, performed 24 hours apart.** Within this subgroup, **30% (*n* = 6)** were classified as having adrenal insufficiency or borderline response on low-dose testing, while showing a normal cortisol response following high-dose, indicating that the high-dose test may mask clinically relevant adrenal dysfunction.

Recovery was dependent on aetiology: g**lucocorticoid-induced** showed the most favorable recovery profile (**53.3%)** within **12 months, while pituitary failure,** and **immunotherapy-related adrenal insufficiency** were associated with delayed recovery.

Conclusions: L**ow-dose test as a more sensitive and physiologically appropriate method** for diagnosing and monitoring central adrenal insufficiency.

Abstract citation ID: lvag096.1405

EP1150 - ECE_3828 - Extended medial wall resection of the cavernous sinus in endoscopic treatment of pituitary adenomas causing acromegaly with cavernous sinus invasion (Knosp I-III)—early clinical results

Barbara Buchalska[1], Maria Maksymowicz[2] and Jacek Kunicki[1]

[1]*Department of Neurosurgery, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland;* [2]*Warsaw, Poland*

Background: Currently, the first-line treatment for acromegaly is surgery—adenoma resection. In patients with invasive adenomas, standard transsphenoidal resection does not provide satisfactory results (remission of acromegaly in 30%-50%). In cases of medial wall invasion of the cavernous sinus, its removal allows for improved treatment outcomes and higher remission rates.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Purpose: The aim of the study was to evaluate the outcomes of endoscopic transsphenoidal resections with removal of the medial wall of the cavernous sinus in the treatment of somatotropin-secreting pituitary adenomas with intermediate and high risk of invasive growth (Knosp I-III) causing acromegaly.

Methodology: This was a retrospective analysis of a series of 21 patients (15 women and 6 men) treated in 2024-2025 with endoscopic transsphenoidal resections for pituitary adenomas with possible invasive growth assessed by the Knosp scale (I-III) and causing acromegaly. The mean age at the beginning of treatment was 53 years (range 25-76 years), with a mean follow-up of 6 months (0-13 months).

Results: Most patients had macroadenomas prior to resection ($n = 11$; 52%). In 11 patients (52%), histopathological examination confirmed invasion of the medial wall of the cavernous sinus. In all patients, the medial wall of the cavernous sinus was removed and gross total resection was achieved. The mean intraoperative blood loss was 180 ml (range 50-450 ml). No neurological or vascular complications were observed postoperatively. Eighteen patients (86%) met the criteria for remission of acromegaly at early postoperative follow-up (2-5 months).

Conclusions: Endoscopic transsphenoidal resections of invasive somatotropin-secreting pituitary adenomas with removal of the medial wall of the cavernous sinus enable effective treatment of acromegaly. Although this method carries an additional risk, it is relatively safe and associated with a low rate of complications.

Abstract citation ID: lvag096.1406

EP1151 - ECE_2827 - Bone proteomic analysis in patients with acromegaly and its clinical correlations

Luigi Demarchis[1], Sabrina Chiloiro[1], Pier Paolo Mattogno[2], Penelope Giambo'[1], Michela Cicchinelli[3], Federico Valeri[2], Domenico Milardi[1], Emanuele Pierpaolo Vodola[1], Laura De Marinis[1], Andrea Urbani[3], Liverana Lauretti[2], Antonella Giampietro[1], Antonio Bianchi[1], Federica Iavarone[3], Francesco Doglietto[2] and Alfredo Pontecorvi[1]

[1]Rome, Italy; [2]Neurosurgery, Catholic University of the Sacred Heart, Fondazione Policlinico Universitario A. Gemelli, Rome, Italy; [3]Department of Basic Biotechnological Sciences, Intensivological and Perioperative Clinics, Catholic University of the Sacred Heart, Fondazione Policlinico Universitario A. Gemelli, Rome, Italy

Background: Bone metabolism is often impaired in patients with acromegaly, with an increased risk of osteoporosis and fragility vertebral fractures, which may also occur independently of the acromegaly biochemical control. Skeletal fragility is probably due to increased bone turnover, with increased bone resorption and impaired bone neoformation. The pathogenetic mechanisms remain not yet fully understood.

Aim of the study: Identify the bone proteome of patients with acromegaly and compare it with a control group of non-acromegaly subjects.

Methods: an analysis by mass spectrometry was conducted on five ethmoid samples (ES) of patients with acromegaly and five ES of patients with non-secreting pituitary tumors (NSPTs). ES were achieved during transsphenoidal surgery for the resection of the pituitary tumors. These samples were analyzed to identify and assay the proteome and to classify them. Among the proteins quantitatively up- and down-regulated (UR and DR) in the group of acromegalic patients compared to patients with NSPT, those with a ratio of variation based on Fold-Change > |1.50| and statistical significance (P-value < .05) were studied.

Results: 312 proteins belonging to each group were identified. As for the acromegalic patient group, compared with the NSPT patient group, 6 proteins with positive Fold-Change (UR) above the threshold value (+1.5) and 12 proteins with negative fold-change (DR) below the threshold value (−1.5) were identified. Their biological function and clinical correlations found in the literature were analyzed: of these 18 proteins, significant correlations inherent to bone metabolism and turnover were found for Profilin-1 (UR), Isoform 5 of Periostin (UR), Apolipoprotein E (DR), Caveolin-1 (DR). A positive correlation was detected between Profilin-1 and Isoform 5 of Periostin concentrations and serum GH and IGF-I levels of our patients' cohort. In parallel, a negative correlation was also detected between Apolipoprotein E and Caveolin-1 concentrations and serum IGF-I levels.

Conclusions: This work aimed to identify proteins with higher and lower expression in the ethmoid bone of patients with acromegaly compared with the control group to better understand bone metabolism and turnover in these patients.

Abstract citation ID: lvag096.1407

EP1152 - ECE_2880 - When histology is silent but ACTH rises: a red flag for pituitary carcinoma in a three-case series

Giacomo Fabio Antonio Grifoni[1], Vittoria Favero[1,2], Paola Doneda[3], Giovanni Battista Lasio[4], Andrea Saladino[5], Renato Cesare Cozzi[2] and Iacopo Chiodini[1,2]

[1]Department of Medical Biotechnology and Translational Medicine, University of Milan., Milan, Italy; [2]Endocrinology Unit, Grande Ospedale Metropolitano Niguarda, Milan, Italy; [3]Neuroradiology Unit, Grande Ospedale Metropolitano Niguarda, Milan, Italy; [4]Neuroscience Department, Neurosurgery Division, ASST Ovest Milano, Legnano Hospital, Legnano, Italy; [5]Pontassieve, FI, Italy

Introduction: Pituitary carcinomas (PCs) are rare tumors, accounting for 0.1%-0.2% of pituitary neoplasms. They're defined by the presence of central nervous system (CNS) or systemic metastases in pituitary neuroendocrine tumors (PitNETs). PCs mainly derive from secreting PitNETs: among these, ACTH-secreting PitNETs show an average degeneration time of 9.5 years. Here, we describe a case series of three patients with ACTH-secreting PitNETs who developed carcinomatous evolution.

Case series: three patients—two males, patients 1 (P1) and 2 (P2), and one female (P3)—were diagnosed with large ACTH-secreting macroPitNETs at age 33, 48 and 64 respectively: none showed histological features suggestive of aggressive PitNET.

While the latency period between Cushing Disease (CD) and PC diagnosis for P2 and P3 was comparable (5 and 4.75 years respectively), in P1 it was 23 years.

All patients underwent transnasal surgery. P1 also required transcranial surgery, medical therapy (cabergoline and pasireotide), conventional radiotherapy, and ultimately bilateral adrenalectomy; P2 and P3 underwent stereotactic radiosurgery and conventional radiotherapy respectively, for persistent CD.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

In P2 and P3 progressive ACTH increases, despite radiological stability (P2) or reduction (P3) of the remnant, prompted restaging through imaging testings (total-body CT, spinal MRI, DOTATOC-PET, FDG-PET) leading to the detection of metastases.

In P1, ACTH assessments were unreliable after bilateral adrenalectomy and diagnosis of PC was incidental: a liver metastasis was discovered during abdominal ultrasound for a colic pain and confirmed as ACTH-positive PitNET on biopsy.

P1 and P2 developed systemic metastases, predominantly involving axial skeleton, besides the liver localisation in P1.

P3 exhibited rapid clinical and biochemical deterioration leading to exitus in few weeks.

Following PC diagnosis in late 2025, P1 and P2 initiated first-line temozolomide therapy and radiotherapy on skeletal metastases. Denosumab was also started and follow-up is still ongoing.

Conclusions: large ACTH PitNETs may undergo insidious malignant transformation. Rising hormone levels (eg, huge ACTH increase), in patients without evident sellar recurrence, serve as a critical indicator of potential tumor dissemination necessitating thorough neuroradiological and systemic evaluation, whereas histological and biomolecular markers prove largely unreliable and ineffective for predicting malignancy

With PC's natural disease course being highly variable, surgery or systemic oncological therapies (eg, temozolomide) may sometimes be precluded, highlighting the lack of therapeutic options for these tumors.

Abstract citation ID: lvag096.1408

EP1153 - ECE_2881 - Evaluation of post-surgical outcomes in prolactinoma patients

Alicja Knysak[1], Nijaguna Mathad[2], Jonathan Hempenstall[2], Christoforos Syrris[2], Jana Bujanova[1] and Ma'en Al-Mrayat[1]
[1]*Endocrinology, Diabetes and Endocrinology, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom;* [2]*Neurosurgery, Wessex Neurological Centre, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom*

Background: Current treatment guidelines for prolactinomas recommend dopamine agonists (DAs) as first-line therapy, reserving surgery and radiotherapy for resistant or intolerant cases. Herein we aimed to evaluate the outcomes for patients with prolactinomas who underwent surgical treatment in our institution (The Wessex Neurological Centre, a tertiary unit in Southampton, UK).

Methods: We performed a retrospective review of 32 patients (17 males, 15 females; mean age 37.5 years) who underwent endonasal endoscopic pituitary surgery for prolactinoma between 2017 and 2025. Tumour types included 27 macroadenomas (84%), 4 microadenoma (13%), and 1 giant adenoma (3%). Cavernous sinus (CS) invasion was present in 14 cases (44%), and 19 tumours (59%) caused optic chiasm compression. Prolactin levels at diagnosis ranged from 251 to 1 026 688 mU/L (our reference range for Male: 55-276; Female: 57-561). 24 patients (75%) received pre-operative DA therapy. Indications for surgery were one or more of: visual compromise ($n = 14$; 44%), pituitary apoplexy ($n = 6$; 19%), DA intolerance ($n = 9$; 28%), DA resistance ($n = 6$; 19%), and cerebrospinal fluid (CSF) leak ($n = 1$; 3%).

Results: Gross total resection was achieved in 21 patients (66%), while 11 (34%) underwent surgery for debulking purposes. Intra-operative CSF leak occurred in 3 patients (9%), and 1 patient developed a post-operative CSF leak requiring surgical repair. 1 patient experienced significant post-operative epistaxis requiring surgical intervention. 7 patients (22%) developed new post-operative pituitary dysfunction, including 3 (9%) with arginine vasopressin deficiency. Histological analysis confirmed lactotroph adenoma in all cases, with co-secretion of growth hormone in 7 tumours (22%). Post-operatively, 19 patients (60%) achieved biochemical remission, including 3 of 4 patients (75%) with microadenomas and 16 patients (57%) with macroadenomas. No residual tumour was visible on post-operative MRI in 20 patients (62%). Persistent disease was observed in 12 patients (38%); 4 underwent repeat surgery (13%) and 2 (6%) received adjuvant radiotherapy. Tumour recurrence was documented in 3 patients (9%) during the follow-up period. Cavernous sinus involvement was observed in 14 (44%) of all patients. Cavernous sinus invasion patients achieving remission were 5 (40%) whilst the rest showed a biochemical remission of 78% (14 of 18 patients) (P value .016 < .05) indicating statistically significant difference of remission between CS invasion or not.

Conclusions: Surgical intervention of prolactinomas yielded significant rates of biochemical remission and low recurrence including in patients with macroadenomas. For carefully selected cases, primary or early secondary surgery may offer an efficacious and safe alternative to traditional long-term pharmacological therapy.

Abstract citation ID: lvag096.1409

EP1154 - ECE_3188 - Gonadotroph pituitary adenomas: clinical features, imaging predictors of recurrence, and treatment outcomes from a tertiary center

Esra Eraslan Aydemir[1], Özge Baş Aksu[1], Asena Gökçay Canpolat[1], Özgür Demir[1], Mustafa Sahin[1], Murat Erdogan[1], Rifat Emral[1], Aylin Heper[2] and Sevim Güllü[1]
[1]*Endocrinology and Metabolism Department, Endocrinology and Metabolism Department, Ankara University Faculty of Medicine, Ankara, Türkiye;* [2]*Medical Pathology Department, Medical Pathology Department, Ankara University Faculty of Medicine, Ankara, Türkiye*

Background: Gonadotroph adenomas constitute the majority of nonfunctioning pituitary adenomas; however, they are often grouped together in surgical series, limiting our understanding of specific prognostic factors. This study aimed to evaluate the preoperative clinical and radiological characteristics of patients with histopathologically confirmed gonadotroph adenomas, identify predictors of treatment response, and assess the efficacy of adjuvant therapies.

Methods: This retrospective study included 78 patients who underwent transsphenoidal surgery at Ankara University Faculty of Medicine between January 2010 and January 2025, with histopathologically confirmed gonadotroph adenoma and a minimum follow-up of six months. Treatment response was categorized as complete surgical response, good residual control (>50% volume reduction), or poor residual control. Multivariable binary logistic regression analysis was performed to identify independent predictors of unfavorable treatment response.

Results: The mean age at surgery was 54.05 ± 13.19 years, with male predominance (73.1%). Visual impairment (71.8%) and headache (42.3%) were the most common presenting symptoms, while 16.7% were incidentally discovered. Central hypogonadism was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

the most frequent preoperative hormonal deficiency (44.9%), followed by central hypocortisolism (32.1%) and central hypothyroidism (28.2%). Panhypopituitarism was present in 12.8% at baseline and increased to 21.8% postoperatively.

Preoperative median tumor diameter was 27 mm (IQR: 22-38) with a median volume of 7.03 cm^3 (IQR: 3.98-14.11). Suprasellar extension was present in 91.0%, optic chiasm compression in 87.2%, cavernous sinus invasion in 42.3%, and sphenoid sinus invasion in 25.6%. Gross total resection was achieved in only 24.4% of patients. Patients with residual tumor had significantly larger preoperative tumor dimensions compared to those achieving gross total resection (median diameter: 28 mm vs 24.5 mm, $P = .011$; median volume: 7.85 cm^3 vs 4.44 cm^3, $P = .008$).

On univariate analysis, sphenoid sinus invasion ($P = .032$) and optic chiasm compression ($P = .033$) were significantly associated with residual tumor presence. Multivariable logistic regression identified sphenoid sinus invasion as the sole independent predictor of unfavorable treatment response (OR = 0.19; 95% CI: 0.046-0.783; $P = .021$). Patients without sphenoid sinus invasion had approximately 5-fold higher odds of achieving favorable residual control. Notably, cavernous sinus invasion, Knosp grade, and Ki-67 proliferation index were not independent predictors of treatment outcome.

Conclusions: Gonadotroph adenomas frequently present with advanced tumor characteristics, resulting in low gross total resection rates. Sphenoid sinus invasion—rather than the traditionally emphasized cavernous sinus invasion—emerged as the sole independent predictor of unfavorable treatment response, providing a new perspective on preoperative risk stratification for this tumor subtype.

Abstract citation ID: lvag096.1410

EP1155 - ECE_3804 - Determinants of diagnostic delay in patients with acromegaly

Soukaina Lahlou, Nassim Essabah Haraj, Malak Iggar, Siham El Aziz and Asma Chadli
Clinical Neuroscience and Mental Health Laboratory, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Ibn Rochd University Hospital, Casablanca, Morocco

Introduction: Acromegaly is a rare endocrine disorder with a slow and insidious course, characterized by a wide clinical heterogeneity. This polymorphic presentation often leads to a significant diagnostic delay, exposing patients to preventable complications and delaying the initiation of appropriate treatment.

Objective: To assess diagnostic delay in patients with acromegaly and to analyze the clinical and biological factors associated with late diagnosis.

Patients and Methods: This was a retrospective cross-sectional study including 81 patients followed for acromegaly. Diagnostic delay was defined as the time interval between the onset of first symptoms and the establishment of the diagnosis. Patients were divided into three groups according to disease duration: less than 5 years, 5-10 years, and more than 10 years. Clinical and biological data were collected from medical records. Statistical analysis was performed using SPSS software.

Results: The mean age at diagnosis was approximately 44 years, with a female predominance. The median disease duration was 9.8 ± 5.5 years. A diagnostic delay greater than 10 years was observed in 42.6% of patients, while 27.9% were diagnosed within 5 years and 29.5% between 5 and 10 years.

Patients with late diagnosis more frequently presented with non-specific symptoms, mainly osteoarticular pain and general symptoms. In contrast, the presence of compressive symptoms was associated with earlier diagnosis, with a tumoral syndrome identified in 100% of patients diagnosed within 5 years.

The mean IGF-1 level was 714 ± 422 ng/mL. No significant correlation was found between disease duration and IGF-1 levels ($P = .15$).

Conclusions: Diagnostic delay in acromegaly remains frequent and often prolonged. It is mainly related to the non-specific nature of early clinical manifestations, highlighting the need for increased clinical awareness to reduce diagnostic delays and improve patient outcomes.

Abstract citation ID: lvag096.1411

EP1156 - ECE_1378 - Value of the LHRH test in the evaluation of precocious puberty

Fatma Ben Abdessalem, Taieb Ach, Imen Halloul, Wiem Saafi, Hamza Fekih, Ghada Saad and Yosra Hasni
Endocrinology, Hôpital Farhat Hached, Sousse, Tunisia

Introduction: Precocious puberty is defined as the appearance of secondary sexual characteristics before age 8 in girls and 9 in boys. The LHRH stimulation test plays a crucial role in identifying the origin of precocious puberty and differentiating true cases from benign variants.

Materials and Methods: This cross-sectional study included 16 cases investigated for precocious puberty. Clinical and hormonal evaluations were performed for all patients.

Results: Twelve girls and four boys made up the 16 participants in the study. At consultation, the average age was five years old (range: one to nine years). Premature pubarche ($n = 7$), premature thelarche ($n = 7$), and increased testicular volume ($n = 2$) were the reasons for consultation. Every patient underwent the LHRH test. With LH peaks ranging from 5 to 94 IU/L and FSH/LH ratios between 0.63 and 4.9, the findings indicated a central origin in six patients. Five patients were diagnosed with pseudo-precocious puberty. Following the LHRH test, the LH peak varied from 0.5 to 3.9 IU/L, and the FSH/LH ratio was between 0.18 and 1. In 5 girls with a mean age of 3 years (1-5 years), premature thelarche was identified. The LHRH test showed LH peaks between 0.8 and 7.2 IU/L and FSH/LH ratios between 0.2 and 2.9.

Conclusions: Precocious puberty may indicate a serious pathology of central or peripheral origin. However, isolated premature thelarche can be considered a normal variant, highlighting the importance of the LHRH test in distinguishing true precocious puberty from simple premature puberty.

Abstract citation ID: lvag096.1412

EP1157 - ECE_1488 - Global prevalence estimates of adult growth hormone deficiency (AGHD): a targeted literature review and meta-analysis [2015-2025]

Subhara Raveendran[1,2], Katja Wiederkehr[3], Chelsea Catsburg[3] and Alden Smith[1]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Ascendis Pharma, Inc, Palo Alto, United States; [2]HEOR, Ascendispharma, Palo Alto, United States; [3]BluePrint Orphan, Inc, New York, United States

Background: Adult growth hormone deficiency (AGHD) is a chronic endocrine disorder that results from inadequate growth hormone secretion and is associated with low bone density, increased body fat, reduced muscle mass, diminished psychosocial functioning, and increased risk of cardiovascular and metabolic dysfunction. Due to heterogeneous diagnostic definitions and limited data sources, population-based estimates of AGHD remain sparse. This research aimed to quantify global AGHD prevalence estimates and treatment rates through a systematic literature review and meta-analysis of recently published epidemiological studies.

Methods: A systematic literature review of PubMed and Embase was conducted to identify studies reporting on the prevalence of AGHD among populations age 18+. Studies were reviewed against exclusion criteria in accordance with PRISMA guidelines and were included if they provided population-based data using comprehensive diagnostic definitions, or if they included cases treated with growth hormone replacement therapy (GHRT). All identified studies were entered into a meta-analysis, which used a random-effects model to estimate pooled prevalence rates; study heterogeneity was quantified using the I^2 statistic.

Results: Six studies with data across Japan, the United States, Italy, France, and Spain were included. Across studies utilizing comprehensive diagnostic definitions ($n = 4$), AGHD prevalence ranged from 27.1 to 37.0 per 100k adults, with an overall pooled global AGHD prevalence of 31.1 per 100k adults (95% CI: 25.9-36.3; $I^2 = 99.2\%$). When considering treated cases only, across populations based on GHRT recipients ($n = 4$), prevalence ranged from 0.7 to 3.5 per 100k adults, with a pooled treated prevalence of 1.9 per 100k adults (95% CI: 1.1-2.7; $I^2 = 99.6\%$). Pooled sub-analyses were not conducted by region due to a lack of estimates, and therefore, differences in prevalence or treatment by region remain unknown.

Conclusions: This meta-analysis estimates that AGHD affects 31 per 100k adults globally, with a substantially smaller fraction receiving GHRT (2 per 100k adults globally). Considerable heterogeneity among studies highlights the need for standardized diagnostic criteria and improved epidemiological surveillance. Future research should refine prevalence estimates, assess regional disparities, and understand barriers to treatment among patients with AGHD. Overall, these findings strengthen the current understanding of AGHD global burden and underscore the need for improved diagnostic practices and broader access to effective GHRT.

Abstract citation ID: lvag096.1413

EP1158 - ECE_1838 - Do immunonegative gonadotroph tumors exhibit a more aggressive behavior than immunopositive ones?

Maria Rodríguez-Bedoya, Jorge Navarro, Johana Sottile, Elena Sansano, Cristina Guillén, Miriam Escalante, Javiera Rodríguez, Francisca María Peiró-Marqués, Eugenia Torregrosa, Elena García, Javier Abarca and Antonio Pico

Endocrinology and Nutrition, General University Hospital of Alicante, Alicante, Spain

Introduction: Non-functioning pituitary tumors represent 30%-40% of pituitary neoplasms. Transcription factor–based classification reclassified many previously considered "null" tumors, with a substantial proportion belonging to gonadotrophs. Among these, most retain immunostaining for LH/FSH (hormone-positive gonadotroph tumors, HPGT), whereas a subgroup lacks hormonal expression (hormone-negative gonadotroph tumors, HNGT). Gonadotroph tumors have also emerged as candidates for targeted therapies, as somatostatin receptor subtype 3 (SSTR3) appears highly expressed. We aimed to explore clinical, radiological, histopathological and molecular differences between HPGT and HNGT.

Material and Methods: We performed a single-center, observational, ambispective study, including adults with histologically confirmed gonadotroph tumors (SF-1 and/or GATA2 positive) diagnosed since 2019. Clinical, radiological and histopathological variables were collected. Signal intensity ratio (SIR) was defined as the ratio of tumor signal intensity to gray matter on T2-weighted MRI sequences. Proliferation was assessed by Ki-67 index using immunohistochemistry (IHC). SSTR3 expression was quantified by RT-qPCR ($2^{-\Delta\Delta Ct}$) using normal pituitary tissue as calibrator. Mann–Whitney U and Chi-square tests were applied.

Results: 64 patients were included (38 HPGT, 26 HNGT). Age was similar (median 58 years [IQR 20] vs 58 [21]; $P > .05$), as sex distribution (women 34.5% vs 34.8%; $P > .05$). HNGT showed trends toward higher apoplexy than HPGT (17% vs 10%; $P > .05$) and panhypopituitarism (44% vs 31%; $P > .05$), whereas visual field impairment tended to be slightly more frequent in HPGT (48% vs 41%; $P > .05$).

Tumor size was similar (27 mm [IQR 19] vs 30 mm [17]; $P > .05$). A trend toward higher cavernous sinus invasion was observed in HNGT (41% vs 24%; $P > .05$), while T2 hyperintensity appeared to be more frequent in HPGT (85% vs 53%; $P > .05$). Ki-67 did not differ (1.10% [0.9] vs 1.0% [1.7]; $P > .05$).

FSH (3.7 [12.17] vs 2.1 [6.97]; $P > .05$) and LH (0.001 [0.01] vs 0.003 [0.01]; $P > .05$) expression did not differ. SSTR3 expression was similar between groups (12.5 [21.5] vs 4.6 [11.07]; $P > .05$).

Recurrence appeared more frequent in HPGT but was not confirmed after follow-up adjustment (Cox HR 0.397; $P = .399$). Three patients in HPGT group and one patient in HNGT received radiotherapy.

Conclusions: No statistically significant differences were observed between HPGT and HNGT for the variables analyzed, potentially influenced by sample size and follow-up. However, HNGT showed a trend toward greater invasiveness without differences in proliferation, whereas HPGT tended to show higher recurrence. Consistent with previous studies, GT tumors demonstrated high expression levels of SSTR3.

Abstract citation ID: lvag096.1414

EP1159 - ECE_3700 - The role of hyperhomocysteinemia in Rathke's cleft cysts: from clinical manifestation to treatment outcomes

Mariana Solovey[1,2], Olena Danevych[1], Mykola Guk[1], Arthur Mumlev[1], Andrii Chukov[1], Nataliia Kobrynska[2] and Oleksii Ukrainets[1]

[1]Romodanov Neurosurgery Institute, Kyiv, Ukraine; [2]Komisarenko Endocrinology and Metabolism Institute, Kyiv, Ukraine

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Rathke's cleft cysts (RCCs) are benign pituitary lesion originated from remnants of Rathke's pouch. The prevalence of RCCs in autopsy studies is reported in 13%-22% of all sellar lesions. The pathogenesis is not fully understood. The relationship between hyperhomocysteinemia and clinical presentation of symptomatic RCCs including headache, arterial hypertension, reproductive disorders have not been reported.

Objective: To discover the relationship between plasma homocysteine levels, clinical presentation and treatment outcomes in the patients with RCCs.

Materials and Methods: We performed a retrospective study of 66 patients that were diagnosed with RCCs: 53 under the conservative management and 13 surgically treated via endoscopic endonasal transsphenoidal approach. Radiological characteristics, clinical presentation, plasma homocysteine and hormones levels according to the age and sex, treatment outcomes were analyzed.

Results: The group of surgically treated patients included 6 males and 7 females. The median age was 35 years (IQR: 17-48.5 years). The clinical presentation included: headache ($n = 11$, 84.6%) with arterial hypertension in 4 patients (30.7%), hypogonadism with decreased levels of FSH, LH or DHEA-s ($n = 5$, 38.5%), hyperprolactinemia ($n = 3$, 23%), GH deficiency ($n = 1$, 7.7%). Postoperative improvement of clinical symptoms was achieved in 6 (46%) patients with normal preoperative homocysteine levels. The persistent symptoms in the rest of patients were strongly associated with elevated plasma homocysteine levels (the mean homocysteine level was 19 ± 5.444 μmol/l). The further homocysteine levels normalization resulted in clinical improvement in all patients.

The group of patients under the conservative management included 35 females and 18 males with the median age of diagnosis of RCC 26 years (IQR: 19.5-36.5 years) and 31 years (IQR: 24-44 years) respectively. Hyperhomocysteinemia was revealed in 21 female patients (60%) and in all 100% male patients. The most common clinical presentation in females were menstrual disorders ($n = 22$, 68.75%) and headache in males ($n = 13$, 76.5%). Correction of homocysteine levels was associated with clinical improvements in the most patients with RCCs and in cyst volume decrease in some cases.

The genetic variants in methylenetetrahydrofolate reductase (MTHFR 677C>T, MTHFR 1298A>C), methionine synthase (MTR 2756A>G), methionine synthase reductase (MTRR 66A>G) were determined in 22 patients with elevated plasma homocysteine levels. Polymorphisms in genes involved in folate metabolism were detected in different combinations in all 22 patients.

Conclusions: Homocysteine level assessment and correction should be considered in optimal management of patients with RCCs. More genetic studies are needed to discover the possible genetic associations of folate metabolism and RCCs development.

Abstract citation ID: lvag096.1415

EP1160 - ECE_1486 - Metabolic effects of recombinant human growth hormone therapy in adults with severe growth hormone deficiency: experience from a single center

Zuzanna Zak-Skryskiewicz, Lukasz Dzialach and Przemysław Witek

Department of Internal Medicine, Endocrinology and Diabetes, Medical University of Warsaw, Warsaw, Poland

Severe adult growth hormone deficiency (GHD) is associated with adverse metabolic disturbances, increased adiposity, and elevated cardiovascular risk. Although recombinant human growth hormone (rhGH) replacement is an established therapy, real-world outcome data from Poland remain scarce.

We conducted a retrospective real-world analysis of adults with severe GHD treated with rhGH within the national drug program at a single tertiary endocrine center. Serum insulin-like growth factor 1 (IGF-1), lipid profile, glycemic indices, and body composition assessed by bioelectrical impedance analysis were evaluated at baseline, after 6 and 12 months of therapy, and at long-term follow-up.

rhGH therapy resulted in a sustained increase in IGF-1 concentrations across all time points, confirming effective dose titration. The biochemical response was inversely related to age, and women achieved higher IGF-1 levels after 12 months compared with men. Patients with childhood-onset GHD demonstrated a greater IGF-1 increase than those with adult-onset disease. Treatment was accompanied by a consistent reduction in total cholesterol and LDL cholesterol throughout follow-up, independent of the number of deficient pituitary axes, with a more pronounced LDL decrease observed in patients with preserved adrenocortical axis function. Glycemic parameters remained overall stable; however, patients with a longer duration of untreated GHD exhibited higher HbA1c levels at 6 and 12 months. After 12 months of therapy, total fat mass and body fat percentage decreased, while relative muscle mass increased. Regional analysis confirmed favorable reductions in fat mass within the trunk and limbs, with no significant changes in absolute muscle mass, bone mass, or total body water.

In conclusion, rhGH replacement therapy in adults with severe GHD under routine clinical practice conditions is associated with beneficial changes in lipid profile and body composition. The treatment response varies according to age, sex, and GHD onset. These real-world findings support the effectiveness of long-term, individualized rhGH therapy in adult GHD.

Abstract citation ID: lvag096.1416

EP1161 - ECE_2937 - Dysregulation of molecular machineries controlling RNA metabolism (spliceosome, RNA-Exosome, and nonsense-mediated decay) in TSHomas: potential pathophysiological relevance

Hugo Huertas Cabrera[1,2], Miguel E. G-Garcia[1,2], Álvaro Flores-Martínez[1,2], Eva Venegas-Moreno[3], Cristina Mª Diaz Perdigones[4], Silvia Maraver[4], María Ángeles Gálvez-Moreno[2,5], Alfonso Soto-Moreno[3], Antonio Carlos Fuentes-Fayos[1,2], Aura D. Herrera-Martínez[2,5] and Raul M. Luque[1,2,6]

[1]Department of Cell Biology, Physiology and Immunology, University of Córdoba, Córdoba, Spain; [2]Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), Reina Sofía University Hospital (HURS), Córdoba, Spain; [3]Unidad de Gestión de Endocrinología y Nutrición, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío CSIC, Universidad de Sevilla, Sevilla, Spain; [4]Endocrinology and Nutrition Service, Virgen de la Victoria University Hospital, Málaga, Spain; [5]Service of Endocrinology and Nutrition, Reina Sofía University Hospital (HURS), Córdoba, Spain; [6]CIBER Pathophysiology of Obesity and Nutrition (CIBERobn), Córdoba, Spain

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Thyrotropin-secreting pituitary tumours (TSHomas) are rare functional pituitary tumors responsible for inappropriate TSH secretion and central hyperthyroidism. Despite recent advances, the molecular mechanisms underlying TSHoma development and progression remain poorly defined. This study aimed at investigating the post-transcriptional regulatory landscape in TSHomas by analyzing the components of all the molecular machineries controlling RNA-metabolism [spliceosome, RNA-Exosome, and Nonsense-Mediated Decay (NMD)], their associations with clinical parameters, and the direct impact of the pharmacological inhibition of the activity of these machineries in TSHoma cells. To that end, microfluidic-based qPCR was used to determine the expression levels of the components of the spliceosome/RNA-Exosome/NMD in 4 TSHomas vs 10 healthy-normal pituitaries (NPs) tissues and to perform clinical correlations. Moreover, as a proof-of-concept, the direct antiproliferative actions of inhibitors of the activity of spliceosome/RNA-Exosome/NMD was evaluated in a patient-derived TSHoma cell-culture. TSHomas exhibited marked dysregulation compared with NPs of multiple components of spliceosome and related splicing-factors [downregulation of major-spliceosome components (*SF3B2/U2AF35/PRPF40A*) and splicing-factors (eg, *SRP30C/EIF4A3/DDX1/TRA2B/HNRPPF*…)], RNA-Exosome (upregulation of *DIS3/DIS3L/MTREX/TTC37*, and downregulation of *WDR61*), and NMD [eg, overexpression of *PABPC1/CNOT3/MAGOHB/…*, and downregulation of NMD-canonical targets (*DDIT3/GADD45B/MAFF/PDRG1/ATF4/ATF3*], being some of these alterations associated with relevant clinical features (eg, tumor-size, TSHB/fT4-levels). Moreover, we demonstrate a clear antiproliferative action of spliceosome/RNA-Exosome/NMD inhibitors in primary patient-derived TSHoma cell-cultures. Altogether, we demonstrated a clinically relevant spliceosome/RNA-Exosome/NMD-associated molecular dysregulation and antiproliferative actions of the activity of these machineries in TSHomas, which could serve as a potential source of novel diagnostic and prognostic biomarkers and therapeutic tools in patients with TSHomas.

Abstract citation ID: lvag096.1417

EP1162 - ECE_2039 - Hypogonadotropic hypogonadism contributes significantly to abnormal metabolic profile in patients with multihormonal hypopituitarism

Paweł Sojka[1,2], Aleksandra Matusiak[1,2], Renata Michalak[2], Andrzej Lewiński[2] and Małgorzata Karbownik-Lewińska[1,2]
[1]*Department of Endocrinology and Metabolic Diseases, Medical University of Łódź, Łódź, Poland;* [2]*Polish Mother's Memorial Hospital – Research Institute, Łódź, Poland*

Background and Objectives: Hypopituitarism is a disorder characterized by a deficiency of one or more pituitary hormones. The aim of our study was to evaluate the impact of each hormonal deficiency and severity (advancement/degree) of hypopituitarism on the metabolic profile.

Materials and Methods: The study group ($n = 131$) comprised 76 subjects with non-compensated multihormonal or isolated hypopituitarism, including growth hormone (GH; $n = 49$), gonadotropin (LH/FSH; $n = 31$), thyrotropin (TSH; $n = 13$), corticotropin (ACTH; $n = 9$), and prolactin (Prl; $n = 17$) deficiencies; healthy individuals served as control ($n = 55$). Standard biochemical parameters and anthropometric measurements were analyzed statistically.

Results: Patients with non-compensated hypopituitarism compared with control group showed a significantly higher prevalence of reduced HDL-C levels ($P = .053$), elevated TG levels ($P = .012$), and obesity ($P = .010$).

In non-compensated growth hormone (GH) deficiency, χ^2 test revealed a higher prevalence of obesity ($P = .016$), which was confirmed in univariate (OR = 2.55 $P = .010$) and multivariate (OR = 2.70 $P = .015$) regression models. Contrary to expectations, no significant differences in the prevalence of lipid abnormalities were found.

In non-compensated hypogonadotropic hypogonadism (gonadotropin deficiency), the χ^2 test showed a higher prevalence of diabetes ($P = .038$), which was confirmed in both univariate (OR = 3.04 $P = .023$) and multivariate (OR = 7.62 $P = .001$) regression models. The χ^2 test showed a higher prevalence of hypertriglyceridemia ($P = .031$), which was confirmed in univariate (OR = 2.72 $P = .020$) regression model. Univariate regression analysis revealed a higher prevalence of obesity (OR = 2.34 $P = .039$).

In the χ^2 test, no significant differences were observed between patients with hypogonadotropic hypogonadism and those with GH deficiency regarding the prevalence of obesity ($P = 1.000$), low HDL-C ($P = .169$), or elevated triglycerides ($P = .562$), whereas diabetes mellitus was more frequent in the hypogonadotropic hypogonadism group ($P = .001$).

No statistically significant changes in the metabolic profile were observed in non-compensated central hypothyroidism (TSH deficiency) or secondary adrenal insufficiency (ACTH deficiency).

Univariate regression analysis revealed that a higher number of pituitary hormone deficiencies was associated with an increased prevalence of reduced HDL-C levels (OR = 1.37, $P = .012$), elevated triglyceride levels (OR = 1.26, $P = .035$), and obesity (OR = 1.29, $P = .012$).

Conclusions: Hypogonadotropic hypogonadism adversely affects the metabolic profile by increasing the risk of obesity and dyslipidemia. Among pituitary hormone deficiencies, it represents the only independent predictor of diabetes. Therefore, hypogonadotropic hypogonadism should be considered a potential predictive factor for an adverse metabolic profile in patients with hypopituitarism. Additionally, more advanced hypopituitarism is associated with a less favorable metabolic profile.

Abstract citation ID: lvag096.1418

EP1163 - ECE_2787 - Prognostic role of granulation pattern in Cushing's disease: clinical and surgical implications

Aysel Unver Ozkahraman[1], Sebnem Burhan[1], Muveddet Banu Yilmaz Ozguven[2], Mehmet Karagulle[3], Buruc Erkan[4,5], Ebubekir Akpinar[4,5], Mutlu Niyazoğlu[1,5] and Esra Hatipoglu[1,5]
[1]*Basaksehir Cam and Sakura City Hospital, Department of Endocrinology and Metabolism, University of Health Sciences, Istanbul, Türkiye;* [2]*Basaksehir Cam and Sakura City Hospital, Department of Pathology, University of Health Sciences, Istanbul, Türkiye;* [3]*Basaksehir Cam and Sakura City Hospital, Department of Radiology, University of Health Sciences, Istanbul, Türkiye;* [4]*Basaksehir Cam and Sakura City Hospital, Department of Neurosurgery, University of Health Sciences, Istanbul, Türkiye;* [5]*Pituitary Disorders Research Center, University of Health Sciences, Istanbul, Türkiye*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: The 2022 WHO classification distinguishes sparsely granulated (SG) from densely granulated (DG) corticotroph pituitary neuroendocrine tumors (PitNETs) based on immunohistochemical granulation patterns. While SG tumors reportedly exhibit more aggressive behavior, their clinical significance and impact on surgical outcomes remain unclear. We compared clinicopathological features and postoperative remission rates between SG and DG corticotroph PitNETs.

Methods: We retrospectively analyzed 33 consecutive patients undergoing transsphenoidal surgery for Cushing's disease (2020-2025). Granulation pattern was determined by cytoplasmic ACTH intensity and keratin (CAM 5.2) distribution per WHO 2022 criteria. Patients were classified as SG ($n = 17$, 51.5%) or DG ($n = 16$, 48.5%). Biochemical remission was defined as morning serum cortisol <5 μg/dL or suppression after 1-mg dexamethasone suppression test within 6 months postoperatively. We compared demographic data, preoperative hormonal parameters (serum cortisol, ACTH, midnight cortisol, salivary cortisol, 24-hour urinary free cortisol, 1-mg DST), tumor characteristics (size, cavernous sinus invasion, Ki-67 index), and remission rates. Statistical analysis used Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables.

Results: Groups were comparable for age (46.7 ± 11.0 vs 49.2 ± 11.7 years, $P = .5$), sex (76.5% vs 75.0% female, $P = 1.0$), and BMI (35.9 ± 6.9 vs 32.0 ± 5.5 kg/m^2, $P = .08$). SG tumors were significantly larger (median 10.5 vs 5.7 mm, $P = .03$), with higher macroadenoma prevalence (58.8% vs 18.7%, $P = .03$). Cavernous sinus invasion showed a non-significant trend in SG tumors (35.3% vs 6.3%, $P = .08$). Ki-67 index and all preoperative biochemical parameters were similar between groups ($P > .05$). Early remission rates at 3 months (82.4% vs 75.0%, $P = .7$) and 6 months (73.3% vs 78.6%, $P = 1.0$) did not differ. Among 23 patients completing ≥12-month follow-up, final remission rates remained comparable (SG: 81.8% [9/11]; DG: 75.0% [9/12]; $P = 1.0$).

Conclusions: Sparsely granulated corticotroph PitNETs demonstrate larger tumor size and greater macroadenoma proportion than densely granulated tumors, suggesting more aggressive growth patterns. However, granulation pattern did not predict biochemical remission rates at any timepoint. These findings indicate that while SG tumors exhibit distinct radiological features, granulation pattern alone may not serve as a reliable prognostic marker for surgical success. The small sample size limits definitive conclusions; multicenter studies with longer follow-up and multivariate analysis are needed to determine whether granulation pattern independently influences long-term outcomes or treatment selection.

Keywords Cushing's disease, corticotroph PitNET, granulation pattern, sparsely granulated, densely granulated, prognosis, remission

Abstract citation ID: lvag096.1419

EP1164 - ECE_1331 - The role of GM3 gangliosides in acromegaly-associated insulin resistance

Amy Coulden[1,2], Ying Di[1], Priyankaa Patel[1], Ella Smith[1], Warwick Dunn[3], Catherine Winder[3], Christian Ludwig[1], Maria Makarova[1], Niki Karavitaki[1,2] and Gabriela Da Silva Xavier[1]

[1]*Department of Metabolism and System Science, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom*

[2]*Department of Endocrinology, Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom;* [3]*Biochemistry, Cell and Systems Biology, University of Liverpool, Centre of Metabolomics Research, Institute of Systems, Molecular and Integrative Biology, Liverpool, United Kingdom*

Background: A significant number of patients with acromegaly develop insulin resistance and diabetes mellitus, the mechanism of which is not fully understood. GM3 gangliosides (GM3), a family of glycosphingolipids which sit within the cell membrane and have important roles within insulin signalling, have previously been mechanistically linked to insulin resistance in patients with diabetes mellitus.

Aim: We aimed to configure the role of GM3 in acromegaly-associated insulin resistance in 3T3-L1 adipocytes and C2C12 myotubes, mouse adipocyte and muscle cell lines, respectively.

Methods: 3T3-L1 adipocytes were exposed to growth hormone (GH) (1 μM) and/or insulin like growth factor 1 (IGF-1) (1 μg/ml) for 48 hours. Insulin signalling was assessed by Western(immuno)blot of AKT phosphorylation (pAKT:AKT). Membrane order was assessed through measures of membrane polarisation by confocal microscopy of DI-4-ANEPPDHQ fluorescence. GM3 content in cellular extracts was measured by NMR spectroscopy. The expression of *ST3GAL5* (which encodes for GM3 synthase, the enzyme responsible for GM3 synthesis) was assessed by qPCR. C2C12 myotubes were also exposed similarly to GH/IGF-1 and expression of *ST3GAL5* was measured.

Results: Exposure of 3T3-L1 adipocytes to elevated concentrations of GH, IGF-1 and the combination of GH/IGF-1 all led to significantly lowered pAKT:AKT (0.3 ± 0.2-fold, 0.5 ± 0.1-fold and 0.5 ± 0.1-fold, respectively) compared to controls, indicating impaired insulin signalling ($P = .01$). Similarly, all three hormonal variations were associated with altered plasma membrane fluidity (1.4 ± 0.04-fold, 1.8 ± 0.1 fold and 1.5 ± 0.08-fold, respectively, $P \leq .0001$). Whilst only IGF-1 (1.4 ± 0.2-fold) and combined GH/IGF-1 (1.4 ± 0.1-fold) altered internal membrane fluidity ($P < .05$).

In 3T3-L1 adipocytes, both IGF-1 and combined GH/IGF-1 increased cellular levels of GM3 [1.4 ± 0.1-fold ($P < .05$) and 1.9 ± 0.4-fold ($P < .05$), respectively] compared to controls. Exposure to elevated GH concentrations also led to increased (1.4 ± 0.1-fold, $P \leq .01$) expression of *ST3GAL5*. Interestingly, combined IGF-1/GH reduced *ST3GAL5* expression 0.8 ± 0.1-fold, $P < .05$, whilst IGF-1 had no effect.

In C2C12 myotubes, GH had no effect on *ST3GAL5* expression, whilst both IGF-1 and combined GH/IGF-1 reduced expression compared to untreated control cells (0.25-fold $\pm$ 0.009 and 0.3-fold $\pm$ 0.05, respectively, $P \leq .0005$).

Conclusions: Taken together, these data indicate that exposure to GH and IGF-1, as seen in acromegaly, inhibits insulin signalling in 3T3-L1 adipocytes potentially via alterations in plasma membrane fluidity and increased GM3 content may be implicated in this process. GH and IGF-1 have some divergent effects in different cell types and fluidity plasma and internal membranes, with IGF-1 being the predominant effector hormone.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1420

EP1165 - ECE_1567 - LC-MS/MS techniques for the analysis of neuroactive and other steroids in various biological matrices

Tereza Skodova, Jana Vitku and Lucie Kolatorova
Department of Steroids and Proteofactors, Institute of Endocrinology, Prague, Czech Republic

Background: Steroid analysis is a rapidly advancing field with significant scientific and clinical potential. Advanced analytical techniques, particularly liquid chromatography with tandem mass spectrometry (LC-MS/MS), allow highly specific, accurate, and sensitive quantification of steroid hormones and related compounds across a variety of biological matrices. Contemporary research focuses on neurosteroids (NS), synthesized de novo in neural tissue, and neuroactive steroids (NAS), peripherally produced steroids that modulate neuronal activity. Changes in NS and NAS reflect disrupted neuroendocrine regulation, particularly in neurological disorders, making them promising biomarkers for understanding, diagnosing, and monitoring these conditions.

Aim: The study aims to develop LC-MS/MS methods for determination of three classes of NS: DHEA metabolites, pregnanolone, and androsterone isomers.

Results: Sample preparation included liquid-liquid extraction using hexan:ethylacetate (3:2) which was used for two developed methods. The first LC-MS/MS enables the analysis of dehydroepiandrosterone (DHEA) and its metabolites—7α-hydroxyDHEA, 7β-hydroxyDHEA, 7-ketoDHEA —together with androgens (testosterone, dihydrotestosterone, androstenedione, and their 11-oxygenated metabolites), corticoids (cortisol, 11-deoxycortisol, 21-deoxycortisol, cortisone, corticosterone, 11-deoxycortico sterone), pregnenolone, progesterone and 17-hydroxypro gesterone. These steroids were chromatographically separated using a Kinetex C18 column (2.6 µm particle size). Pregnanolone isomers (pregnanolone, allopregnanolone, isopregnanolone, and epipregnanolone) and androsterone isomers (androsterone, epiandrosterone, etiocholanolone, and epietiocholanolone) were not adequately separated using this method and column. Because these compounds share identical multiple reaction monitoring (MRM) transitions, they cannot be distinguished by mass spectrometry alone; therefore, further method optimization was required. Several separation columns were tested including Kinetex C18 (2.6 and 1.7 µm particle sizes), Kinetex Biphenyl (2.6 µm) and Kinetex F5 (2.6 µm), under various temperatures (30 °C, 40 °C, 50 °C), flow rates, and gradient conditions. The best isomer separation was achieved using the Kinetex F5 column at 30 °C with an initial gradient composition of 30:70 (water:MeOH).

Conclusions: Two LC-MS/MS methods were developed for the analysis of DHEA metabolites, pregnanolone and androsterone isomers, and 21 other streroids. Quantification can be performed from a single sample using two LC-MS/MS methods—one employing a Kinetex C18 column and the other a Kinetex F5 column. The developed methods will be applied to a broad spectrum of biological matrices, including plasma, cerebrospinal fluid, and both human and animal tissues. Comprehensive profiling of NS and NAS is expected to enhance our understanding of their roles in the pathophysiology and treatment of neurological disorders.

Acknowledgement: Supported by NW25J-04-00127 and NU23-04-00551 of Czech Ministry of Health.

Abstract citation ID: lvag096.1421

EP1167 - ECE_2239 - The somatotroph activation may define the aggressive biology of silent corticotroph tumors

Cristina Guillen[1], María Eugenia Torregrosa-Quesada[1], Johana Sottile[2], Jorge Navarro[2], Jorge Frances[1], Francisca María Peiró-Marqués[1], Elena García[1], Joaquin Serrano[1], Javier Abarca Olivas[1] and Antonio Pico[1]
[1]*Hospital General Universitario Dr. Balmis, Alicante, Spain;* [2]*Instituto de Investigación Biomédica de Alicante (ISABIAL), Alicante, Spain*

Introduction: Silent Corticotroph Tumors (SCTs) are clinically distinguished from Silent Gonadotroph Tumors (SGTs) by their higher rate of recurrence and aggressive behavior. After we noticed unexpectedly high IGF-1 levels in our SCT group, we decided to explore the somatotroph axis in these tumors. We thought that somatotroph activation could be an important biological feature related to the natural aggressiveness of the corticotroph lineage. We assessed both the basic dynamics and functional reserve using specific secretagogues.

Methods: We studied 58 patients, including 27 with SCTs and 31 with SGTs. 1) We compared baseline somatotroph levels of IGF-1 and GH between SCTs and SGTs; 2) To see if the activation was caused by the classic GHRH pathway or the alternative Ghrelin pathway, we conducted the Glucagon Stimulation Test (GHRH-dependent) on a subgroup of 14 patients (6 SCTs and 8 SGTs) and the specific Macimorelin Test (GHSR-dependent) in SCT patients ($n = 7$).

Results: SCT patients showed significantly higher baseline IGF-1 levels (175.1 ± 56.4 vs 105.8 ± 65.8 ng/mL, $P = .0002$) and a two-fold increase in baseline GH levels (0.42 vs 0.19 ng/mL). The SCT group had a reintervention rate seven times higher than the SGT control group (21.4% vs 3.3%, $P = .08$). Our tests showed that the Glucagon test produced a similar GH response in both groups (SCT Peak: 1.26 ± 1.15 ng/mL vs SGT Peak: 0.98 ± 1.65 ng/mL, $P = .17$). However, SCTs were particularly sensitive to the alternative pathway. Stimulation with Macimorelin caused a strong GH release in SCTs (Peak: 1.88 ng/mL), significantly better than the response to Glucagon ($P = .0078$).

Conclusions: The higher levels of IGF-1 and GH, compared with SGTs, along with a strong response to Macimorelin, indicate a specific functional increase of the somatotroph axis, likely triggered by the GHSR pathway. This unique biological profile appears to be a characteristic of the corticotroph lineage and may help explain the aggressive behavior and higher recurrence rates seen in this group. We are currently extending Macimorelin testing to the SGT group and conducting molecular analysis (RT-qPCR) to confirm this mechanism.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1422

EP1168 - ECE_3937 - An elusive sellar germinoma: clinical and histopathological challenges

Alice Monsanto[1], Gustavo Rodrigues[1], Tânia Carvalho[1], Ana Margarida Sobral[2], Bárbara Jesus[1], Adriana Duarte[1], Mariana Coelho[1], Mariana Lavrador[1], Mara Ventura[1], Daniela Guelho[1] and Leonor Gomes[3]

[1]Department of Endocrinology, Diabetes and Metabolism, Unidade Local de Saúde de Coimbra, Coimbra, Portugal; [2]Unidade Local de Saúde de Coimbra, Coimbra, Portugal; [3]Coimbra, Portugal

Introduction: Intracranial germ cell tumors are rare and represent a diagnostic challenge, particularly when an extensive lymphocytic reaction obscures tumor cells.

Case report: A 23-year-old male with gynecomastia and decreased libido. Investigation revealed hypogonadotropic hypogonadism (FSH 1.08 IU/L [1.4-18.1], LH 0.55 IU/L [1.5-9.3], total testosterone 19.0 ng/dL [241.0-827.0]). Cranial CT scan revealed an expansive supra- and intrasellar lesion, spontaneously hyperdense, with moderate homogeneous contrast enhancement. A clarification sellar MRI showed enlargement of the adenohypophysis with an hourglass morphology measuring 15 × 10 × 14 mm, loss of posterior pituitary bright spot on T1-weighted images, and reduced contrast uptake relative to normal glandular parenchyma, with contact with the optic chiasm.

Further evaluation: hyperprolactinemia (75.3 ng/mL) and GH deficiency (IGF-1 103 ng/mL) and vasopressin deficiency, with polyuria (5 L/day) and urinary osmolarity 230 mOsm/kg. Serum tumor markers were negative (AFP 3.50 ng/mL, β-hCG 2.0 mIU/mL). Baseline campimetry was normal.

Progressively developed central hypothyroidism (FT4 0.53 ng/dL [0.7-1.5]; TSH 1.8 uUI/mL [0.35-4.94]), secondary adrenal insufficiency (cortisol 2.6 ug/dL), and visual symptoms (incomplete right inferior temporal quadrantanopsia and incomplete left temporal hemianopsia). MRI revealed an dimensions increasing (17 × 13 × 14 mm).

Transsphenoidal resection was performed with neuropathologicaly revealing adenohypophyseal fragments with preserved lobular architecture and a discrete lymphocytic infiltrate, along with connective tissue showing a dense, predominantly lymphocytic inflammatory infiltrate with reactive lymphoid follicle formation. Immunohistochemical: B lymphocytes (CD20) and T lymphocytes (CD3), CD138-positive plasma cells. Background staining without well-defined cellular elements for PLAP, CD117, and D2-40, with very rare cells expressing OCT4 and SALL4. No positivity for CAM5.2, AFP, or hCG.

Discussion/conclusions: The pathological findings are highly suggestive of an intracranial germ cell tumor, showing reactive follicular lymphoid hyperplasia with focal immunohistochemical expression of PLAP, OCT4, and SALL4, without features of pituitary adenoma or craniopharyngioma. These findings plus clinical presentation (young male, diabetes insipidus, panhypopituitarism, loss of the posterior pituitary bright spot, bitemporal visual field defects) strongly suggest germinoma with extensive lymphocytic reaction. Germinomas are highly immunogenic tumors that elicit a dominant peritumoral immune response with massive lymphocytic infiltration, occasionally obscuring neoplastic cells and leading to misdiagnosis. Additional investigations are on going (CSF cytology and tumor markers; postoperative MRI). This case underscores the diagnostic challenges of CNS germ cell tumors when peritumoral immune reactions dominate the histological picture and emphasizes the importance of integrating clinical, radiological, and immunohistochemical findings when tumor cells are sparse.

Abstract citation ID: lvag096.1423

EP1169 - ECE_2981 - Effects of treatment on bone metabolism and structure in patients with excess and deficiency of growth hormone: a preliminary report

Arnika Wydra[1,2], Jagoda Alicja Rogowska[1,2], Maria Stelmachowska-Banas[2], Alicja Duquenne[1,2], Wojciech Zgliczyński[2] and Izabella Czajka - Oraniec[2]

[1]Doctoral School of Translational Medicine, Centre of Postgraduate Medical Education, Warsaw, Poland; [2]Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland

Background: Both the excess of growth hormone in acromegaly (Acro) and its deficiency (GHD) may lead to impaired bone metabolism and bone mineral density (BMD) and fragility. However, the exact mechanism remains unclear.

Purpose: To evaluate the effects of Acro and GHD treatment on bone metabolism and structure, including bone turnover markers, BMD and bone microarchitecture.

Methodology: In this single-center study 52 patients were recruited: 20 with Acro and 32 with GHD. During the follow-up period, 6 patients with Acro and 7 patients with GHD met the exclusion criteria.

Consequently, 14 Acro patients (9 males, 5 females) and 25 GHD patients (13 males, 12 females) remained under observation. Calcium, phosphorus (serum and urine), PTH, 25-hydroxy- and 1,25-dihydroxy-vitamin D and bone turnover markers: serum b-cross laps (Ct-x), procollagen type I N-terminal propeptide (P1NP), bone alkaline phosphatase (BALP), sclerostin (Scl) and Dikkopff-1 (Dkk-1), and BMD and TBS measured by dual-energy X-ray absorptiometry were assessed baseline and after 6 months (a6m) of adequate treatment.

Results: Median age was 48 (IQR: 26.75) and 28.5 (IQR: 16) in Acro and GHD group, respectively. Median baseline GH and IGF-1 levels in Acro were 12.5 ug/L and 689 ug/L (3.1 × ULN), respectively. In the GHD group median baseline IGF-1 was 74.9 ug/L (0.86 × LLN). A6m of adequate treatment a decrease in IGF-1 in the Acro group and an increase in the GHD group were observed (225.5 ng/ml (0.97 × ULN) and 185.2 ng/ml (0.71 × ULN) respectively).

In Acro a6m of treatment we observed a reduction in serum calcium (2.5 vs 2.42 mmol/L; $P = .04$) and phosphorus (1.42 vs 1.1 mmol/L; $P < .001$), urine calcium (5.53 vs 2.94 mmol/24 h; $P < .001$) in 24-hour urine collection. We also observed an increase in PTH (29.9 vs 45.0 pg/mL; $P = .023$) and 25(OH)D (26.92 vs 35.6 ng/ml; $P = .002$). A6m of treatment we did not observe statistically significant changes in bone turnover markers or BMD.

In GHD there was an increase in serum phosphorus (1.02 vs 1.19 mmol/L; $P = .002$), and increase in 24-hour urine calcium and phosphorus (3.95 vs 5.66 mmol/L; $P = .004$ and 17.71 vs 22.93 mmol/L; $P = .02$, respectively). A6m of treatment an increase in BALP (70.5 vs 78.4 U/L; $P = .034$) and Scl (47.6 vs 64.6 pg/ml; $P = .034$) was observed. There were no notable changes in PTH, 25(OH)D or BMD a6m.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: We present initial results of the study showing the impact of GH and IGF-1 changes on bone turnover in both groups.

Abstract citation ID: lvag096.1424

EP1170 - ECE_3127 - Hematologic predictors of prolonged glucocorticoid replacement in endogenous Cushing's syndrome: a nationwide cohort study from the clalit health services database

Shruti Shah[1], Nidhi Agrawal[2], Shiri Kushnir[3], Tzipora Shochat[4], Maria Fleseriu[5] and Amit Akirov[6,7]
[1]NYU Grossman School of Medicine, New York, United States; [2]Department of Medicine, NYU Langone Health, New York, United States; [3]Research Authority, Rabin Medical Center, Beilinson Hospital, Petach Tikva, Israel; [4]Biostatistics Unit, Rabin Medical Center, Beilinson Hospital, Petach Tikva, Israel; [5]Pituitary Center, Departments of Medicine and Neurological Surgery, Oregon Health & Science University, Portland, United States; [6]Rabin Medical Center, Beilinson Hospital, Institute of Endocrinology, Petach Tikva, Israel; [7]Gray Faculty of Medical & Health Sciences, Tel Aviv University, Tel Aviv, Israel

Purpose: The duration of glucocorticoid (GC) replacement following curative treatment of endogenous Cushing's syndrome (CS) is highly variable, and there are no validated markers to guide tapering or predict prolonged dependency. Hematologic indices reflect cortisol exposure and immune regulation, yet their role in postoperative adrenal recovery has not been examined. We evaluated clinical and hematologic predictors of GC duration, stratified by disease etiology and GC formulation.

Methods: This nationwide retrospective cohort included patients with endogenous CS diagnosed between 2000 and 2023 in the Clalit Health Services database in Israel. Patients with adrenocortical carcinoma, ectopic CS, or prior supraphysiologic steroid use were excluded. Duration of GC therapy following curative pituitary or adrenal surgery was categorized as <20 months or ≥20 months based on the cohort median of 19.3 months. Baseline hematologic indices, including white blood cell count, neutrophils, lymphocytes, and neutrophil-to-lymphocyte ratio (NLR), were derived from values recorded within 24 months prior to diagnosis. Analyses included Wilcoxon and chi-square tests, Kaplan–Meier survival estimates, and Cox proportional hazards modeling with subgroup analyses by etiology and GC type.

Results: Among 103 patients (mean age 43.8 ± 13.7 years; 76.7% women), 41 had Cushing's disease (CD), 56 had adrenal CS, and 6 were of indeterminate etiology. Fifty-one patients (49.5%) required ≥20 months of GC replacement (median 47.6 vs 8.3 months). Patients requiring prolonged therapy were older (47.8 ± 14.5 vs 39.8 ± 11.7 years, $P = .0045$) and had lower baseline neutrophils (6.79 ± 3.12 vs 7.74 ± 2.75 × 10^9/L, $P = .050$) and NLR (3.99 ± 3.06 vs 4.90 ± 2.64, $P = .026$). In CD, prolonged therapy was associated with lower neutrophils, lower NLR, and lower total leukocytes, whereas no hematologic differences were observed in adrenal CS. Hydrocortisone use was more frequently associated with prolonged replacement than prednisone (75.0% vs 43.4%). Baseline cortisol measures and comorbidities were not predictive. Overall survival did not differ by GC duration, but among CD patients, prolonged therapy was associated with lower survival (log-rank $P = .045$).

Conclusions: Older age and lower baseline neutrophils and NLR were associated with prolonged postoperative GC dependency, particularly in pituitary disease. These findings suggest that routinely available hematologic markers may help anticipate delayed adrenal recovery and support individualized tapering strategies, warranting prospective validation.

Abstract citation ID: lvag096.1425

EP1171 - ECE_1534 - Analysis of the clinical characteristics of patients receiving growth hormone treatment at the National Children's Hospital of Costa Rica, in the period between January 2008 and December 2023

Liseth Gabriela Delgado Castro, Fred Cavallo Aita, Jose Edmond Esquivel Vargas and Paulo Perez Damasco
Caja Costarricense de Seguro Social, San José, Costa Rica

Background: Recombinant human growth hormone therapy has been used at the Children´s National Hospital in Costa Rica since 1987. This study aims to analyze the clinical and epidemiological characteristics of patients treated with rhGH from 2008 to 2023, and to evaluate treatment effectiveness in the Costa Rican pediatric population.

Methods: An observational, descriptive, and retrospective study was conducted including 672 patients treated in the Endocrinology outpatient clinic at the National Children's Hospital. Clinical, anthropometric, biochemical, and treatment-related variables were collected. Differences were analyzed according to diagnosis and treatment status (active, completed, or discontinued), and predictors of a satisfactory response; defined as achieving a final height within ≤2 SD below the genetic target, were identified. Nonparametric tests, chi-square, and binary logistic regression were applied.

Results: The most frequent diagnosis was GH deficiency (63.1%), followed by Turner syndrome (16.8%), small for gestational age (SGA) (14.4%), and other diagnoses (5.7%). The median age at treatment initiation was 107.5 months, lower in SGA patients (69 months), who also had the most compromised initial height Z-score (−3.2). Of the total, 43% completed treatment, 36.9% remained on active therapy, and 20.1% had discontinued. Treatment adherence was significantly lower among those who discontinued (45.9%, $P < .001$). Among the 289 patients who completed treatment, 52.2% achieved a satisfactory final height. Significant predictors of treatment success included male sex (OR 3.0, $P = .013$), regular adherence (OR 6.08, $P = .010$), higher initial height Z-score (OR 4.48, $P < .001$), better genetic height potential (OR 2.39, $P = .018$), and lower GH peak (OR 0.77, $P = .003$). Adverse events were reported in 9.1% of patients, with no association with GH dose or diagnosis. Although a significant correlation is observed between baseline IGF-1 and peak of GH un the insulin tolerance test, its low magnitude prevents IGF-1 from being used as a substitute for the stimulation test in most cases. However, markedly low values could be useful for identifying priority candidates for diagnostic confirmation.

Conclusions: These findings are consistent with international registries such as KIGS, GeNeSIS, and NordiNet, and emphasize the importance of early diagnosis, sustained adherence, and appropriate diagnostic selection to optimize treatment outcomes with rhGH.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1426

EP1172 - ECE_3030 - Effects of dopamine agonist treatment on IGF-1 levels in patients with prolactinoma

Karolina Cylke-Falkowska[1,2], Aleksandra Toporowska-Siwiak[1], Wojciech Zgliczyński[1] and Maria Stelmachowska-Banaś[1]

[1]*Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland;* [2]*Doctoral School of Translational Medicine, Centre of Postgraduate Medical Education, Warsaw, Poland*

Introduction: Prolactinomas account for 40%-50% of pituitary adenomas. Dopamine agonists (DAs) are the first-line treatment in vast majority of patients due to their efficacy in reducing prolactin (PRL) secretion and tumor size; however, their long-term effect on insulin-like growth factor-1 (IGF-1) levels remains unclear.

Aim: To determine the impact of DAs treatment on IGF-1 concentrations in patients with prolactinoma.

Patients and Methods: This retrospective, single-center study included 45 consecutive patients with prolactinoma treated with DAs, with available IGF-1 measurements at baseline and follow-up. Patients with mixed PRL–GH tumors and clinical features of acromegaly were excluded.

Results: The male-to-female ratio was 0.96 and mean age at diagnosis was 41.5 ± 17 years. The median baseline PRL concentration in all patients was 520 ng/ml. Microadenomas were present in 12 patients (27%), while macroadenomas were observed in 33 patients (73%). During DAs treatment, the mean IGF-1 level increased from 193.5 ± 87 ng/ml to 229 ± 97.8 ng/ml (from $0.74 \pm 0.28 \times$ the upper limit of normal (ULN) for age to $0.89 \pm 0.32 \times$ ULN) after the mean 14.6 ± 11.6 months. The increase was significant ($P < .001$). BMI of patients did not change significantly, and showed no correlation with IGF-1 levels.

Twenty -two patients (9 women, 13 men) received bromocriptine treatment. There was a significant decrease in PRL concentration to a median of 13.7 ng/ml with normalization achieved in 16 patients (72%). The baseline IGF-1 levels were within the reference range in most patients, whereas 3 patients were above the ULN. During bromocriptine treatment, the mean IGF-1 levels increased from 188.2 ± 107 ng/ml to 208.7 ± 92.5 ng/ml (from $0.74 \pm 0.34 \times$ ULN to $0.85 \pm 0.37 \times$ ULN) after the mean 13.4 ± 8 months; however the increase was not significant ($P > .05$). After bromocriptine treatment IGF-1 concentration exceeded the ULN in 7 (33%) patients.

Twenty-three patients (14 women, 9 men) were treated with cabergoline. PRL normalization was achieved in 17 patients (74%), with a median PRL concentration of 13.7 ng/ml. During cabergoline treatment the mean IGF-1 concentration increased from 198.7 ± 63.9 ng/ml to 248.4 ± 100.7 ng/ml (from $0.73 \pm 0.2 \times$ ULN to $0.92 \pm 0.27 \times$ ULN), $P < .05$ after the mean 15.7 ± 14.3 months.

Conclusions: DAs therapy of prolactinoma was associated with an increase IGF-1 levels which was particularly pronounced in patients treated with cabergoline. The mechanism underlying the increase in IGF-1 concentration requires further research.

Abstract citation ID: lvag096.1427

EP1173 - ECE_1889 - Effects of a novel set of somatostatin/cortistatin analogues on pituitary neuroendocrine tumors

Federica Mangili[1], Nicole Panseri[2], Donatella Treppiedi[1], Genesio Di Muro[2], Marco Locatelli[3,4], Erika Peverelli[1,2] and Giovanna Mantovani[1,2]

[1]*Endocrinology Unit, Fondazione Irccs Ca Granda Ospedale Maggiore Policlinico, Milano, Italy;* [2]*Department of Excellence 2023-2027, University of Milan, Milan, Italy;* [3]*Neurosurgery Unit, Fondazione IRCCS Ca Granda Ospedale Maggiore Policlinico, Milan, Italy;* [4]*Dalmine, BG, Italy*

Pituitary neuroendocrine tumors (PitNETs) comprises the 10%-25% of all intracranial neoplasms and first-line therapeutical approach is represented by surgery, whereas an effective pharmacological therapy for resistant and relapsing disease is still lacking.

Somatostatin (SS) receptors (SSTs) constitute the main suitable pharmacological targets for PitNETs therapy with SST ligands (SRLs). Nevertheless, a large proportion of tumors are unresponsive or resistant to conventional therapies, highlighting the need of personalized strategies. Recently, the endogenous neuropeptide cortistatin (CST), that shares with SS actions and affinity to SSTs, emerged as an anti-inflammatory player, showing potential antitumoral behavior in different NETs. Furthermore, an effect of CST in regulating GH and ACTH secretion has been demonstrated.

This study aims to test the effects of CST and a novel set of SS/CST analogues that display broader SSTs affinity, in both GH-secreting PitNET cell line GH3 and primary cultures, and ACTH-secreting PitNET cell line ATt-20/D16v-F2, comparing them with classical SRLs octreotide and pasireotide.

The antimitotic ability of CST was also tested in human primary cultured non-functioning PitNETs.

CST 100 nM reduced cell proliferation in both GH3 (−40.8(42.6)%, $P < .01$) and ATt-20/D16v-F2 (−25.7(20.3)%, $P < .05$) cells. A significative antimitotic action was exerted by all SS/CST a*nalogs 1, 2, 3 and 4* in both cell lines. A*nalog5* was effective only in GH3 cells. To note, a*nalog1* showed a stronger efficacy with respect to octreotide in GH3 ($P < .05$).

SS/CST *analog2* and *analog5* inhibited also GH3 migration (−74.6(45.8)%, $P < .01$; −67.4(13.8)%, $P < .01$), GH secretion (−41.9(21.4)%, $P < .05$; −28.2(23.7)%, $P < .05$), and increased cell apoptosis (+1.43(0.39)-fold, $P < .05$; +1.38(0.51)-fold,$P < .05$). CST and *analog2* antisecretory effect was also confirmed in 3 different human primary cultured GH-PitNETs cells.

Antimigratory action in ATt-20/D16v-F2 was also exerted by both CST (−39.1(29.2)%, $P < .05$) and SS/CST *analog1* (−44.7(29.8)%, $P < .05$), this last showing also pro-apoptotic effect (+1.22(0.18)-fold,$P < .01$).

Similarly, CST (−36.59(36.9)%, $P < .05$) and *analog2* (−28.43(23.1)%, $P < .05$)exerted antimitotic action in 8 out of 11 different NF-PitNETs cultured cells tested.

To conclude, our study represents an alternative approach that provides the use of novel molecules, based on a wider interaction with SSTs profile of expression, paving the way for a more flexible and adaptive pharmacological approach for patients with PitNET.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1428

EP1175 - ECE_1430 - Metastatic germ cell cancer presenting as hypophysitis: a rare clinical case report

Martyna Juskiene, Ieva Baikštienė, Radvilė Matukaitienė and Birutė Žilaitienė
Department of Endocrinology, Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas Clinics, Kaunas, Lithuania

Introduction: Hypophysitis is a rare endocrine disorder characterized by inflammation of the pituitary gland, resulting in hypopituitarism. The most common causes include autoimmune (lymphocytic), infection-related, and medication-induced forms. Metastatic hypophysitis is exceptionally rare, with limited data regarding its prevalence.

Case: A 29-years-old male presented with a two-year history of general weakness, polydipsia and polyuria. Initial investigations revealed severe hypopituitarism with a low basal cortisol (29 nmol/L), IGF-1, growth hormone, gonadotropins, testosterone and thyroxine, with elevated prolactin (951 mU/L). With a suspected diagnosis of hypopituitarism, central hypothyroidism, hypogonadotropic hypogonadism, secondary adrenal insufficiency, the patient was admitted to the Department of Endocrinology. Treatment with levothyroxine and hydrocortisone was initiated. Further evaluation revealed polyuria with hypostenuria. A positive desmopressin test confirmed diabetes insipidus and additional treatment initiated.

To clarify the cause of panhypopituitarism, a brain CT scan (as it was faster than an MRI) revealed changes in the corpus callosum, a thickened pituitary stalk (~4.3 mm), and thickening of the right optic nerve in the prechiasmatic segment. A suspected diagnosis of Langerhans cell histiocytosis was made. Due to the identified changes, a consultation with a neuro-ophthalmologist was sought—no visual fields or OND changes were identified.

Thoracic, abdominal, and pelvic CT scans revealed multiple para-aortic and paracaval lymph nodes, suggesting a possible lymphoproliferative disorder. Given the limited accessibility for tissue verification, threpine biopsy was performed, demostrating normal hematopoesis.

To refine the diagnosis, a brain MRI was performed, revealing changes in the corpus callosum, left corona radiata, both anterior limbs of the internal capsules, the ependyma of the third ventricle, chiasmatic optic nerve, and the right optic nerve region, suggesting central nervous system lymphoma and less likely germinoma. A stereotactic biopsy confirmed germinoma. Testicular ultrasound did not reveal any abnormalities, and tumor markers AFP, βHCG, LDH were within normal limits.

Following multidisciplinary neuro-oncology board discussion, neoadjuvant chemotherapy eith the CARB-VP regimen was initiated. Patient received three chemotherapy cycles followed by cranial radiotherapy with a total dose of 44 Gy. After completion of oncological treatment, testosterone replacement therapy was started.

Patient is in follow up since April 2024, continious MRI demonstrated significant regression of periventricular, suprasellar, and adjacent tumor infiltration. Patient remains in remission and continues regular imaging surveillance every six months.

Conclusions: Hypophysitis due to germ cell cancer is rare and diagnostically challenging condition. Timely diagnosis, multidisciplinary collaboration, and comprehensive treatment approach are essential for managing this condition and improving patient's quality of life.

Abstract citation ID: lvag096.1429

EP1176 - ECE_1536 - Long-term pasireotide treatment in the setting of advanced chronic kidney disease and hemodialysis

Adnan Zaina[1] and Sameer Kassem[2]
[1]*The Azrieli Faculty of Medicine, Clalit Medical Health Care Services, Endocrinology, Bar-Ilan University, Safed, Israel;* [2]*Carmel Medical Center, Internal Medicine, Technion Israel Institute of Technology, Haifa, Israel*

Introduction: Transsphenoidal surgery (TSS) remains the primary treatment for acromegaly. Pharmacological therapy is essential for achieving biochemical control in patients with persistently elevated IGF-1 levels after surgery or when surgery is not feasible. Somatostatin analogs (SSAs), such as octreotide and lanreotide, are widely used. Pasireotide (PAS-LAR) and Pegvisomant (PEGV) are additional options, particularly for patients resistant to or partially responsive to first-generation SSAs. Other treatments include radiotherapy and dopamine receptor agonists. We report the first case of acromegaly in a patient with CKD on hemodialysis who achieved long-term biochemical control with PAS-LAR.

Case presentation: A 73-year-old woman diagnosed with acromegaly in April 1996 due to a pituitary macroadenoma underwent TSS. Pathology revealed a pituitary adenoma that stained positively for GH. Postoperatively, MRI showed a partially empty sella without tumor remnant, and GH and IGF-1 levels normalized. From 1999 to 2005, a pituitary tumor remnant gradually increased, with IGF-1 at 38.9 nmol/L (normal range 10 to 33 nmol/L) and GH at 5.83 μg/L. A repeat TSS was performed in March 2005. Because GH and IGF-1 levels remained high postoperatively, lanreotide autogel 60 mg monthly was initiated and up-titrated to 120 mg, causing gastrointestinal symptoms after each injection. In 2008, an MRI showed tumor shrinkage; however, because IGF-1 remained high in July 2009, treatment was switched to PEGV 10 mg daily, with the dose increased to 20 mg daily. A dramatic decline in IGF-1 levels was observed (32.9 nmol/L; normal range 10-33 nmol/L).

Due to poor compliance, the patient discontinued PEGV. Between 2013 and 2016, successive MRIs showed a right pituitary mass measuring $1.3 \times 1.1 \times 1.1$ cm, with elevated IGF-1 levels. Endoscopic transsphenoidal re-exploration of the pituitary was performed, and no tumor was identified.

PAS-LAR 40 mg monthly was initiated in May 2017 and up-titrated to 60 mg. A normalized IGF-1 level of 168 ng/mL (normal range: 20 to 244 ng/mL) was achieved, with a random GH level of 1.31 μg/L. The patient has been adherent to monthly treatment since initiation. She has had CKD due to longstanding hypertension since 2005, progressing to advanced CKD requiring hemodialysis since May 2012, with prior hospitalization for severe anemia and hemicolectomy for a cecal tubule-villous adenoma.

Conclusions: Managing acromegaly in patients with CKD on hemodialysis is challenging. Long-term use of PAS-LAR in this patient subgroup appears safe for controlling disease activity. Further research in this area is needed.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1430

EP1177 - ECE_1572 - Challenges in the treatment of aggressive somatotrophic pituitary adenoma

Aleksandra Markovic[1,2], Mirjana Bojic[1], Ivona Risovic[1,2], Jelena Malinovic Pancic[1,2], Sanja Milanovic[1], Bojana Caric[1,2], Milena Brkic[2] and Tamara Dojcinovic[1,2]
[1]University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina; [2]Faculty of medicine University of Banja Luka, Banja Luka, Bosnia and Herzegovina

Introduction: Aggressive adenomas are large and invasive tumors that exhibit unusually rapid growth and/or continue to grow despite surgical treatment, drug therapy, and radiotherapy. However, large tumors, as well as invasive tumors, are not always aggressive, and this diagnosis can only be established after clinical monitoring, in which tumor growth dynamics and response to therapy are crucial for defining aggressiveness.

Case presentation: We present the case of a 37-year-old female patient with an aggressive invasive pituitary somatotropic macroadenoma. The tumor was detected at the time when it produced symptoms related to compression of surrounding structures, including headaches and visual disturbances, as well as amenorrhoea due to secondary hypogonadotropic hypogonadism.

In July 2024, the first MRI of the pituitary gland was performed, revealing a macroadenoma measuring 25 × 48 × 28 mm, expanding the sella turcica, exerting suprasellar compression of the optic chiasm, and circumferentially encasing the carotid arteries, with mild compression of the surrounding brain parenchyma. A neurosurgical consultation was obtained, and two transsphenoidal surgical procedures were performed; however, disease remission was not achieved. After the second surgery, a long-acting somatostatin analogue was introduced, as the tumor was considered inoperable. During further follow-up, an extremely active disease course was observed, characterized by persistently very high levels of growth hormone and IGF-1, accompanied by hypogonadotropic hypogonadism and secondary hypothyroidism. In addition to the long-acting somatostatin analogue, a dopamine agonist was also introduced. Follow-up MRI of the sellar region performed in February 2025 revealed residual tumor. The patient was discussed at a multidisciplinary team meeting, and radiotherapy was indicated. After completion of radiotherapy, partial regression of the tumor mass was achieved; however, biochemical disease activity remained significant. Due to the unavailability of second-generation somatostatin analogues and growth hormone receptor antagonists in our country, treatment with higher doses of somatostatin analogue was continued.

Conclusions: This case highlights the complexity of the therapeutic approach to aggressive pituitary adenomas, as well as the need for individualized and multidisciplinary treatment planning and the importance of continuous clinical follow-up.

Keywords aggressive pituitary adenoma, somatotroph adenoma, acromegaly, invasive pituitary tumor, multidisciplinary management

Abstract citation ID: lvag096.1431

EP1178 - ECE_1627 - Diagnostic challenges in a case of "mild" acromegaly

Irina A. Vaychulis
Internal Medicine Department, South-Ural State Medical University, Chelyabinsk, Russia

Presence and type of hormonal secretion are the key factors for treatment choice in patients with pituitary adenomas. However, in some cases, the detection of hormonal activity of pituitary tumors is not so obvious.

Female patient has been followed by endocrinologist (since the age of 54 years) with euthyroid multinodular goiter, arterial hypertension and dyslipidemia, well controlled by small doses of antihypertensive drugs and statins. At the age of 63 years, during her regular visit to the same endocrinologist, she mentioned the recently appeared swelling of the fingers, numbness and pain in both hands. Carpal tunnel syndrome was diagnosed by neurologist. Her TSH, fT4, CBC, rheumatoid factor, anti-CCP, fasting BG levels were unremarkable. Despite the absence of rough typical features and any noticeable changes in her appearance, testing for acromegaly was administered by endocrinologist. Moderate elevation of IGF-1 up to 222-217 (ULN 174) ng/ml at two consecutive measurements, in combination with normal basal GH, ACTH and prolactin levels were revealed. OGTT with 75 g glucose demonstrated normal 2-h postload BG and slightly insufficient suppression of GH to the minimum value of 0.59 (GH nadir cutoff < 0.4) ng/ml. Pituitary macroadenoma with maximal size of 1.4 cm was found at MRI. Patient had no visual field defects and was not inclined to consider neurosurgery. Short acute octreotide test was recommended to estimate sensitivity to somatostatin analogues, but the next two measurements of basal IGF-1 levels, performed at one month interval, showed the results within the normal range. Three months later, moderate elevation of IGF-1 (up to 185 ng/ml) was registered again. Repeated MRI showed no change in size of pituitary adenoma after 11 months.

Conclusions: Typical somatotropinoma is a slowly growing tumor, which remains undiagnosed for many years, and often first identified at advanced stage, presenting with large pituitary mass, multiple complications, high IGF-1 and unsuppressed GH levels. This case demonstrates diagnostic challenges in acromegaly with subtle, non-specific suspicious clinical signs/associated comorbidities (in the absence of typical acromegaly phenotype) and minimal, non-stable IGF-1 hypersecretion with normal basal GH and near normal suppression of GH. Such discordance can be interpreted as a "mild" form of disease, or explained by relatively early detection of classic, slowly progressing somatotropinoma. Taking into account inconsistent IGF-1 results, cyclic acromegaly pattern can also be discussed. Medical practitioners should be aware of acromegaly with mild clinical manifestations to avoid delay in diagnosis and to individualize therapy.

Abstract citation ID: lvag096.1432

EP1179 - ECE_2855 - A rare case of gonadotroph adenoma in a young woman

Claudia Angela Lasorella[1], Caterina Policola[1], Alessio Michetti[1], Andrea De Simone[1], Ettore Maggio[1], Gianluca Cera[1], Alessandro Romano[1], Erika Motolese[1], Pietro Locantore[1], Francesco Doglietto[2] and Alfredo Pontecorvi[1]
[1]Rome, Italy; [2]Unità di Neurochirurgia, Università Cattolica del Sacro Cuore-Fondazione Policlinico "A. Gemelli" IRCCS, Rome, Italy

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Functioning gonadotroph adenomas (FGA) represent 2%-10% of pituitary adenomas. It is characterized by ovarian follicles and cysts, hyperestrogenism and endometrial hyperplasia. Gold standard therapy is surgery.

Case presentation: A 40-year-old woman referred to us for abdominal pain, increased ovarian volume and hypomenorrhea. Hormonal evaluation showed hyperestrogenism and inappropriate FSH value. Second level tests documented secreting pituitary adenoma. Pelvic ultrasonography and MRI showed ovarian hyperstimulation syndrome (OHSS). Brain MRI revealed a pituitary lesion with increased uptake to 18-FDG-PET/TC. Patient underwent neurosurgery and histology showed a pituitary macroadenoma. Immunohistochemistry was positive for LH, FSH, p53, CK-CAM5.2, chromogranin.

Conclusions: Multiple ovarian cysts are frequently suggestive for polycystic ovary syndrome. A complete hormonal asset is necessary for differential diagnosis. Generally, women with FGA present hyperestrogenism, with inappropriate levels of FSH and LH and could also present OHSS. A complete biochemical, imaging and histological evaluation is necessary to confirm FGA diagnosis.

Abstract citation ID: lvag096.1433

EP1180 - ECE_3089 - Masked adrenal insufficiency in Wolfram syndrome: a rare endocrine phenotype

Sanda Cho, Tahir Omer, Rawia Adoma and Mosea Song
Diabetes and Endocrinology, Bedford Hospital, Bedford, United Kingdom

Background: Wolfram syndrome is a rare, inherited neurodegenerative disorder characterised by diabetes mellitus, optic atrophy, and progressive central nervous system involvement. While posterior pituitary dysfunction, particularly central diabetes insipidus, is well recognised, anterior pituitary hormone deficiencies are uncommon. ACTH deficiency is an exceptionally rare manifestation, with only a few reported cases. We describe a case of evolving secondary adrenal insufficiency in Wolfram syndrome, highlighting diagnostic challenges in rare neuroendocrine disease.

Case presentation: A 24-year-old woman with a known diagnosis of Wolfram syndrome attended routine diabetes follow-up with persistent fatigue, low energy, and chronically low blood pressure. Several weeks earlier, she had presented to the emergency department for worsening lethargy and hypotension, where blood pressure was recorded at 75/50 mmHg with a mild metabolic acidosis. She was treated with intravenous fluids and discharged following clinical improvement.

Given ongoing symptoms, adrenal function was assessed. Early-morning serum cortisol was repeatedly low (76 nmol/L and 71 nmol/L). An urgent short Synacthen test (SST) demonstrated preserved adrenal responsiveness, with cortisol rising from 105 nmol/L at baseline to 461 nmol/L at 30 minutes and 560 nmol/L at 60 minutes. The patient denied prior exposure to exogenous glucocorticoids.

The discrepancy between low basal cortisol levels and normal dynamic testing prompted further hypothalamic–pituitary evaluation. A repeat 9 AM cortisol one week later improved to 219 nmol/L. Anterior pituitary function was otherwise preserved, with normal thyroid function, gonadotrophins, and prolactin. Plasma ACTH was low at 5 ng/L (reference range 5-49 ng/L), supporting evolving secondary adrenal insufficiency. Pituitary MRI was requested.

Discussion: ACTH deficiency represents one of the rarest endocrine manifestations of Wolfram syndrome. When reported, it appears to reflect progressive hypothalamic–pituitary neurodegeneration rather than autoimmune pathology. Proposed mechanisms include impaired hypothalamic corticotrophin-releasing hormone secretion, selective vulnerability of pituitary corticotrophs, and chronic endoplasmic reticulum stress related to WFS1 dysfunction. Early disease may present with impaired basal ACTH secretion despite preserved adrenal reserve, leading to misleadingly normal SST responses. This case underscores limitations of dynamic testing alone and highlights the importance of longitudinal biochemical surveillance in rare neurodegenerative endocrine disorders.

Conclusions: This case adds to the limited literature describing ACTH deficiency in Wolfram syndrome. Clinicians should maintain vigilance for evolving pituitary–adrenal dysfunction in symptomatic patients. Serial assessment is essential, and the patient was advised on sick-day steroid rules while awaiting repeat testing, avoiding premature long-term glucocorticoid replacement.

Abstract citation ID: lvag096.1434

EP1181 - ECE_3410 - AVPD as a rare endocrine complication of temozolomide

Lia Anguelova[1], Mike Matheou[1], Bahram Jafar-Mohammadi[1], Christine May[1], Robin Joseph[2] and Aparna Pal[1]
[1]*Endocrinology, OCDEM, OCDEM, Oxford, United Kingdom;* [2]*Oxford, United Kingdom*

A 67-year-old man with no significant past medical history presented in June 2025 to the emergency department with acute neurological symptoms including facial droop and dysarthria. Neuroimaging revealed a multifocal glioblastoma involving the right cerebral hemisphere. Staging investigations demonstrated no evidence of extracranial metastatic disease. The patient underwent awake craniotomy followed by adjuvant radiotherapy (60 Gy in 30 fractions) and was commenced on temozolomide.

Following four weeks of the first cycle of temozolomide, the patient re-presented three weeks later with focal seizure activity. Biochemistry demonstrated hypernatremia (serum sodium 148 mmol/L), elevated plasma osmolality (305 mOsm/kg), and inappropriately dilute urine (urine osmolality 213 mOsm/kg), with otherwise normal renal function and electrolytes. On further questioning, the patient reported a one-month history of abrupt onset polydipsia and polyuria, consuming more than 4 litres of fluid daily and waking overnight to drink, which was uncharacteristic for him.

A diagnosis of AVPD was made and the patient was commenced on Desmopressin, resulting in resolution of symptoms, reduction in fluid intake to approximately 2 litres per day, and normalisation of serum electrolytes.

The case was reviewed at the pituitary multidisciplinary team meeting to assess for potential structural or treatment-related causes. Imaging demonstrated that tumour lesions were remote from the hypothalamic–pituitary axis, with no evidence of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

pituitary involvement, metastasis, or radiotherapy-related injury. In the absence of alternative causes, temozolomide was considered the most likely precipitating factor.

Temozolomide-associated AVPD is rare and is not recognised as a standard adverse effect in major prescribing references. A small number of isolated case reports describe the development of AVPD during temozolomide therapy, typically occurring days to weeks after treatment initiation and following exclusion of infection, tumour progression, or new intracranial pathology. The underlying mechanism remains unclear.

The patient is currently receiving his fourth cycle of temozolomide and remains clinically stable on ongoing desmopressin therapy, allowing continuation of chemotherapy. Given reports of potential reversibility following temozolomide cessation, he has been closely safety-netted and is undergoing regular biochemical and clinical follow-up.

Abstract citation ID: lvag096.1435

EP1182 - ECE_2501 - Beta radio-guided surgery in patients with pulmonary neuroendocrine tumors eligible for radical surgery

Piero Paravani[1], Francesco Collamati[2], Riccardo Mirabelli[3,4], Francesca Nicolanti[5], Matteo Tiracorrendo[6], Daniela Prosperi[7], Enrico D'ippolito[7], Chiara Lauri[7], Valeria Bentivoglio[7], Chiara Bolzan[8], Camilla Mancini[1], Valentina Brainovich[8], Massimiliano Mancini[9], Mohsen Ibrahim[6], Alberto Signore[7], Riccardo Faccini[5] and Antongiulio Faggiano[1]

[1]Endocrinology Unit, Department of Clinical and Molecular Medicine, Sapienza University of Rome, Sant'Andrea Hospital, ENETS Center of Excellence, Rome, Italy; [2]Section of Rome, Italian Institute For Nuclear Physics, INFN, Rome, Italy; [3]Section of Rome, National Institute of Nuclear Physics (INFN), Rome, Italy; [4]Department of Basic and Applied Sciences for Engineering, Sapienza Università di Roma, Rome, Italy; [5]Department of Physics, University of Rome La Sapienza, Rome, Italy; [6]Department of Thoracic Surgery, Sant'Andrea Hospital, Sapienza University, Rome, Italy; [7]Nuclear Medicine Unit, Sant'Andrea University Hospital of Rome, Department of Medical-Surgical Sciences and Translational Medicine of "Sapienza", University of Rome, Rome, Italy; [8]Medical Physics Dept., Sant'Andrea Hospital Rome, Rome, Italy; [9]Morphologic and Molecular Pathology Unit, Sant'Andrea Hospita, Rome, Italy

In Pulmonary neuroendocrine tumors (NETs), when feasible, surgical resection represents the gold standard of treatment. Achieving a radical resection remains the primary therapeutic goal, with great impact on overall survival. Radio-Guided Surgery (RGS) has been developed as an adjunctive technique to support surgeons obtaining complete tumor removal. RGS involves the administration of a radiotracer, followed by intraoperative detection of the emitted radiation. To overcome intrinsic limitations to gamma-sensitive detection systems, novel devices employing β-decaying isotopes with direct β detection have recently been developed. This approach has already been explored in small bowel NETs, showing encouraging results.

The present study, designed as a first-in-human, in vivo clinical trial, aims to evaluate the impact of intraoperative β-detector use during surgery for pulmonary NET. Inclusion criteria are: 1) presence of lung nodules positive on 68Ga-DOTA-TOC PET and consistent with pulmonary NETs, with or without preoperative histological diagnosis; 2) eligibility for radical surgical resection; 3) ECOG PS 0-2; 4) written informed consent.

Enrolled patients receive an intravenous injection of approximately 1 MBq/kg of 68Ga-DOTA-TOC at the beginning of surgery. The surgical procedure is performed according to standard clinical practice. During the operation, the β probe is used in vivo to sample the lung nodule and regional lymph node stations. Based on the detected signal, tissues are classified as "probe-positive" or "probe-negative" and compared with definitive histopathological findings. The diagnostic performance of the technique will be evaluated by calculating sensitivity, specificity, and positive and negative predictive values.

To date, three patients have been enrolled, two males and one female, aged 69, 58, and 43 years, respectively. All patients had pulmonary nodules suspicious for NETs and underwent anatomical lung resection with systematic hilar and mediastinal lymphadenectomy (anatomical trisegmentectomy of culmen, left upper lobectomy, middle lobectomy). Intraoperative uptake was observed in one patient at the site of the pulmonary nodule. No lymph node uptake was detected in any of the patients. Consistently, the only patient with uptake was diagnosed with a pulmonary NET (mitotic index < 1/2 mm^2, Ki-67 < 1%, absence of necrosis) with negative lymph nodes (pT1bpN0, Stage IA2). Similarly, no lymph nodes were found to be "probe-positive" and pathological on histology. The remaining two patients were diagnosed with non-NET, namely a biphasic sarcoma and a sclerosing pneumocytoma, both with 68Ga-DOTA-TOC PET uptake.

Completion of recruitment is expected by 03/2026.

Abstract citation ID: lvag096.1436

EP1183 - ECE_1972 - Immune checkpoint inhibitor-related hypophysitis: a single tertiary center cohort

Ruth Karov[1], Esther Osher[2,3] and Yona Greenman[1,3]

[1]Tel Aviv Souraski Medical Center, Institute of Endocrinology Metabolism and Hypertension, Tel Aviv, Israel; [2]Tel Aviv, Israel; [3]Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Background: Immune checkpoint inhibitor (ICI)-related hypophysitis is a clinically high-impact immune-related adverse event. Presentation is frequently nonspecific and may be misattributed to malignancy or cancer therapy, while ACTH deficiency can be rapidly life-threatening if unrecognized. We describe a real-world cohort from a tertiary Endo-Oncology Clinic to inform timing, imaging yield, co-occurring irAEs, and outcomes.

Methods: We retrospectively reviewed medical records of adult cancer patients evaluated in the Endo-Oncology Clinic at Tel Aviv Sourasky Medical Center with ICI-related hypophysitis (ICI initiation: 30-December-2018-05-May-2025; hypophysitis diagnosis: 10-May-2020-04-January-2026). Patients who received systemic glucocorticoids for >2 months in proximity to diagnosis were excluded.

Results: We identified 35 patients with suspected ICI-related hypophysitis; six were excluded due to systemic glucocorticoid therapy for >2 months near diagnosis, leaving 29 patients for analysis. Mean age at diagnosis was 65.8 ± 11.8 years and 62% were female. Most patients received PD-1/PD-L1 inhibitors (82%) while 17% received PD-1 + CTLA-4. Median time from ICI initiation to hypophysitis was 265 days (IQR 189-344; range

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

97-714) and was shorter with PD-1 + CTLA-4 versus PD-1/PD-L1 (156 [152-164] vs 295 [229-366] days; $P < .001$). Fatigue/weakness occurred in 90% and hyponatremia in 31%. Median morning cortisol was 0.49 µg/dL (IQR 0.28-0.96) with low ACTH (median 1.50 pg/mL, IQR 1.50-2.62; $n = 22$). Pituitary MRI was performed in 17/29 and showed abnormalities in 7/17 (41%). ACTH deficiency was isolated in most patients; central hypothyroidism occurred in 3% and gonadotropin deficiency in 10% (17% NA/not assessed). Other irAEs were recorded in 48%, most commonly thyroiditis (34%). No adrenal axis recovery was documented.

Conclusions: In our tertiary-center cohort, ICI-related hypophysitis typically developed months after ICI initiation and was dominated by persistent ACTH–cortisol deficiency, and showed earlier onset under PD-1 + CTLA-4, with moderate MRI yield and frequent co-occurring irAEs. These findings support a low threshold for endocrine evaluation in symptomatic ICI-treated patients and structured long-term follow-up for adrenal insufficiency.

Abstract citation ID: lvag096.1437

EP1184 - ECE_2174 - Tradeoff between pituitary stalk preservation and tumor control in craniopharyngioma surgery

Shingo Fujio, Ryutaro Makino, Jun Sugata, Tomoko Hanada and Ryosuke Hanaya
Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan

Introduction: Maximizing the extent of tumor resection and preserving endocrine function are often conflicting goals in the surgical management of craniopharyngiomas. Therefore, whether the pituitary stalk, the presumed site of tumor origin, should be preserved remains debatable.

Patients and Methods: Since the introduction of high-definition endoscopy in 2012, 49 surgical procedures have been performed in 45 patients with newly diagnosed craniopharyngiomas at our institution (26 men and 19 women, median age; 47 years). Surgical approaches included transsphenoidal surgery (34 patients), craniotomy (13 patients), and endoscopic cyst fenestration (two patients). Factors associated with pituitary function and tumor control were analyzed at the final follow-up, focusing on the impact of pituitary stalk preservation.

Results: Preoperatively, five patients (11%) had diabetes insipidus and 20 (44%) had anterior pituitary dysfunction. Intraoperatively, the pituitary stalk was transected in 12 patients (27%). At the final follow-up, anterior pituitary dysfunction involving at least one hormonal axis was observed in 34 patients (76%) and diabetes insipidus in 26 patients (58%).

Among the 33 patients in whom the pituitary stalk was preserved, 19 (58%) required reoperation or radiotherapy; however, tumor control was ultimately achieved in all cases. Additionally, anterior pituitary dysfunction occurred in 22 patients (67%) and diabetes insipidus in 14 (42%). Multivariate analysis revealed that postoperative anterior pituitary function was significantly associated with age ($\beta = -.0095$, $P = .02$), but not with tumor size or histological subtype. No cases of delayed pituitary dysfunction were observed after radiotherapy. Contrastingly, all 12 patients who underwent pituitary stalk transection developed postoperative panhypopituitarism, whereas only two (17%) required additional treatment for tumor control.

Discussion: Although preservation of the pituitary stalk does not guarantee complete preservation of endocrine function, it helped reduce the incidence of diabetes insipidus. Although stalk preservation is associated with a higher likelihood of requiring additional treatment, durable tumor control can be achieved through multidisciplinary management. These findings support a staged treatment strategy that prioritizes functional preservation, while maintaining effective tumor control.

Abstract citation ID: lvag096.1438

EP1185 - ECE_2240 - Dysregulation of nonsense-mediated decay and RNA-exosome machineries: two molecular sculptors of pituitary tumour pathophysiology

Ana De La Rosa-Herencia[1,2], Miguel E. G-Garcia[1,2], Álvaro Flores-Martínez[1,2], Eva Venegas[3], Paloma Moreno-Moreno[2,4], Judith López-Fernández[5,6], Antonio J. Fuentes[1,2], Luiz E Wildemberg[7,8], Leandro Kasuki[7,8], Mônica Gadelha[7,8], Alfonso Soto[3], María Ángeles Gálvez-Moreno[2,4], Antonio Carlos Fuentes-Fayos[1,2] and Raul M. Luque[1,2,9]
[1]Department of Cell Biology, Physiology and Immunology, University of Córdoba, Cordoba, Spain; [2]Reina Sofía University Hospital (HURS), Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), Cordoba, Spain; [3]Hospital Universitario Virgen del Rocío/Unidad de Gestión de Endocrinología y Nutrición, Instituto de Biomedicina de Sevilla (IBiS)/CSIC/Universidad de Sevilla, Sevilla, Spain; [4]Service of Endocrinology and Nutrition, Reina Sofía University Hospital (HURS), Cordoba, Spain; [5]Department of Medicine, University of La Laguna, Tenerife, Spain; [6]Service of Endocrinology, Canarias University Hospital, Tenerife, Spain; [7]Endocrinology Division, Medical School and Hospital Universitario Clementino Fraga Filho, Neuroendocrinology Research Center, Universidade Federal do Rio de Janeiro, Rio De Janeiro, Brazil; [8]Neuroendocrine Unit, Neuropathology and Molecular Genetics Laboratory, Secretaria Estadual de Saúde, Instituto Estadual do Cérebro Paulo Niemeyer, Rio De Janeiro, Brazil; [9]CIBER Pathophysiology of Obesity and Nutrition (CIBERobn), Cordoba, Spain

Despite recent advances in the management of pituitary tumors (PiTs), limited therapeutic strategies are available which highlights the urgent need to identify new molecular targets to improve the management of these patients. This study focuses on systematically characterizing, for the first time, the expression levels of the molecular components of two molecular machineries controlling gene expression, the Nonsense-Mediated Decay (NMD) and RNA-Exosome, in somatotropinomas (GHomas) and non-functioning PiTs (NFPTs) along with their relationship with clinical features. We also evaluated the therapeutic potential of inhibiting the activity of these molecular machineries in GHoma and NFPT cell-models. Our results revealed an overall upregulation of the components of the NMD and RNA-Exosome machineries in GHomas, while a more heterogeneous profile was found in NFPTs, compared with non-tumour pituitary glands. We identified two key factors as the most clinically relevant NMD and RNA-Exosome components, as their high expression wwere associated with critical oncogenic pathways and their *in vitro* silencing in GHoma and NFPT cell-models reduced multiple cancer hallmarks [eg, viability/proliferation, GH-secretion, oncogenic marker expression (*CDK2*/*VEGFA*/*POU1F1*…)]. Moreover, we provide solid evidence demonstrating

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

that targeting the activity of the NMD machinery with a specific inhibitor (NMDi alone or in combination with lanreotide) might translate into a beneficial effect on patients with GHomas and NFPTs, an observation that certainly warrants further clinical investigation. Altogether, our results demonstrate a clinically relevant NMD and RNA-exosome associated molecular dysregulation in GHomas and NFPTs, which could serve as a potential source of novel diagnostic/prognostic biomarkers and therapeutic targets.

Abstract citation ID: lvag096.1439

EP1186 - ECE_2461 - Different tumors, different burdens: long-term outcomes of pituitary hormone replacement in craniopharyngiomas and non-functioning pituitary adenomas

Nunzia Prencipe, Francesca Mocellini, Daniela Cuboni, Alessandro Maria Berton, Michela Sibilla, Valentina Gasco, Emanuele Varaldo, Fabio Bioletto, Alice Martinotti, Gianluca Aimaretti and Silvia Grottoli
Division of Endocrinology Diabetology and Metabolism, Department of Medical Sciences, "AOU Città della Salute e della Scienza di Torino" University Hospital, Torino, Italy

Background: Craniopharyngiomas (CF) and non-functioning pituitary adenomas (NFA) are causes of acquired hypopituitarism. Their different involvement of the hypothalamic–pituitary axis may influence long-term hormone replacement needs and the risk of complications related to under- or over-replacement therapy. Comparative long-term data in these patients are scarce.

Objective: To compare endocrine replacement requirements and long-term complications potentially related to pituitary hormone replacement in patients with CF and NFA.

Methods: We retrospectively analyzed 144 patients (66 CF, 78 NFA; 44 female) followed at a tertiary referral center. Inclusion criteria were the presence of ≥3 pituitary hormone deficiencies, excluding growth hormone deficiency, to ensure a homogeneous cohort with advanced hypopituitarism. Median follow-up was 12 years (range 1-50), with a median of 4 years of stable hormone replacement therapy. Hormonal status, type and dose of replacement therapies, treatment modifications, and metabolic and cardiovascular outcomes were assessed at diagnosis and at last follow-up.

Results: All CF patients underwent neurosurgery, whereas three NFA patients not; radiotherapy rates were comparable. CF patients were younger at diagnosis (median 35.5 vs 55.5 years, $P < .0001$). At baseline, anterior pituitary deficits were comparable by design, while arginine vasopressin deficiency (AVP-D) was more prevalent in CF ($P = .0005$). At last follow-up, AVP-D remained significantly higher in CF (80% vs 22%, $P < .0001$).

CF patients required higher doses of levothyroxine (median 1.25 vs 0.98 μg/kg/day, $P = .0001$) and recombinant human growth hormone (0.005 vs 0.003 mg/kg/day, $P = .001$), and showed a trend toward higher desmopressin doses. Desmopressin treatment was associated with a higher prevalence of electrolyte disturbances, but with lower rates of hypertension and coronary artery disease, independently of dose. Higher levothyroxine doses were associated with weight gain, whereas lower doses were observed in hypertensive patients. Testosterone replacement required more frequent dose adjustments in CF patients ($P = .014$).

At final follow-up, hypertension was more frequent in NFA patients ($P = .003$). Conversely, CF patients showed higher rates of obesity ($P = .04$) and weight gain ($P = .002$), while weight reduction was more common in NFA patients ($P = .001$). No differences were observed in diabetes mellitus, dyslipidemia, atrial fibrillation, thromboembolic events, or mortality.

Conclusions: In patients with severe hypopituitarism, CF are associated with greater hypothalamic involvement, higher hormone replacement requirements, and increased susceptibility to complications related to replacement imbalance, particularly weight gain and water–electrolyte disorders. NFA patients exhibit a higher prevalence of hypertension, probably due to older age. These findings highlight the importance of tumor-specific, individualized strategies for long-term pituitary hormone replacement.

Abstract citation ID: lvag096.1440

EP1187 - ECE_2820 - PitNETs: clinical characteristics and outcomes following surgical resection from single-center perspective

Aleksandra Derwich-Rudowicz[1], Abdulrahman Ammoun[1], Ikram Ghalmi[1], Ellen Haagensen[1], Matthew Steplewski[1], Norbert Wąsik[2], Marek Ruchala[1] and Nadia Sawicka-Gutaj[1]
[1]Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznan, Poland; [2]Department of Neurosurgery, Poznan University of Medical Sciences, Poznan, Poland

Background: Pituitary tumors (PitNETs) are a heterogeneous group of central nervous system lesions, which account for 13.5%-20% of all primary brain tumors. The aim of the study was to analyze clinical characteristics and postoperative outcomes of patients undergoing PitNET resection.

Material and Methods: This was longitudinal observational study. Medical records of patients diagnosed with PitNET who were hospitalized pre- and postoperatively at the Department of Endocrinology, Poznan, Poland, between January 2018 and December 2023 were reviewed. All patients underwent surgical resection of a pituitary tumor. Routine postoperative follow-up was scheduled 3-6 months after surgery. The statistical analysis was performed with MedCalc Software Ltd, with significance level set as $P < .05$.

Results: The study included 94 patients, 51 women (54%) and 43 men (46%), with a mean age of 53.7 ± 14.7 years. Non-functioning pituitary adenomas (NFPA) were the most common subtype (63.8%), followed by GH-secreting (18.1%), ACTH-secreting (12.8%), PRL-secreting (4.3%), and TSH-secreting tumors (1.1%). Most tumors were macroadenomas (71%), with microadenomas and giant adenomas comprising 14% and 15%, respectively. Hypopituitarism was observed in 63% of patients, most commonly affecting the gonadotrophic axis (64%), followed by corticotrophic (31%), thyrotrophic (28%), and somatotrophic (4%) axes. Tumor volume after surgery was reduced significantly ($P < .0001$). Postoperative evaluation demonstrated no radiological evidence of residual tumor in 45% of patients. The prevalence of headaches significantly decreased after surgery (difference −17.1%, 95% CI: −30.5 to −3.6; $P = .024$), the same as optic chiasm compression (difference −40.9%, 95% CI: −53.0 to −28.9; $P < .0001$). Lower LH levels were associated with a higher likelihood of hypopituitarism ($\beta = -.128$, SE = 0.043, Wald = 8.83, $P = .003$), corresponding to an odds ratio of 0.88 (95% CI: 0.81-0.96) per unit increase in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

LH. The number of impaired pituitary axes did not differ significantly before and after surgery ($P = .335$). Postoperative metabolic changes included a significant increase in body mass index, with a median rise of 0.64 (95% CI: 0.14-1.07; $P = .015$), as well as a significant increase in body weight, with a median gain of 2.0 kg (95% CI: 0.5-3.5; $P = .004$).

Conclusions: Surgical resection significantly reduced tumor volume and relieved mass-effect symptoms, despite continued axis dysfunction. Lower LH levels pre-surgery might be associated with a higher risk of hypopituitarism. Postoperative weight gain highlights the need for metabolic monitoring.

Abstract citation ID: lvag096.1441

EP1188 - ECE_2845 - Craniopharyngiomas at a tertiary referral center: a descriptive study

Francisca Leitão H., Miguel Marques, Daniel Duarte, Marta Almeida, Ana Quítalo, Ana Gonçalves Ferreira, Henrique Vara Luiz and Maria Carlos Cordeiro
Unidade Local de Saúde de Almada-Seixal, Almada, Portugal

Introduction: Craniopharyngiomas are rare epithelial tumors of the sellar and suprasellar region, accounting for 2%-5% of intracranial neoplasms. Although histologically benign, their proximity to critical adjacent structures often leads to significant morbidity. Two main histological variants are recognized: adamantinomatous and papillary. Management is complex and requires a multidisciplinary approach to balance tumor control and quality of life.

Objective: This study aimed to describe the characteristics and outcomes of patients diagnosed with craniopharyngioma at a tertiary referral center.

Methods: A retrospective descriptive study was conducted including all patients diagnosed with craniopharyngioma in our institution between 2019 and 2025. Demographic, clinical, radiological, histopathological, surgical, and follow-up data were collected from medical records. Surgical remission was defined as the absence of residual tumor on postoperative magnetic resonance imaging (MRI) and the absence of early recurrence.

Results: A total of 32 patients were included: 62.5% male and 37.5% female, with a mean age at diagnosis of 35.8 years. Of these, 35% were pediatric and 65% were adult cases. The most common symptoms at presentation were headache (16, 50%), visual disturbance (16, 50%), and endocrine dysfunction (6, 18.8%), of whom 5 had panhypopituitarism. Tumor location was suprasellar in 12 (37.5%) and both sellar and suprasellar in 20 cases (62.5%). The mean tumor volume was 6.15 cm.

All patients underwent surgical resection, with surgical remission achieved in 12 cases (37.5%). A transsphenoidal approach was performed in 18 patients (56.3%), while craniotomy in 14 (43.8%). Histopathological analysis revealed the adamantinomatous subtype in 24 cases (75%) and the papillary subtype in 8 cases (25%). Postoperative complications included diabetes insipidus (21, 65.6%), hypothalamic obesity (10, 31.3%), and endocrine dysfunction (29, 90.6%), of whom 27 developed panhypopituitarism. Neurocognitive dysfunction was observed in 4 patients (12.5%). Adjuvant radiotherapy was performed in 14 patients after surgery, of whom 5 achieved tumor remission. During a median follow-up of 6 years, tumor recurrence occurred in 15 cases (88%); among these, 60% required additional surgery, 13% radiotherapy alone, and 27% both modalities.

Conclusions: The management of craniopharyngiomas remains challenging due to high recurrence rate and frequent endocrine and hypothalamic sequelae. Despite their benign histology, these tumors are associated with significant long-term morbidity. Our center's experience highlights the importance of multidisciplinary management and lifelong follow-up to optimize tumor control and quality of life.

Abstract citation ID: lvag096.1442

EP1189 - ECE_3026 - A comparative evaluation of immunoinflammatory blood biomarkers in Cushing's disease and nonfunctioning pituitary adenomas

Hatice Ozisik[1], Adil Bahadir[2], Su Ozgur[3], Ezgi Ulas[1], Mehmet Yigit[4], Sevki Cetinkalp[1] and Mehmet Erdogan[4]
[1]Endocrinology, Ege University, Izmir, Türkiye; [2]The University of Texas MD Anderson Cancer Center, Houston, Texas, United States; [3]Translational Pulmonary Research Center-EgeSAM, Ege University, Izmir, Türkiye; [4]Izmir, Türkiye

Introduction: Cushing's disease (CD), caused by adrenocorticotropic hormone–secreting pituitary adenomas, is characterized by pituitary-dependent chronic hypercortisolism with marked effects on immune and hematological parameters. Excess cortisol leads to leukocytosis, neutrophilia, and lymphopenia, resulting in a distinct immunological profile that may be reflected in peripheral blood cell–derived inflammatory indices. Nonfunctioning pituitary adenomas (NFPAs), although hormonally inactive, may also exert systemic effects through mass-related pituitary dysfunction and tumor-associated inflammation. This study aimed to comparatively evaluate peripheral blood–derived immunoinflammatory markers in patients with Cushing's disease and nonfunctioning pituitary adenomas and to assess their discriminative and independent associations.

Methods: This retrospective study included 108 patients, comprising 19 patients with Cushing's disease and 89 patients with nonfunctioning pituitary adenomas. Standard laboratory parameters derived from complete blood counts were used to calculate immunoinflammatory indices, including commonly used ratios neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), eosinophil-to-lymphocyte ratio (ELR), platelet-to-neutrophil ratio (PNR), mean platelet volume to absolute lymphocyte count ratio (MPV/ALC), systemic immune-inflammation index (SII), systemic inflammatory response index (SIRI), pan-immune-inflammation value (PIV), derived NLR, and the fibrosis-4 (FIB-4) index. Intergroup comparisons, receiver operating characteristic (ROC) analyses, and multivariable logistic regression adjusted for age and sex were performed.

Results: Patients with Cushing's disease were significantly younger than NFPA patients (median age: 43 vs 60 years, $P < .001$) and exhibited a more pronounced pro-inflammatory hematological profile. Compared with the NFPA group, patients with CD had significantly higher leukocyte and neutrophil counts and lower lymphocyte percentages, resulting in elevated NLR, SIRI, SII, PIV, and derived NLR (all $P < .05$). ROC analysis showed modest-to-moderate distinctive performance for these indices

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(AUC range: 0.66-0.69), while FIB-4 showed the highest distinctive accuracy (AUC = 0.78). FIB-4 was included as a surrogate marker of cortisol-related metabolic and hepatic involvement. In multivariable logistic regression analyses adjusted for age and sex, only SIRI remained independently associated with Cushing's disease (odds ratio 2.42, 95% confidence interval 1.19-4.90, $P = .014$).

Conclusions: Peripheral blood–derived immunoinflammatory markers demonstrate distinct differences between Cushing's disease and nonfunctioning pituitary adenomas and show moderate disc ability. Among these markers, SIRI emerges as the only robust immunoinflammatory index independently associated with Cushing's disease, suggesting its potential utility as an easily accessible adjunctive biomarker reflecting disease-related immune dysregulation. Prospective studies with larger cohorts are warranted to confirm these findings and clarify their clinical applicability.

Abstract citation ID: lvag096.1443

EP1190 - ECE_3870 - Paradoxical IGF-1 and GH elevation: diagnostic challenges beyond acromegaly

Oana Pietrareanu[1], Iulia Florentina Burcea[1,2], Ramona Dobre[1,2], Raluca Pirvu[1], Andreea Gorun[1] and Catalina Poiana[1,2]
[1]'C.I. Parhon' National Institute of Endocrinology, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania

Introduction: Acromegaly is traditionally diagnosed based on elevated insulin-like growth factor 1 (IGF-1) and failure of growth hormone (GH) suppression during an oral glucose tolerance test (OGTT). Nevertheless, discordant biochemical profiles between IGF-1 and GH are increasingly encountered, complicating diagnostic decision-making and raising concerns regarding overdiagnosis or delayed recognition of true disease. Understanding these paradoxical patterns is essential to optimize diagnostic accuracy and avoid unnecessary interventions.

Methods: We performed a retrospective observational study including patients evaluated for suspected acromegaly, between 2022 and 2025. Inclusion criteria were biochemical discordance between IGF-1 concentrations and GH on confirmatory testing, availability of pituitary MRI, and exclusion of confounding physiological conditions such as pregnancy or puberty. Hormonal evaluation comprised age- and sex-adjusted IGF-1 levels, GH nadir during OGTT, and 24-hour GH secretion profiles. Clinical features, metabolic comorbidities, imaging findings, and longitudinal biochemical evolution were systematically analysed.

Results: Six patients (median age 44 years) met inclusion criteria, displaying heterogeneous patterns of GH–IGF-1 discordance. The most prevalent phenotype was persistently elevated IGF-1 despite OGTT GH nadir < 0.4 ng/ml ($n = 3$), all associated with pituitary microadenomas and multiple metabolic or endocrine comorbidities. Longitudinal follow-up of up to three years demonstrated stable tumor size and no increase in IGF-1 (×ULN) and stable GH dynamics despite sustained IGF-1 elevation. Additional discordant patterns included high-normal IGF-1 with increased 24-hour GH secretion, but preserved OGTT supression ($n = 1$), normal IGF-1 with failure of GH suppression during OGTT ($n = 1$), and low-normal IGF-1 with elevated GH secretion in the absence of pituitary tumor imaging evidence ($n = 1$). These findings highlight the complexity of GH pulsatile secretion, assay limitations, and individual variability within the GH–IGF-1 axis.

Conclusions: In this retrospective case series of patients with discordant IGF-1/GH profiles, integrating dynamic testing, 24-hour GH profiling, pituitary MRI, and longitudinal follow-up supported a surveillance strategy when no clinical, biochemical, or structural progression was observed. These findings highlight the value of a multimodal, individualized approach when IGF-1 and GH measures diverge. Limitations include the small sample size, single-center retrospective design, and potential assay-related variability.

Abstract citation ID: lvag096.1444

EP1191 - ECE_1348 - Clinical relevance of genetic diagnosis in congenital hypogonadotropic hypogonadism

Andreu Campos Peris, Guillermo Serra Soler, Ramón Zafra Jiménez, Alejandro De la Cruz Bonilla, Maria Ubeda Dilme, Alicia Sanmartín Sánchez, Francisca Caimari Palou, Elena Mena Ribas, Santiago Tofé Povedano and Iñaki Argüelles Jiménez
Hospital Universitario Son Espases, Palma, Spain

Introduction: Congenital isolated hypogonadotropic hypogonadism (CHH) is a rare genetic disorder that is associated with deficient secretion and/or action of the Gonadotropin-releasing hormone (GnRH). The incidence is estimated to be 1:15.000-50.000 with a male-to-female ratio of 5:1. CHH spectrum of clinical expression ranges from complete absence of sexual development to partial completion of puberty. It can be associated with multisystem anomalies such as anosmia (known as Kallman syndrome). Timely diagnosis and treatment are crucial for fertility preservation.

Pathogenic variants in more than 60 genes have been identified as the cause of CHH. Genetic testing can help lead to an early diagnosis, providing prognostic information and allowing genetic counseling to be adapted.

Our objective was to reassess patients with diagnosis of CHH without initial genetic testing or with negative results from previous genetic testing panels.

Methods: A descriptive retrospective observational study was conducted in a series of eight patients with CHH. Genetic re-evaluation was performed using a next-generation gene panel associated with CHH. Clinical variables, magnetic resonance imaging (MRI) findings, presence of offspring, and genetic results were collected for statistical analysis.

Results: All 8 patients were men, (current mean age 51.9 ± 13.3 years). The mean age at diagnosis of CHH was 24.3 ± 13.3 years. Genetic reassessment was performed after an average of 24.4 years from initial diagnosis (range 14-34 years). The genetic study identified pathogenic variants in four patients (50%). Among the two patients (25%) who had undergone previous genetic testing with negative results, the updated genetic panel identified a pathogenic variant in one case, whereas the other remained negative. *GNRHR, ANOS1, SOX10, PROK2,* were the genes identified.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Regarding the phenotype, two patients (25%) presented anosmia and one hyposmia (12.5%). Anomalies in MRI were observed in three patients (37.5%). Gonadotropin therapy was administered to six of the eight patients (75%), with the aim of pubertal induction in two cases and fertility induction in four cases. Three of eight (37.5%) patients had offspring.

Conclusions: Genetic testing in CHH is challenging; however, it allows an earlier and more precise diagnosis. This enables timely initiation of hormonal therapy, optimizing pubertal development and reproductive function. In addition, genetic testing provides prognostic information that supports tailored genetic counselling. Therefore, the implementation of new genetic panels supports personalized medicine and enhances patients' quality of life.

Abstract citation ID: lvag096.1445

EP1192 - ECE_2409 - Assessment of the allostatic load index and psychological and psychiatric status in patients with pituitary tumours

Aleksandra Jawiarczyk-Przybyłowska[1], Martyna Strzelec[1], Justyna Kuliczkowska-Płaksej[1], Dorota Szczesniak[2], Agnieszka Zembska[1], Katarzyna Kolačkov[1], Natalia Sloka[1], Anna Brona[1], Aleksandra Zdrojowy-Wełna[1], Iga Zendran[1], Malgorzata Rolla[1] and Marek Bolanowski[1]
[1]*Department of Endocrinology and Internal Diseases, Medical University in Wroclaw, Wroclaw, Poland;* [2]*Division of Psychotherapy and Psychosomatic Medicine, Department of Psychiatry, Medical University in Wroclaw, Wroclaw, Poland*

Background: Chronic exposure to pathogenic stress factors results in multisystemic deterioration and adverse physiological changes resulting in the development of allostatic load (AL). Stress is a key contributor to the development and progression of numerous diseases, including endocrine disorder.

Purpose: This study aimed to assess the allostatic load index (ALI) and psychological and psychiatric status in patients with pituitary tumours and compare the results to a control group.

Methodology: The research group included 58 patients diagnosed with hormonally active pituitary tumours and 52 control subjects without pituitary dysfunction. The AL index (ALI) was determined using 16 parameters categorized into anthropometric parameters, cardiovascular markers, lipid and carbohydrate metabolism parameters, and inflammatory and hormonal markers. Standardized clinimetric tools were used to evaluate the psychological and psychiatric status in patients with pituitary tumours (WHOQOL-BREF scale, GHQ-28 scale, GAD-7 scale, INTERMED questionnaire, PHQ-9 scale, PSS-10 scale)

Results: Patients with pituitary tumours exhibited a significantly higher ALI compared to the control group, regardless of the endocrine activity of the adenoma ($P < .001$). Based on the analysis of clinimetric data, we found that patients in the study group exhibited significantly poorer psychological and social functioning, lower self-esteem, and more pronounced depressive and somatic symptoms compared to the control group. In every fourth patient with a pituitary tumour, a score of at least 10 points was obtained on the PHQ-9 scale, indicating the presence of moderate or severe depression. In the control group, depressive symptoms were eight times less frequent.

Conclusions: The findings support the utility of the ALI as of the AL index as an integrated measure for evaluating the cumulative impact of stress in pituitary diseases. Mental health disorders are a significant concern among patients with pituitary tumours and require special attention in clinical practice. Every patient diagnosed with a pituitary tumour should undergo screening for depression.

Keywords allostatic load, pituitary tumour, clinimetric tools, depression

Abstract citation ID: lvag096.1446

EP1194 - ECE_2633 - When appearances deceive: a silent somatotroph macroadenoma with acromegaloid features and low IGF-1

Emily Mayar and Sing Yang Sim
Brighton & Sussex University Hospitals NHS Trust, Brighton, United Kingdom

A 45-year-old gentleman was referred to the endocrinology department after presenting with recurrent epistaxis, headache, third cranial nerve palsy and a right-sided diplopia. A subsequent pituitary MRI identified a giant pituitary macroadenoma. On presentation, he exhibited acromegaloid features, including frontal bossing, spade-like hands and coarse facial characteristics suggestive of a GH-secreting tumour despite the absence of hyperhidrosis or rapid weight gain. Ophthalmologic assessment revealed mild enlargement of the right blind spot with preserved visual fields.

Initial MRI imaging demonstrated a large sellar and suprasellar mass with mass effect on the chiasm extending into the right cavernous sinus and paranasal sinuses. The differential diagnoses initially included nasopharyngeal malignancy and lymphoma; however, biopsy of nasal tissue revealed only benign adenoid tissue. Preoperative endocrine blood tests showed low serum free testosterone (5.4 nmol/L), TSH 1.37 mU/L (0.27-4.2), T4 15.6 pmol/L (11-22), FSH 3.8 IU/L, LH 4.1 IU/L, a normal short synacthen test and elevated prolactin 4107 mIU/L (86-324) prompting initiation of cabergoline at a dose of 500 micrograms weekly. Surprisingly, his IGF-1 was low preoperatively (13.1 nmol/L; 15.5-33.1) highlighting a biochemical discrepancy between clinical appearance and the hormonal profile.

The patient underwent endoscopic transsphenoidal resection in March 2025. Postoperatively, he experienced transient diabetes insipidus requiring DDAVP which subsequently resolved. Visual function and pituitary hormones remained largely preserved; hydrocortisone was administered temporarily due to borderline cortisol levels (178 nmol/L). He remained under follow-up in our combined pituitary clinic where management options including observation versus conventional fractionated radiotherapy were discussed with him in view of the postoperative residual tumour within the cavernous sinus.

Histopathology confirmed a PIT1-lineage somatotroph adenoma. His immunohistochemistry was positive for GH yet negative for other pituitary hormones, with a low proliferative index (Ki67 < 2%), consistent with a silent somatotroph adenoma.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

This case highlights the diagnostic challenge of silent somatotroph adenomas. They represent 2-4% of surgically removed pituitary adenomas often discovered incidentally or through mass effect symptoms. Compared to functioning somatotroph adenomas, they are more aggressive with higher Ki67 index, greater local invasiveness, higher recurrence rate and a female predominance. Patients may exhibit acromegaloid features despite normal IGF-1 levels. Recognition of this entity is crucial, as the absence of overt hormonal hypersecretion can delay diagnosis, yet large tumour mass effects can cause significant morbidity. Integrated clinical, radiological and histopathological assessment will be key here.

Abstract citation ID: lvag096.1447

EP1195 - ECE_2882 - Urea for treating hyponatremia and and its impact on nutritional status: a case report

Lucía Estévez Asensio[1,2,3], Maria del Puerto Bernoy González[1,2,3], Hugo Pereira Gregorio[1,2,3], Jaime González Gutierrez[1,2,3], Paloma Perez Lopez[1,2,3], Pablo Fernández Velasco[1,2,3], Juan Jose Lopez Gomez[1,2,3], Daniel De Luis Roman[1,2,3] and Emilia Gomez Hoyos[1,2,3]

[1]Valladolid, Spain; [2]Centro de Investigación de Endocrinología y Nutrición, Universidad de Valladolid, Valladolid, Spain; [3]Centro de Investigación Biomedica en Red (CIBEROBN) de la Obesidad y Nutrición, Instituto de Salud Carlos III, Valladolid, Spain

Introduction and Aim: Hyponatremia is the most common electrolyte disorder, and even mild forms are associated with increased morbidity and mortality. The most frequent etiology is the syndrome of inappropriate antidiuretic hormone secretion (SIADH). The traditional first-line therapy for SIADH is fluid restriction (FR). However, approximately 39%-55% of patients with SIADH do not respond adequately to FR. Consequently, there is increasing interest in identifying safe and well-tolerated treatments for the long-term management of hyponatremia. Urea, an oral osmotic diuretic, may represent a safe and effective alternative treatment, and newer flavoured formulations could improve patient adherence.

Methods: We report the case of a 64-year-old woman with moderate chronic hyponatremia and disease-related malnutrition. Her medical history included T4N2M0oropharyngeal carcinoma treated with chemoradiotherapy four years earlier and emphysematous chronic obstructive pulmonary disease (COPD). She was clinically euvolemic and asymptomatic, with a serum sodium concentration of 129 mmol/L (plasma osmolality 257 mosm/L). Complementary diagnostic tests were consistent with chronic hyponatremia due to SIADH of pulmonary etiology (COPD) diagnosis.

Results: Fluid restriction was not feasible due to patient's xerostomia secondary to prior chemoradiotherapy. Ambulatory treatment with oral urea was initiated at a dose of 15 g/day dose, resulting in progressive correction of hyponatremia (pNa 136 mmol/L at the 3-month follow-up visit; pNa 135 mmol/L at the 20-month follow-up visit) and adequate long-term tolerance. In addition, hypercaloric high-protein oral nutritional supplements and physical activity were prescribed. No adverse effects (eg, dysgeusia, nausea) or overcorrection of hyponatremia were observed. A morphofunctional assessment of the patient's nutritional status was performed at baseline and during outpatient follow-up, showing no deterioration in nutritional status (Table 1).

Table 1 Morphofunctional nutritional assessment

Parameter	Baseline Visit	3-Month Follow-up Visit
BMI	16.62 kg/m^2	17.31 kg/m^2
Handgrip Strength	22 kg	27 kg
Resistance	736.4	703.5
Reactance	77.2	77.8
Phase Angle	5.9 °	6.3 °
Fat Mass (%)	11.20	11.50
Skeletal Muscle Mass (%)	58.59	59.75

Conclusions: This case illustrates that urea is an effective, safe, and well-tolerated therapeutic option for the management of hyponatremia due to SIADH. Furthermore, the improved palatability of newer formulations does not negatively impact nutritional status, as relaxation of fluid restriction facilitates the intake of oral nutritional supplements.

Abstract citation ID: lvag096.1448

EP1197 - ECE_3004 - Multiple treatment strategies in a patient with ACTH-dependent Cushing's syndrome

Anna Brona[1], Aleksandra Zdrojowy-Welna[1], Barbara Stachowska[1], Aleksandra Jawiarczyk-Przybyłowska[1], Justyna Kuliczkowska-Płaksej[1], Jowita Halupczok-Żyła[2] and Marek Bolanowski[1]

[1]Endocrinology and Internal Medicine, Endocrinology and Internal Medicine, Wroclaw Medical University, Wroclaw, Poland; [2]Wroclaw, Poland

We would like to present a 31-year old patient with Cushing's disease who has undergone all types of treatment, ie, surgery, radiotherapy and pharmacotherapy.

The patient was diagnosed with ACTH-dependent Cushing's syndrome in 2022, at the age of 27. The first symptoms of the disease had probably appeared about 8 years before. On admission the patient presented with a moon face, abdominal obesity with thinning limbs, purple striae, thin skin, petechiae, scalp hair loss, oedema of the feet. She complained of easy bruising, proximal muscular weakness and menstrual irregularities. She had already been diagnosed with hypertension, diabetes and hypertriglyceridemia. The comorbidities were managed with multidrug pharmacotherapy, ie, bisoprolol 7.5 mg, indapamide 1.5 mg, lercanidipine 10 mg, pantoprazole 20 mg, ezetimibe 10 mg, fenofibrate 267 M mg (once a day), metformin 1000 mg (three times a day), empagliflozin 10 mg (once a day), insulin lispro with insulin lispro protamine suspension 25 16 IU in the morning, 18-20 IU before dinner. After confirming the diagnosis of ACTH-dependent Cushing's syndrome (pituitary tumor 17 × 10 × 20 mm) she was operated on. Due to the invasion of the right sinus cavernous the complete removal of the tumor was not possible. After surgery the symptoms of hypercortisolemia persisted, thus she was referred to the radiotherapy division for stereotactic surgery with Cyberknife. She was dismissed from pasireotide therapy because of poor diabetes control. In January 2023 therapy with osilodrostat was introduced. It was well tolerated and improved diabetes control. In June 2025 the patient

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

agreed to switch to therapy with pasireotide to address the tumor size. This therapy caused severe hyperglycemia that could not be well managed because of the financial background. In October 2025 therapy with osilodrostat was restarted. After 2.5 months diabetes control improved and the patient continues therapy with osilodrostat. Now, the treatment of diabetes includes insulin aspart lispro with insulin degludec 14 IU in the morning, and insulin aspart before meals depending on glucose level.

The last MRI of the pituitary was performed in January 2025 (tumor size 9 × 6 × 12 mm).

Our case highlights the difficulties of management of ACTH-dependent Cushing's disease due to macroadenoma and the role of combined therapy. The long -existing hypercortisolemia before surgery contributed to symptoms and complications of Cushing's disease that are still present (ie, central obesity, hypertension, and hypertriglyceridemia).

Abstract citation ID: lvag096.1449

EP1198 - ECE_1182 - Pituitary stalk interruption syndrome: case series from a tertiary care center in South India

Sai Subrahmanyam Pappu, Neelaveni Kudugunti and Rakesh Sahay
Osmania General Hospital, Hyderabad, India

Introduction: Pituitary Stalk Interruption Syndrome is a rare disorder with incidence of 0.5 per 100000 births. Ectopic posterior pituitary (EPP) is the cardinal feature. MRI shows a triad of-thin/absent stalk, EPP, Anterior pituitary hypoplasia.

GH deficiency is seen in almost 100% cases. Isolated sparing of TSH has also been described. DI is very rare.

We describe 12 cases of PSIS that presented to a tertiary care center.

Case summary:

	Age/Gender	Presenting complaint	Height SDS	GH(Peak)(ng/ml)	T3/T4/TSH	LH/FSH	Cortisol(mcg/dl)	MRI
1	4/m	Hypoglycemic seizures Micropenis cryptorchidism	−3.95	2.83	97 ng/dL 7.3 mcg/dl 1.105 mIU/mL	Post Hcg T: 208 ng/dL	21.77	EPP/Thin infundibulum/ Pituitary Hypoplasia
2	18/m	Short stature Stalled puberty	−6	1.01	90 ng/dL 8.3 mcg/dl 2.1 mIU/mL	1.23/2.25 T: 266 ng/dL	21.27	EPP/Thin infundibulum/ Pituitary Hypoplasia
3	16/f	Short stature Delayed puberty	−4.5	1.8	T4 3.5 mcg/dl TSH 3.5	1.26/2.95 E2 13.09 pg/mL	On Replacement	EPP/Thin infundibulum/Pituitary Hypoplasia
4	15/f	Short stature stalled puberty	−4	0.4	T4 9.9 mcg/dl TSH 6.72	0.52/1.62 E2 < 5 pg/mL	26.7	EPP/Thin infundibulum/Pituitary Hypoplasia
5	4/m	Hypoglycemic seizures	−3	0.41	T4 8. mcg/dl TSH 2.7		23	EPP/Absent Stalk/ Ant. Pituitary Hypoplasia
6	1 mo/m	Hypoglycemic seizures Neonatal jaundice		Random 2.74	T4 2.96 mcg/dl TSH 3.28	2.14/1.43 T: 116 ng/ml	Critical sample 1.88	EPP/Thin infundibulum/Ant. Pituitary Hypoplasia
7	11/m	Short stature micropenis	−3.5	0.5	FT4 0.7 ng/ml TSH 2.5		27.80	EPP/Absent Stalk/ Pituitary Hypoplasia
8	11/m	Short stature micropenis	−5.2	0.19	FT4 0.97 ng/ml TSH 1.47		23.25	EPP/Absent Stalk/ Pituitary Hypoplasia
9	12/m	Short stature micropenis	−3.21	0.235	T4 6 mcg/dl TSH 1.8		24	EPP/hypoplastic infundibulum
10	8/f	Short stature	−4.38	0.20	T4 13.1 mcg/dl TSH 3.86		24.86	EPP/Absent Stalk/ Ant. Pituitary Hypoplasia
11	7/f	Short stature	−3.95	0.5	T4 11.1 mcg/dl TSH 4.86		21	EPP/Absent Stalk/ Ant. Pituitary Hypoplasia
12	4/m	Short stature micropenis	−3.06	1.03	T4 9.8 mcg/dl TSH 3.4		26	EPP/Absent Stalk/ Ant. Pituitary Hypoplasia
13	1/m	Asymptomatic, 3 siblings affected	−1.58	1.5	T4 12. mcg/dl TSH 2.4		32	EPP/Absent Stalk/ Ant. Pituitary Hypoplasia

Discussion: All subjects had GH deficiency, 2 subjects had central hypocortisolism. 3 subjects had central hypothyroidism.

The 2nd most common hormonal defect was hypogonadotropic hypogonadism.

4 siblings had isolated GH deficiency.

Early childhood and neonatal presentation was with hypoglycemia.

Children and adolescents presented with short stature and delayed puberty.

Conclusions: Our cohort highlights the entire spectrum of PSIS from neonatal hypoglycemia to childhood short stature and delayed puberty.

Abstract citation ID: lvag096.1450

EP1199 - ECE_1472 - High prevalence of moderate-severe obstructive sleep apnoea in acromegaly and the impact of surgical or medical treatment on its severity: a systematic review and meta-analysis

Jagraj Thandi[1], Matthew Craggs[2], Hanae Magari[3], Supichaya Narongchartsopon[4], Grace Yu Ling Tan[5], Daniel Cuthbertson[2,6], Sonya Craig[2] and Kirstie Anderson[7]
[1]*School of Medicine, University of Sunderland, Sunderland, United Kingdom;* [2]*Aintree University Hospital, Liverpool, United Kingdom;* [3]*School of Dentistry, Tohoku University, Sendai, Japan;* [4]*Medical School, Newcastle University, Newcastle upon Tyne, United Kingdom;* [5]*Stockton-on-Tees, University Hospital of North Tees, United*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Kingdom; [6]Department of Metabolic and Cardiovascular Medicine, University of Liverpool, Liverpool, United Kingdom; [7]Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom

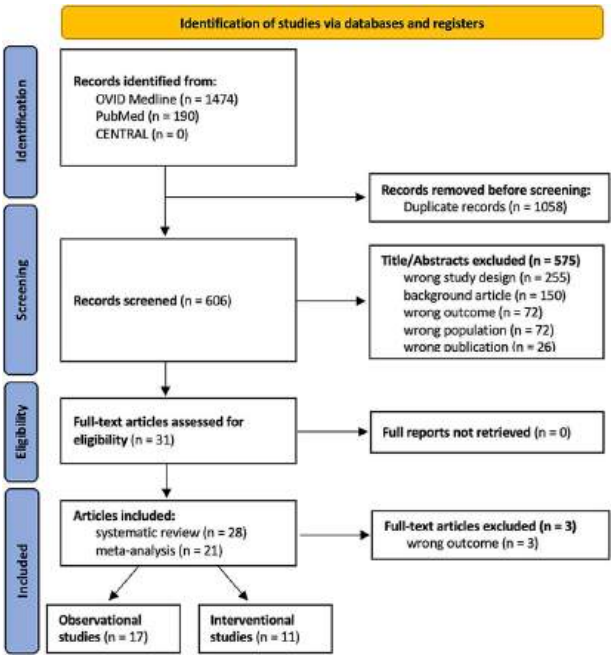
Background: Acromegaly causes significant multimorbidity and mortality, with 50% of patients responding to first-line somatostatin analogue (SSA) therapy. Untreated acromegaly often causes obstructive sleep apnoea (OSA), primarily due to pharyngeal/glossal hypertrophy from IGF-1–mediated tissue growth. Improved understanding could enable earlier detection, better management, and reduced cardiovascular and respiratory complications in acromegaly.

Aims: To perform a systematic review and meta-analysis to assess the impact of acromegaly disease activity and treatment on OSA severity.

Methods: Studies comparing active and inactive post-treatment acromegaly patients were included, assessing OSA prevalence, apnea-hypopnea index (AHI), growth hormone (GH) excess, and respiratory disturbance index (RDI). Cardiovascular events, cerebral microbleeds, and macroglossia were also reviewed. Literature searches followed PRISMA guidelines, using these MeSH terms—"acromegaly", "obstructive sleep apnea", "cardiovascular" and "respiratory" across OVID Medline, EMBASE, CENTRAL, and Cochrane databases (1980-2025). Only English-language studies were included. Study selection, data extraction, and narrative synthesis were performed, with meta-analysis where data permitted. Reporting bias was assessed using the ROBINS-I tool.

Results: From 606 identified articles, 31 underwent full-text review, 28 were included in the systematic review (17 observational, 11 interventional; 695 patients) and 21 in the meta-analysis. OSA prevalence remained high in post-treatment acromegaly (active = 44.0%-87.5% vs inactive = 14.0%-58.0%). Meta-analysis showed moderate mean AHI (~15-20 events/hour) for active and inactive disease, with 40%-65% exhibiting moderate-to-severe OSA. Central sleep apnoea occured in 10% of patients but correlated with higher GH/IGF-1 levels. Sleep quality was often poor, with 60%-70% reporting daytime somnolence; although screening tools underestimated severity compared with polysomnography sleep studies (PSG). Acromegaly OSA was driven by oropharyngeal soft-tissue hypertrophy, macroglossia, uvular/soft-palate thickening, tonsillar enlargement, and lateral pharyngeal wall thickening, which correlate with OSA severity and not serum IGF-1 levels. Cardiovascular complications included resistant hypertension, left ventricular hypertrophy, and arrhythmias detected during sleep studies. However, major adverse cardiovascular events (MACE) such as myocardial infarction, stroke, and death were not reported. Therefore, consistent OSA severity predictors included male sex, older age, longer disease duration, higher BMI, and craniofacial/soft-tissue hypertrophy, whereas biochemical disease activity (serum IGF-1 concentrations) showed inconsistent associations.

Conclusions: Cross-sectional meta-analysis found no significant difference in OSA prevalence or AHI between active and inactive disease. However, longitudinal studies showed significant reductions in AHI and OSA severity following surgical or medical control, particularly within the first year. Persistent OSA despite treatment highlights the need for repeat OSA assessments for those with ongoing symptoms despite acromegaly treatment.



Abstract citation ID: lvag096.1451

EP1200 - ECE_1684 - The utility of anti-rabphilin-3A antibody measurement in autoimmune hypothalamic-pituitary inflammation

Naoko Iwata, Momoka Inoue, Yusuke Kato, Jun Yoshida, Tetsuro Tsumura, Haruki Fujisawa and Yoshihisa Sugimura
Nagoya, Japan

Background: Pituitary inflammation is a chronic inflammatory disorder of the pituitary gland caused by autoimmune, systemic diseases, medications, infections, and other factors. It includes lymphocytic adenohypophysitis, lymphocytic infundibulo-neurohypophysitis (LINH), IgG4-related hypophysitis (IgG4-RH), and immune-related adverse events (irAE) induced by immune checkpoint inhibitors (ICI) in pituitary gland. However, reliable non-invasive diagnostic markers, particularly for posterior pituitary involvement, remain limited. We previously identified anti-rabphilin-3A antibodies as a diagnostic marker for LINH and reported the involvement of rabphilin-3A in the disease pathogenesis. This study evaluated the clinical utility of measuring anti-rabphilin-3A antibodies in pituitary inflammation other than LINH.

Case 1: A 52-year-old male. He had experienced frequent urination for several years. In August 2023, he started chemotherapy with FOLFOX + Pmab for sigmoid colon cancer with multiple liver metastases. From October 2023, he developed dry mouth and polyuria with polydipsia. Endocrine evaluation revealed preserved anterior pituitary function, while the hypertonic saline loading test showed low AVP response. Pituitary MRI showed no enlargement of the pituitary gland or pituitary stalk, with loss of posterior pituitary bright spot. Based on these findings, idiopathic arginine vasopressin deficiency (AVP-D) was diagnosed. Anti-rabphilin-3A antibodies were positive.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Case 2: An 84-year-old male developed joint pain and anorexia in May 2025. Endocrine evaluation including the stimulation tests demonstrated decreased secretion of anterior pituitary hormones and AVP-D. Pituitary MRI showed enlargement of the pituitary gland and pituitary stalk, with blurred T1WI and homogeneous contrast enhancement. Serum IgG4 was elevated at 190.1 mg/dL. Pituitary stalk thickening improved after hydrocortisone therapy, leading to a diagnosis of suspected IgG4-RH. Anti-rabphilin-3A antibodies were positive.

Case 3: A 62-year-old male. Nivolumab therapy initiated in January 2017 for lung squamous cell carcinoma. In April 2018, he developed generalized fatigue. Laboratory tests revealed severe hyponatremia, prompting further endocrine evaluation. Endocrine evaluation revealed isolated ACTH deficiency as an irAE. Serum IgG4 was normal. MRI showed no enlargement of the pituitary gland or pituitary stalk. AVP-D was absent. Anti-rabphilin-3A antibodies were negative.

Discussion: In our study, anti-rabphilin-3A antibodies were positive in cases of idiopathic AVP-D and suspected IgG4-RH, but negative in ICI-induced isolated ACTH deficiency without AVP-D. These findings suggest rabphilin-3A may be involved in autoimmune mechanisms underlying AVP-related hypothalamic-posterior pituitary disorders, including idiopathic AVP-D and IgG4-RH. Measuring anti-rabphilin-3A antibodies may aid in distinguishing these disorders from tumors. Conversely, ICI-induced pituitary dysfunction without AVP-D may involve autoimmune mechanisms targeting antigens other than rabphilin-3A.

Abstract citation ID: lvag096.1452

EP1201 - ECE_2150 - Intracranial dissemination in aggressive immature PIT-1 lineage pituitary tumor: a consequence of repeated transcranial surgery?

Aysel Unver Ozkahraman[1], Rukiye Dilara Tekin Uzman[1], Huseyin Karatay[2], Ebubekir Akpinar[3,4], Buruc Erkan[3,4], Mutlu Niyazoğlu[1,4] and Esra Hatipoglu[1]

[1]Department of Endocrinology and Metabolism, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkey; [2]Department of Pathology, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkey; [3]Department of Neurosurgery, University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkey; [4]Pituitary Disorders Research Center, University of Health Sciences, Istanbul, Turkey

Introduction: Immature PIT-1 lineage pituitary neuroendocrine tumors (PitNETs) are rare, high-risk neoplasms recognized in the World Health Organization 2022 classification. We present a case requiring five surgeries and multimodal treatment, ultimately developing intracranial dissemination.

Case Presentation: A 40-year-old woman presented nine years ago with menstrual irregularity. Hormonal evaluation revealed hypogonadotropic hypogonadism, central hyperthyroidism (FT4: 2.30 ng/dL [N: 0.93-1.7], FT3: 8.3 pg/mL [N: 2.0-4.4], TSH: 6.53 μIU/mL [N: 0.27-4.20]), and secondary adrenal insufficiency (PRL and IGF-1 were normal). Pituitary MRI demonstrated a 43 mm sellar mass. First transsphenoidal surgery (TSS) revealed PIT-1 positivity with diffuse prolactin (PRL) immunoreactivity and focal TSH staining. Adrenal function recovered postoperatively.

Six months later, a 25 mm residual tumor prompted transcranial resection, showing PRL expression (60%) with negative TSH staining, the tumor was endocrinologically non-functioning. Five months later, tumor regrowth to 37 mm necessitated a third TSS; pathology showed PRL positivity with Ki-67 of 5%. Octreotide therapy failed to achieve tumor control.

Three years later after the third surgery, tumor progression to 55 mm with Knosp grade 4 invasion and recurrence of central hyperthyroidism were noted. Transcranial resection revealed PIT-1, GATA-3, PRL positivity with Ki-67 of 15%, consistent with immature PIT-1 lineage PitNET. Gamma Knife and cabergoline were initiated.

Three years later, while the sellar tumor regressed, a new frontal lobe mass measuring ($21 \times 23 \times 30$ mm), isointense on T1- and T2-weighted sequences, was identified. Endocrine evaluation revealed non-functioning status. Resection revealed PIT-1 positivity, patchy PRL expression, Ki-67 of 18%, and 15 mitoses per 10 high-power fields. Systemic imaging including Gallium-68 labeled DOTA-Tyr3-octreotate positron emission tomography/computed tomography excluded distant metastasis, supporting intracranial tumor dissemination. Conventional radiotherapy was administered following this fifth surgery.

One year after the final surgery, the patient remains hormonally and clinically stable with no recurrence on cabergoline 1 mg weekly maintenance therapy.

Discussion: Immature PIT-1 lineage tumors are aggressive PitNETs with complex endocrine presentations. Central hyperthyroidism, as observed in our patient, is a recognized hormonal manifestation. Despite consistent prolactin immunopositivity, hyperprolactinemia was never observed, highlighting immunohistochemical-hormonal discordance. The progressive Ki-67 increase from 5% to 18% underscores malignant potential. Repeated transcranial approaches may have contributed to dissemination via subarachnoid exposure. This case emphasizes close surveillance, multimodal treatment, and careful surgical approach selection in aggressive PitNETs.

Keywords immature PIT-1 lineage tumor, central hyperthyroidism, intracranial dissemination, aggressive pituitary tumor

Abstract citation ID: lvag096.1453

EP1204 - ECE_3109 - Evaluation of serum IL-1β levels in acromegalic patients with hepatic steatosis

Hatice Ozisik[1], Adil Bahadir[2], Tarik Inci[3], Su Ozgur[4], Sinem Aslan[3], Melih Bektas[3], Ezgi Ulas[3], Mehmet Yigit[3], Nazlican Seren[3], Erhan Canbay[3], Gaye Hamarat[3], Gökçen Ünal Kocabaş[3], Banu Sarer Yurekli[3], Nur Selvi Gunel[3] and Eser Yildirimi Sozmen[3]

[1]Endocrinology, Ege University, Izmir, Turkey; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, United States; [3]Izmir, Turkey; [4]Translational Pulmonary Research Center-EgeSAM, Ege University, Izmir, Turkey

Introduction: Acromegaly is a chronic endocrine disorder caused by excessive secretion of growth hormone (GH) and insulin-like growth factor-1 (IGF-1), and is frequently associated with metabolic complications, including hepatic steatosis. Hepatic involvement in acromegaly is considered a manifestation of metabolic syndrome and may progress to fibrosis, commonly assessed using non-invasive indices such as the Fibrosis-4 (FIB-4) score. Although chronic low-grade inflammation has been proposed as a contributing mechanism in acromegaly-related metabolic dysfunction, the role of circulating inflammatory mediators remains incompletely understood. This study aimed to

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

evaluate inflammatory markers in patients with acromegaly and controls to explore their relationship with hepatic and metabolic parameters.

Methods: A total of 90 participants were included: 48 patients with acromegaly (53.3%) and 42 healthy controls (46.7%). Demographic characteristics, hormonal and metabolic parameters, and abdominal ultrasonography findings were recorded. Serum interleukin-1 beta (IL-1β) and nuclear factor kappa B (NF-κB) levels were measured using enzyme-linked immunosorbent assay. Patients with acromegaly were additionally evaluated according to disease activity (controlled vs uncontrolled). Group comparisons were performed using non-parametric statistical methods. Correlation analyses and exploratory receiver operating characteristic (ROC) analyses were conducted.

Results: Patients with acromegaly were older than controls (median 54 vs 45 years, $P < .001$), while sex distribution was similar ($P = .343$). Markers of metabolic burden were higher in the acromegaly group, including fasting glucose ($P = .009$) and HbA1c levels ($P < .001$). The FIB-4 index was significantly elevated in patients with acromegaly (median 0.94 vs 0.63, $P < .001$), and ultrasonographic hepatic steatosis was more frequent ($P = .030$).

Serum IL-1β levels were significantly lower in patients with acromegaly compared with healthy controls (median 866 vs 2006 pg/mL, $P < .001$). NF-κB levels were also significantly lower in the acromegaly group ($P = .013$). Overall correlation analyses demonstrated weak associations between IL-1β and hepatic or hormonal parameters, which were not consistently maintained in subgroup analyses. In ROC analysis, IL-1β showed good distinctive ability for distinguishing acromegaly from controls (AUC = 0.80), whereas FIB-4 demonstrated modest performance (AUC = 0.72). The ability of FIB-4 to distinguish controlled from uncontrolled acromegaly was limited (AUC = 0.68).

Conclusion: Despite increased hepatic and metabolic burden in acromegaly, circulating inflammatory markers did not indicate classical inflammatory activation. This pattern may reflect immunomodulatory effects of chronic GH/IGF-1 excess rather than a conventional pro-inflammatory state. Given the age difference between groups, findings should be interpreted with caution. These results highlight the complexity of immune–metabolic interactions in acromegaly.

Abstract citation ID: lvag096.1454

EP1205 - ECE_2331 - Assessment of sex-specific urinary steroid changes induced by ketoconazole in Cushing's syndrome

Arturo Vega-Beyhart[1], Qiang Zhao[1], Gregori Casals[1], Marta Araujo Castro[2], Mireia Mora[1], Aida Orois[1], Cintia Santillan[1] and Felicia Alexandra Hanzu[1]
[1]*Endocrinology and Nutrition, Hospital Clínic De Barcelona, Barcelona, Spain;* [2]*Endocrinology and Nutrition, Hospital Universitario Ramón Y Cajal, Madrid, Spain*

Background: Sex differences in ketoconazole (KTZ) pharmacodynamics have been demonstrated in animal models, but not in humans. In Cushing's syndrome (CS), sex-specific effects of KTZ on urinary steroid profiles remain unexplored. This study evaluated whether intrapersonal KTZ-induced urinary steroid reductions differ by sex.

Methods: Adults (>18 years) with active CS from Hospital Clínic de Barcelona providing one adequate 24-h urine sample during untreated disease and one during KTZ maintenance (≥400 mg/day for ≥3 months) were included. Urinary free cortisol (UFC) and 34 urinary steroids were quantified using GC–MS. Absolute and percentage intrapersonal reductions (baseline – treatment) were calculated for each metabolite, and fold changes (FC) for steroid classes. Changes were compared between females and males to evaluate sex-specific effects of KTZ.

Results: 23 patients were included (12 females; 11 males). Age at inclusion was comparable (females: 44 ± 12; males: 47 ± 15 years old). KTZ doses did not differ (females: 400 [200-600] mg/day vs males: 400 [400-600] mg/day; $P = .20$). Patients achieving UFC below ULN during treatment was similar between sexes (35% in females vs 37% in males). However, a trend toward greater UFC reduction was observed in males (42% [19%-80%], 142 µg/day [6-397]) compared with females (24% [15%-51%], 22 µg/day [10-94]; $P = .13$).

Several metabolites exhibited divergent changes, increasing in females while decreasing in males. This pattern was observed for b-cortol (females: +42% [3-170] vs males: −20% [5-35]; $P = .006$), tetrahydrocortisone (females: +32% [4-165] vs males: −29% [2-60]; $P = .021$), and 5α-tetrahydrocortisol (females: +76% [13-201] vs males: −13% [−22 to 20]; $P = .021$). Moreover, several metabolites showed significantly greater reductions in males than in females, including 5α-tetrahydrocorticosterone (−35% [7-65] vs −18% [5-34]; $P = .022$), 11β-hydroxyandrosterone (−65% [33-77] vs −24% [10-60]; $P = .032$), 20β-dihydrocortisol (−43% [15-77] vs −20% [15-38]; $P = .043$), and 16α-hydroxy-DHEA (−72% [52-89] vs −5.7% [2-68]). No metabolite had significantly greater reduction in females. Finally, FC of glucocorticoid-derived compounds class differed significantly with an overall reduction in males (0.89 [0.75-1.27]) and an increase in females (1.26 [0.91-1.92]; $P = .013$).

Conclusion: Ketoconazole induces sex-specific urinary steroid responses in Cushing's syndrome, with greater glucocorticoid reductions observed in males.

Abstract citation ID: lvag096.1455

EP1207 - ECE_3847 - Pituitary adenoma with hyperprolactinemia and hyperandrogenism-associated menometrorrhagia in a 28-year-old woman: a case report

Salome Batsashvili[1], Ana Avkopashvili[2] and Maia Rekhviashvili[3]
[1]*Endocrinology, European University, Aversi Clinic, Tbilisi, Georgia;* [2]*Endocrinology, Aversi Clinic, Tbilisi, Georgia;* [3]*First Medical Clinic, Tbilisi, Georgia*

Introduction: Pituitary adenomas are a common cause of hyperprolactinemia and may lead to clinically significant reproductive dysfunction through disruption of the hypothalamic–pituitary–gonadal axis. This case highlights the interaction between pituitary and reproductive endocrine disorders and emphasizes the importance of integrated endocrine evaluation in patients with persistent menstrual dysfunction.

Case Presentation: A 28-year-old woman with a history of autoimmune thyroiditis (diagnosed at age 11) and vitiligo presented with fatigue, dyspnea, generalized weakness, dizziness, reduced exercise tolerance, and menometrorrhagia. Additional symptoms included recurrent headaches, hair loss, and hirsutism. Hematological assessment confirmed chronic iron-deficiency

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

anemia with profound ferritin depletion. Obstetric history included two pregnancies delivered via cesarean section; the patient denied a history of miscarriages. Family history was significant for thromboembolic disorders.

The patient's body mass index was within the normal range. Laboratory evaluation revealed elevated DHEA sulfate and free testosterone levels, consistent with hyperandrogenism, along with persistent hyperprolactinemia. Other hormonal investigations, including thyroid function tests, cortisol, and gonadotropins, were within normal limits. Adrenal imaging was performed as part of the hyperandrogenism workup. A vascular abnormality was detected during evaluation, and the patient was referred for angiologic assessment. Pituitary imaging was subsequently performed and confirmed a pituitary microadenoma measuring 2.8 × 2.5 mm. Notably, the patient had no prior diagnosis of pituitary pathology.

The patient was managed with a multidisciplinary approach involving endocrinology, gynecology, and hematology. Iron deficiency anemia was treated with iron replacement therapy, with monitoring of hemoglobin and ferritin levels. Given hyperprolactinemia in the setting of pituitary microadenoma, dopamine agonist therapy was initiated. Gynecologic management was planned to control ongoing menometrorrhagia and prevent recurrent iron depletion, with individualized assessment considering the patient's family history of thromboembolic disorders. Clinical follow-up with repeat hormonal assessment and surveillance pituitary imaging was arranged.

Conclusions and Perspectives: This case emphasizes that pituitary microadenoma–associated hyperprolactinemia can be the central driver of complex reproductive endocrine dysfunction in young women. When accompanied by clinically significant hyperandrogenism, marked by hirsutism, hormonal imbalance may contribute to persistent menometrorrhagia and lead to chronic iron-deficiency anemia with substantial functional impairment. Early recognition of pituitary-related endocrine disturbance and systematic evaluation of coexisting hyperandrogenic states are essential to ensure timely treatment and improve long-term outcomes through coordinated multidisciplinary care.

Abstract citation ID: lvag096.1456

EP1210 - ECE_3539 - Steroidomic profiling in women with multiple sclerosis

Radmila Kancheva[1,2], Eva Kubala Havrdová[3], Ludmila Kancheva[1], Marta Velíková[1], Josef Vcelak[4], Radek Ampapa[5], Michal Židó[6], Ivana Štětkářová[6], Jana Libertínová[7], Michala Vosátková[8] and Martin Hill[1]

[1]Institute of Endocrinology, Steroid Hormones and Proteohormones, Prague, Czech Republic; [2]Institute of Endocrinology, Prague, Czech Republic; [3]Department of Neurology, First Faculty of Medicine, Charles University, Prague, Czech Republic; [4]Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic; [5]Jihlava Hospital, MS Center, Jihlava, Czech Republic; [6]Department of Neurology 3FM CU and UHKV, Third Faculty of Medicine, Charles University, Prague, Czech Republic; [7]Second Faculty of Medicine, Charles University, MS Center, Prague, Czech Republic; [8]Clinical Biochemistry, Institute of Endocrinology, Prague, Czech Republic

Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative disease of the central nervous system that predominantly affects women of reproductive age. Steroid hormones and their metabolites exert profound immunomodulatory, neuroprotective, and neuromodulatory effects and may influence both susceptibility to MS and disease progression. However, a comprehensive and systematic characterisation of circulating steroid profiles in women with MS has been lacking. This study aimed to perform an extensive steroidomic analysis in women with MS in order to identify disease-associated alterations in steroid biosynthesis and metabolism.

Using a gas chromatography–tandem mass spectrometry platform, complemented by immunoassay for estradiol, a broad spectrum of unconjugated and conjugated steroids was quantified in serum samples from women with MS prior to disease treatment and from age-matched healthy controls. In addition to steroid concentrations, multiple molar ratios were calculated to reflect the activity of key steroidogenic enzymes and pathways, including those involved in adrenal, gonadal, and neurosteroid synthesis.

Women with MS exhibited an overall trend towards lower circulating levels of unconjugated steroids, particularly neuroprotective and immunomodulatory ones, while conjugated steroids were relatively preserved. This resulted in significantly increased ratios of conjugated to unconjugated steroids, suggesting altered steroid sulfation. Disturbances were observed along the pathway to cortisol synthesis, with evidence of impaired conversion of pregnenolone and 17-hydroxypregnenolone, alongside elevated cortisol and cortisone levels consistent with overactivation of the hypothalamic–pituitary–adrenal axis. Additionally, reduced levels of estradiol, androgens, progesterone metabolites, and key neuroactive steroids such as allopregnanolone were detected, indicating compromised neurosteroidogenesis.

Despite generally reduced steroid levels in patients compared with controls, positive correlations were found between several steroid concentrations and clinical indices of disease severity, suggesting the presence of counter-regulatory mechanisms activated during disease progression. Together, these findings demonstrate widespread alterations in the steroidome of women with MS and support a contributory role of disrupted steroid metabolism in MS pathophysiology. Steroidomic profiling may therefore provide valuable insights into disease mechanisms and hold potential for biomarker development.

Funding: This work was supported by the Czech Research Health Council (grant number NU20-04-00450) and by the Ministry of Health of the Czech Republic under the conceptual development of research organisation MH CZ DRO – Institute of Endocrinology, 00023761.

Abstract citation ID: lvag096.1457

EP1211 - ECE_3181 - Clinical and genetic aspects of growth hormone deficiency in children: the role of VDR polymorphisms

Mariana Ryznychuk[1] and Olena Bolshova[2]

[1]Bukovinian State Medical University, Chernivtsi, Ukraine; [2]SI "V.P. Komisarenko Institute of Endocrinology and Metabolism of the National Academy of Medical Sciences of Ukraine", Kyiv, Ukraine

In recent years, vitamin D (vit. D) and the vitamin D receptor gene (*VDR*) have attracted considerable scientific interest due to their involvement not only in calcium–phosphorus homeostasis but

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

also in growth regulation. Vitamin D is known to influence the differentiation of somatotroph cells in the pituitary gland, hepatic production of insulin-like growth factor 1 (IGF-1), and physiological processes of cartilage remodeling. The *VDR* gene contains several polymorphic variants, among which BsmI (rs1544410), TaqI (rs731236), and ApaI (rs7975232), located in the 3′ untranslated region, are the most extensively studied. These polymorphisms may modulate VDR expression and mRNA stability, thereby affecting the biological activity of vitamin D.

The aim of this study was to assess the effect of combined VDR gene polymorphisms (BsmI, TaqI, and ApaI) on hormonal, metabolic, and biochemical parameters in children with growth hormone deficiency (GHD).

Materials and Methods: The study included 42 children with confirmed GHD. Genotyping of *VDR* polymorphisms was performed using PCR followed by restriction fragment length polymorphism analysis and agarose gel electrophoresis.

Results: The most frequent combined genotype was the heterozygous variant (G/A + T/C + A/C), observed in 55.56% of patients, whereas the homozygous pathological genotype (A/A + C/C + A/A) was the least common (16.66%). Children carrying the pathological homozygous genotype demonstrated the lowest basal and stimulated growth hormone levels, indicating a more pronounced hormonal deficiency. Decreased serum 25(OH)D concentrations were identified in all genotype groups. Vitamin D deficiency predominated in children with the normal genotype, while insufficiency was more frequently observed in carriers of heterozygous and homozygous variants.

Correlation analysis revealed significant associations between vit. D levels and IGF-1, growth hormone, body mass index, bone age, and height standard deviation score (Ht-SDS). In children with the homozygous pathological genotype, a strong inverse relationship between IGF-1 and Ht-SDS was detected. Biochemical blood parameters, including calcium, phosphorus, creatinine, urea, and cholesterol, did not differ significantly between genotype groups and remained within normal reference ranges. Regression analysis confirmed a significant influence of bone age on IGF-1 and stimulated GH levels, as well as a close association between IGF-1 and stimulated GH.

Conclusions: Analysis of *VDR* genotypes demonstrated that the GATCAC combination was the most prevalent among children with GHD (55.56%). These findings highlight the substantial contribution of genetic factors to the pathogenesis of GHD and support the feasibility of personalized diagnostic and therapeutic approaches.

Abstract citation ID: lvag096.1458

EP1212 - ECE_1144 - The role of Epithelial Mesenchymal Transition (EMT) modulators in giant invasive Pituitary Neuroendocrine Tumors (PitNets); is there a real connection?

Gamze Akkus[1], Erdem Ince[2], Eralp Cetinalp[2], Puren Yucel[2], Merve Avluklu[3], Aslı Boz[2] and Seyda Erdogan[2]
[1]Endocrinology, Cukurova University, Adana, Turkey; [2]Cukurova University, Adana, Turkey; [3]Adana, Turkey

Backgorund: Epithelial Mesenchymal Transition is a process that changes the cell from an epithelial to mesenchymal phenotype driven by a network transcription factors. Although it is well known the role of EMT markers in other solid tumors such as ovarian, breast and small cell lung cancers. There has been a paucity in the literature regarding the possible role of EMT markers in invasive pituitary tumors

Methods: We evaluate the expression of EMT-related markers (E-CAD, N-CAD, SNAI1, SNAI2 and TWIST) in fifty invasive PitNets. To clarify relation between the expression of these markers and clinical characteristics or remission rates of PitNets is main purpose of our study.

Results: Among the 50 patients included in the study, 24 (48%) were male and 26 (52%) were female, with a mean age of 51.1 ± 14.2 years. Endocrine remission was achieved in 24 patients (48%), and tumor size was equal to or greater than 4 cm in 22 patients (44%). While 15 ($n = 30\%$) of the PitNets were as null cell adenomas, the others were as GH-secreting ($n = 11$, 22%), prolactinoma ($n = 9$, 18%) and gonadotroph adenomas ($n = 15$, 30%). GAPDH was used as an internal control for normalization of gene expression levels. Although the ΔCt values of E-CAD, N-CAD, SNAI1, and SNAI2 showed statistically significant differences among groups ($P < .001$), the relative expression levels calculated by the $2^{-\Delta\Delta Ct}$ method did not differ significantly ($P > .05$). No significant differences in gene expression were observed according to the presence or absence of endocrine remission ($P = .244$, $P = .614$, $P = .595$, $P = .573$, and $P = .808$, respectively).

Conclusion: We could not demonstrate the associations between E-CAD, N-CAD, SNAI1, SNAI2, and TWIST gene expression and clinical course or endocrine remission of giant invasive PitNets functional or nonfunctional. Further studies with large sample size may be needed for in-depth understanding this physiopathological mechanism.

Abstract citation ID: lvag096.1459

EP1213 - ECE_2256 - The telomerase/shelterin system is impaired in acromegaly and Cushing´s disease: potential pathophysiological relevance

Ignacio Gil-Duque[1,2,3], Miguel E. G-Garcia[1,2,3], Ana De La Rosa-Herencia[1,2,3], Aura D. Herrera-Martínez[2,3,4], David Cano Gonzales[5], Miguel Ángel Núñez-Santos[1,2,3], Manuel D. Gahete[1,2,3], Álvaro Flores-Martínez[1,2,3], María Ángeles Gálvez-Moreno[2,3,4], Alfonso Soto-Moreno[5], Antonio C. Fuentes-Fayos[1,2,3] and Raul M. Luque[1,2,6]
[1]Córdoba, Spain; [2]Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), Reina Sofia University Hospital, Córdoba, Spain; [3]Reina Sofía University Hospital (HURS), Córdoba, Spain; [4]Service of Endocrinology and Nutrition, Reina Sofía University Hospital (HURS), Córdoba, Spain; [5]Unidad de Gestión de Endocrinología y Nutrición, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Sevilla, Spain; [6]CIBER Pathophysiology of Obesity and Nutrition (CIBERobn), Córdoba, Spain

Pituitary Tumours (PiTs) present significant challenges in diagnosis and treatments due to their heterogeneity and complex pathophysiology and endocrine comorbidities. Current therapies (i.e., surgery, radiotherapy, and/or pharmacological treatment) frequently become ineffective over time, leading to low quality of life and recurrence rates. Therefore, identifying alternative medical tools for these rare pathologies is crucial. In this context, the alteration of the telomerase/shelterin molecular complexes

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

has been associated with cancer pathophysiology and progression; however, their role in PiTs remains poorly understood. Here, we uncovered a profound dysregulation in the expression of key components of the telomerase/shelterin systems in growth-hormone and adrenocorticotropic-hormone producing PiTs [GHomas ($n = 50$) and ACTHomas ($n = 19$), respectively] versus non-tumour pituitary tissues ($n = 10$), and identified critical dysregulated components associated with key clinical features (i.e., sinus invasion, visual alteration, cephalea, etc.). Moreover, we demonstrated that the inhibition of the telomerase activity (using BIBR1532) in primary patient´s derived cell-cultures and available cell-line models (GH3 and AtT-20) might serve as a potential therapeutic tool by reducing cell-proliferation and stem-cell capacity through the modulation of key oncogenic processes, including GH/ACTH synthesis, cell-cycle, and DNA Damage Repair (DDR) pathways. Notably, we also demonstrated that BIBR1532, in combination with somatostatin-analogues, exerted a synergic anti-proliferative effect in GH3 and AtT-20 cells. Altogether, our results demonstrate a profound and clinically relevant telomerase/shelterin-associated molecular dysregulation in GHomas and ACTHomas, which could serve as a potential source of novel diagnostic/prognostic biomarkers and therapeutic targets, offering a new avenue to improve the management of patients with these PiTs.

Abstract citation ID: lvag096.1460

EP1214 - ECE_1257 - Impact of intensive iron chelation on pituitary iron load and endocrine recovery in transfusion-dependent thalassemia major: a structured review

Ashraf Soliman, Shayma Ahmed, Mohamed Yassin, Fawziya Alyafei, Nada Alaaraj and Noor Hamed
Pediatric Endocrinology, Hamad Medical Center, Doha, Qatar

Background: Transfusion-dependent β-thalassemia major (TDT) leads to progressive iron accumulation in endocrine organs, with the anterior pituitary among the earliest affected. Pituitary iron overload contributes to hypogonadotropic hypogonadism, GH deficiency, delayed puberty, and glycemic dysregulation. Although MRI permits non-invasive assessment of pituitary iron, the reversibility of endocrine dysfunction with intensive chelation remains incompletely characterized.

Objective: To evaluate the impact of intensive iron chelation on pituitary iron burden, endocrine function, and glucose homeostasis in TDT patients, emphasizing age-related variability in recovery.

Methods: A structured review of MRI-based pituitary iron studies from 1990-2025 was conducted. Nine eligible longitudinal and cross-sectional studies (458 patients, ages 7-32 years) reporting pre- and post-chelation endocrine outcomes and pituitary T2/T2*/R2 measurements were analyzed.

Results: Across all studies, pituitary iron overload correlated strongly with impaired hypothalamic–pituitary–gonadal (HPG) and GH–IGF-1 axis function. **Noetzli et al.** demonstrated that increased R2 values predicted hypogonadism, reduced pituitary volume, and attenuated LH/FSH responses. **Christoforidis et al.** reported concurrent reductions in GH peak responses and pubertal delay in adolescents with high pituitary iron.
Endocrine Recovery: Intensive chelation—including high-dose deferoxamine, combined deferoxamine–deferiprone, or escalated deferasirox—produced measurable improvements in hormonal function:

- **Gonadotropins:** Up to **37%** of patients showed improved LH/FSH responses, and **21%** demonstrated pubertal progression following 2-3 years of intensification.
- **GH–IGF-1 axis:** Multiple studies reported increases in IGF-1 levels and improved GH secretory profiles after chelation, particularly in younger patients (<12 years), consistent with partial restoration of somatotroph activity.
- **Prolactin:** Mild PRL increases were observed in some series, suggesting recovering pituitary reserve.

Glycemic Outcomes: Intensive chelation was also associated with improved glucose metabolism:

- **Farmaki et al.** documented significant reductions in fasting glucose, improved insulin sensitivity, and decreased frequency of impaired glucose tolerance after achieving near-normal total body iron.
- Patients with high baseline pancreatic iron showed partial normalization of OGTT responses after 2-4 years of combined chelation.
- Glycemic recovery was strongly age-dependent, with younger patients experiencing greater reversibility.

Age Dependence: Across all analyses, endocrine recovery was far more pronounced in children and adolescents than adults; structural pituitary atrophy in older individuals limited full normalization.

Conclusions: Intensive iron chelation substantially reduces pituitary iron burden and can restore components of the HPG, GH–IGF-1, and glycemic regulatory axes—especially when initiated early. Early MRI surveillance and timely escalation of chelation are critical for preserving long-term endocrine and metabolic health in TDT.

Abstract citation ID: lvag096.1461

EP1215 - ECE_2009 - Hidden liver involvement in acromegaly: a non-invasive assessment of metabolic dysfunction–associated steatotic liver disease

Rosa Pitino[1], Chiara Mele[1], Martina Romanisio[1], Sara Sturnia[1], Alice Ferrero[1], Laura Veneto[2], Gianluca Aimaretti[1], Cristina Rigamonti[2], Paolo Marzullo[1], Flavia Prodam[1,3] and Marina Caputo[1,3]
[1]Endocrinology, Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy; [2]Division of Internal Medicine, Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy; [3]Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy

Background and Aim: Acromegaly is associated with multiple metabolic complications; however, its relationship with metabolic dysfunction-associated steatotic liver disease (MASLD) remains poorly defined. This study aimed to assess the prevalence and severity of MASLD and liver fibrosis in acromegalic patients and to explore their association with hormonal burden, disease characteristics, and metabolic comorbidities.

Patients and Methods: In this monocentric observational study, 26 acromegalic patients (F:M 1.6:1; median age 62 years) were

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

evaluated. Clinical data, disease duration and activity, metabolic complications, and hormonal parameters (GH, IGF-I at baseline and follow-up, and ΔIGF-1 from baseline to last follow-up) were collected. The probability of liver fibrosis was assessed using the Fibrosis-4 index (FIB-4), applying age-adjusted cut-off (>1.3 in ≤65 years and >2.0 in older ones). All patients underwent vibration-controlled transient elastography (VCTE), assessing the Controlled Attenuation Parameter (CAP) for steatosis, Liver Stiffness measurement (LSM) and Spleen Stiffness measurement (SSM). Steatosis was defined as a CAP value >248 dB/m. LSM values <10 kPa, in the absence of other clinical or imaging signs, were considered to rule out compensated advanced chronic liver disease (cACLD). SSM <21 kPa excluded clinically significant portal hypertension (CSPH), according to Baveno VII criteria.

Results: Most patients (80.8%) had undergone pituitary surgery and disease remission was achieved in 42.3% of patients at last follow-up. Among patients with active disease, 46.2% were treated with SSRLs, 3.8% with cabergoline, and 7.7% with pegvisomant. Metabolic complications were frequent, including secondary diabetes (53.8%), dyslipidemia (69.2%), and hypertension (50.0%). Median FIB-4 value was 1.34 (IQR 1.11-1.98), with 38.5% of patients exceeding age-related cut-offs. Median CAP was 244 dB/m (IQR 221-297), and steatosis diagnosed in 42.3% of patients (severe 30.8%). Median LSM was 4.4 kPa (IQR 3.7-4.9), with 23.1% of patients showing LSM between 5 and 9.9 kPa. None of the patients had cACLD. Median SSM was 19.1 kPa (IQR 15.9-27.6). MASLD was diagnosed in 38.4% of patients. Baseline IGF-I levels were correlated with CAP values ($\rho = 0.63$; $P = .002$), indicating an association between steatosis and hormonal burden.

Conclusions: MASLD is highly prevalent in acromegalic patients and should be considered among metabolic complications. The association with baseline IGF-I supports a link between chronic hormonal excess and ectopic fat accumulation.

Abstract citation ID: lvag096.1462

EP1216 - ECE_2664 - A masquerader in the sella: cavernous sinus ICA aneurysm causing panhypopituitarism

David Lopez-Lazaro[1], Shebina Liz Mathews[1], Muhammad Sohail Akhtar[1,2] and Cornelius Fernandez James[3]

[1]Diabetes & Endocrine, Pilgrim Hospital Boston(United Lincolnshire Hospitals NHS Trust), Boston, United Kingdom; [2]Diabetes & Endocrinology, Boston, United Kingdom; [3]Boston, United Kingdom

Introduction: We present a sellar lesion which was later identified to be an internal carotid artery (ICA) aneurysm. Although the pituitary function was normal at presentation, the patient developed symptomatic panhypopituitarism after four years. This highlights the importance of long-term endocrine surveillance in these patients.

Case Presentation: An 87-year-old lady presented in 2021 with headache and right 6th nerve palsy. CT head revealed a sellar/suprasellar lesion with right parasellar extension, initially suspected as a macroadenoma, but subsequent MRI Pituitary followed by CT angiography confirmed it as a bilateral cavernous sinus ICA aneurysm (right 15 × 19 mm; left 10 × 9 mm), with significant mass effect on the pituitary gland. Her pituitary profile was normal at that time (Cortisol 372 nmol/L, TSH 2.6 mIU/L, FT4 14.6 pmol/L, FSH 45.3 IU/L, IGF-1 11.4 nmol/L, prolactin 373 mIU/L). She was managed conservatively after neurosurgical input.

Repeat CT angiography in 2023 showed progression of the right ICA aneurysm (25 × 15 mm), with a relatively stable left ICA aneurysm (14 × 10 mm). In 2025, she presented with COVID-19 pneumonia and hyponatraemia (Sodium 125). Endocrine workup showed evidence of panhypopituitarism (Cortisol 47 nmol/L, ACTH <5 ng/L, TSH 0.83 mIU/L, FT4 2.9 pmol/L, IGF-1 2.1 IU/L, Prolactin 455 mIU/L). She responded well to hydrocortisone and levothyroxine replacement.

Discussion: Hypopituitarism is most commonly caused by sellar or parasellar tumours. Vascular lesions like ICA aneurysms are an important differential diagnosis of hypopituitarism, as they could mimic non-functioning pituitary macroadenomas. Early detection avoids potentially disastrous complications resulting from manipulation of such aneurysms during transsphenoidal or other pituitary operations. Cavernous segment (C4) ICA aneurysms account for only a small number (2%-9%) of all intracranial aneurysms. They account for <0.17% of all hypopituitarism cases. The hypopituitarism is usually permanent even after surgical interventions. Chronic mass effect from vascular lesions can cause delayed panhypopituitarism over the years. The mechanisms for delayed hypopituitarism include persistent mechanical compression, microvascular compromise, local inflammation and the pituitary microenvironment changes caused by the mass effect from the vascular lesion.

Conclusion: Chronic mass effect from vascular lesions can lead to delayed panhypopituitarism over the years. Lifelong endocrine follow-up is crucial for patients with any sellar mass causing anatomical displacement of the pituitary gland. Early recognition and timely neurosurgical intervention are important in preventing life-threatening endocrine crisis and neurological complications.

Abstract citation ID: lvag096.1463

EP1218 - ECE_3135 - Hyperprolactinemia in women with primary empty sella or primary partial empty sella

Bernadetta Kałuża[1,2], Mariusz Furmanek[3,4], Jan Domański[1,2], Aleksandra Żuk-Łapan[1,2], Jerzy Walecki[4,5] and Edward Franek[1,2,6]

[1]Department of Internal Medicine, Endocrinology and Diabetology, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland; [2]Department of Internal Medicine, Endocrinology and Diabetology, Medical University of Warsaw, Students Scientific Group of the Medical University of Warsaw, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland; [3]Department of Pediatric Radiology, Medical University of Warsaw, Warsaw, Poland; [4]Department of Radiology, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland; [5]Department of Radiology, National Medical Institute of the Ministry of the Interior and Administration, Centre of Postgraduate Medical Education, National Institute of Medicine of the Ministry of the Interior and Administration, Warsaw, Poland; [6]Department of Human Epigenetics, Mossakowski Medical Research Centre Polish Academy of Sciences, Warsaw, Poland

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Hyperprolactinemia is one of the most common examples of hormonal imbalance in females with empty or partial empty sella. This imbalance is associated with suppressed dopamine secretion, resulting from intrasellar structures being compressed by the suprasellar cistern. The aim of this study was to assess factors that potentially increase the risk of hyperprolactinemia in women.

Material and Methods: We conducted a prospective analysis, including pituitary magnetic resonance imaging and blood hormone level testing, in 34 women with empty or partial empty sella turcica.

Results: Hyperprolactinemia was observed in four patients (11.8%). Univariate logistic regression analysis demonstrated a significant relationship between patients' body weight (OR 0.84 [0.708-0.997]; $P = .045$) and hyperprolactinemia, with no such relationship shown by other evaluated parameters: pituitary craniocaudal diameter [mm] (OR 1.741 [0.646-4.695]; $P = .27$), pituitary anterior–posterior diameter [mm] (OR 0.637 [0.333-1.217]; $P = .172$), pituitary right–left diameter (OR 0.891 [0.666-1.193]; $P = .439$), pituitary volume [mm^3] (OR 1.001 [0.991-1.011]; $P = .828$), stalk displacement (OR 0.801 [0.765-6.175]; $P = .801$), age (OR 0.884 [0.781-1.001], $P = .05$), or body mass index (OR 0.597 [0.338-1.053]; $P = .075$).

Conclusions: Females with a lower body weight and empty or partial empty sella may be more prone to developing hyperprolactinemia and, therefore, require regular clinical and hormonal assessments.

Abstract citation ID: lvag096.1464

EP1219 - ECE_2202 - Diabetic ketoacidosis as the first manifestation of acromegaly in an 18-year-old patient: a case report

Katerina Stefanaki[1], Konstantinos Barkas[2], Stefania Magkou[3], Ioannis Boutsikos[4], Paraskevi Kazakou[4], Panagiota Zacharaki[1], Olympia Michalopoulou[4] and Stavroula A. Paschou[1]

[1]Department of Clinical Therapeutics, Endocrine Unit and Diabetes Center, National and Kapodistrian University of Athens, Alexandra Hospital, Athens, Greece; [2]Department of Neurosurgery, National and Kapodistrian University of Athens, G.H Nikea-Piraeus "St. Panteleimon", Athens, Greece; [3]Medical School, National and Kapodistrian University of Athens, Athens, Greece; [4]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Alexandra Hospital, Athens, Greece

Background: Diabetic ketoacidosis (DKA) is an endocrinological emergency defined by hyperglycemia, anion gap metabolic acidosis and ketosis, while it often constitutes the earliest presentation of diabetes mellitus (DM). Acromegaly represents a rare endocrine disease characterized by excessive production of growth hormone (GH), typically caused by a GH-secreting pituitary adenoma. This disease is most frequently diagnosed between the fourth and fifth decades of life, presenting with a wide range of manifestations, including acral enlargement, soft tissue edema, facial feature deformities, and acrochordons. DM constitutes a frequent complication of acromegaly, predominantly attributable to GH–induced insulin resistance. By contrast, diabetic ketoacidosis represents an uncommon sequela in individuals with acromegaly and coexisting T2DM.

Case Report: We present a case of an 18-year-old Caucasian man who arrived at the emergency department of our clinic with decreased level of consciousness, increased blood pressure, tachypnea (Kussmaul pattern), and tachycardia. For the past three days, the patient had experienced multiple episodes of vomiting and diarrhea without prior medical history. On physical examination, multiple abscesses were found on trunk, scapular and right axillary region, cystic acne, and skin fistulas. Admission blood tests confirmed metabolic acidosis (pH = 6.91, pCO2 = 8 mmHg, HCO3 = 3 mmol/L, Glu = 582 mg/dL, Cl = 110 mmol) with increased anion gap (30) and ketonemia [serum ketones = 6 mmol (<0.6 mmol/l)]. Although the patient was managed successfully based on the established guidelines for DKA, he failed to regain consciousness. Brain CT and MRI revealed a sizable (3.9 cm × 3.3 cm × 3.7 cm) heterogeneous mass in the posterior cranial fossa suggestive of pituitary macroadenoma. Anti-staphylococcal therapy was administered, and abscesses were surgically drained. Endocrine investigation primarily identified elevated levels of ACTH, IGF, GH, cortisol, and increased C-peptide. The patient was referred for neurosurgical management, followed by the subtotal excision of the mass. Histopathology revealed a well-differentiated neuroendocrine tumor expressing GH and ACTH. Post-operatively, the patient exhibited panhypopituitarism with diabetes insipidus and he received hydrocortisone, levothyroxine, testosterone and desmopressin. Insulin and metformin therapy were subsequently initiated for glycemic management.

Conclusions: Although DKA is a rare complication in patients with T2DM and acromegaly, the uniqueness of the present case lies in the occurrence of DKA in an 18-year-old patient with undiagnosed acromegaly, initially suspected of having T1DM. The intricate nature of this case provides a meaningful opportunity to reflect on diagnostic and therapeutic challenges.

Abstract citation ID: lvag096.1465

EP1220 - ECE_3603 - An unusal presentation of Crooke cell adenoma

Joana Vinhais[1], Beatriz R. Pereira[1], Ana Cláudia Martins[1], David Verissimo[1], Catarina Ivo[1], Mafalda Marcelino[1], Dolores Passos[1], Luis Lopes[1], Dalia Forte[2], Amets Sagarribay[2], João Jácome de Castro[1] and João Nunes Silva[1]

[1]Serviço de Endocrinologia, Hospital das Forças Armadas, Lisboa, Portugal; [2]Serviço de Neurocirurgia, ULS São José, Lisboa, Portugal

Introduction: Crooke cell adenomas (CCA) are a rare subtype of corticotroph pituitary adenomas. CCA are usually invasive macroadenomas and can present with Cushing's disease or can be clinically asymptomatic.

Case Report: A 54-years-old male without relevant past medical history was referred to our endocrinology outpatient clinic after a pituitary macroadenoma was detected on CT performed due to complaints of sinusitis. CT revealed a sellar mass with supra- and infra-sellar extension, marked enlargement of sella turcica, and bone erosion, consistent with macroadenoma. Patient denied headaches or visual changes but reported periocular oedema and tearing for four months, easy bruising and decreased libido. He denied erectile disfunction or weight change. Physical examination showed mild facial plethora,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

periocular oedema and conjunctival hyperaemia, ecchymosis of the upper limbs, and normal BMI (24.9 kg/m^2). Visual fields evaluation by confrontation were normal. Blood work showed glycemia 92 mg/dL, Na+ 144 mmol/L (136-145), K+ 5.3 mmol/L (3.5-5.5), cortisol 26.3 µg/dL (3.7-19.4), ACTH 161 pg/mL (<46), IGF-1 164 ng/mL (55-248), TSH 0.6 uUI/mL (0.350-4.940), fT4 1.27 ng/dL (0.8-1.76), total testosterone 2.4 ng/mL (2.54-8.53), LH 1.63 mUI/mL (0.57-12.07), FSH 4.6 mUI/mL (0.95-11.95), Prolactin 10.6 ng/mL (3.46-19.40).

Pituitary MRI confirmed a well-defined macroadenoma with infra-, supra- and latero-sellar extension (predominantly to the left). There was remodelling of the sellar floor, involvement of sphenoidal sinus, posterior fossa and the prepontine cistern, and compression of the optic chiasma, anterior diencephalon and third ventricle.

The patient was referred for evaluation in neurosurgery department, however, three days later he developed new-onset diplopia and headache. Ophthalmologic evaluation in the emergency department revealed left abducens nerve paresis and CT showed stability of the tumour.

Given the rapid clinical evolution, salivary and 24 h-urinary cortisol were not performed. One week later transsphenoidal surgery was performed and histological diagnosis was Crooke cell adenoma, positive for PIT 1, Chromogranin A, cytokeratin CAM 5.2, and weakly positive for ACTH with Ki-67 <3%.

Conclusion: This atypical presentation of CCA with periocular oedema and conjunctival hyperaemia, likely resulted from compression of venous structures, highlighting the invasive nature of these adenomas. Although these tumours may retain some corticotroph function, reflected by weak ACTH and chromogranin A positivity, their clinical manifestations are often dominated by mass effect rather than hormone excess.

Abstract citation ID: lvag096.1466

EP1221 - ECE_1718 - Etiology and clinical profile of patients with endogenous Cushing Syndrome: a single center experience

Shahini Winson Gnanathayalan, Manilka Sumanatilleke and Uditha Bulugahapitiya
Endocrinology and Diabetes, National Hospital of Sri Lanka, Colombo, Sri Lanka

Introduction: The clinical presentation of Cushing Syndrome (CS) is variable and non-specific in many cases. Prompt clinical suspicion is the essence not to miss the diagnosis of genuine Cushing syndrome and to avoid extensive evaluation in pseudo-Cushing states (non-neoplastic hypercortisolism).

Objective: To assess clinical characteristics of Cushing syndrome diagnosed at Endocrine department, National Hospital Sri Lanka

Methods: We performed a retrospective evaluation of 20 patients with CS, diagnosed during September 2022—March 2024.

Results: Twenty adult patients (15 females, 5 males, age 21-60 years, mean age with SD 39.6 ± 13 years) were diagnosed to have CS during this period. Seventeen cases (85%) were ACTH dependent (Cushing Disease (CD) – $n = 15$, ectopic Cushing syndrome (ECS) – $n = 2$) while 3 (15%) were ACTH independent (Adrenocortical carcinoma (ACC) – $n = 2$, primary pigmented nodular adrenal disease – $n = 1$). Pituitary macroadenoma was seen in 40% of CD cases. The cases of ECS were secondary to thymic-carcinoid tumor and olfactory-neuroblastoma.

The most common presenting complaints in CD were abdominal obesity with weight gain followed by a new onset or worsening of diabetes mellitus or hypertension. One young male was diagnosed to have CD when he was evaluated for fragility fracture of hip. Persistent severe symptomatic hypokalemia was the first clue to evaluate toward the possibility of CS in both patients with ECS. Among cases of ACC, one presented with generalized monomorphic acne and the other one had adrenal incidentaloma. Typical cushingoid appearance was present in all patients with CD but absent in both patients with ECS and in one patient with ACC. At least one clinical feature with the highest discriminatory value (facial plethora – 35%, easy bruising- 35%, thin skin – 45%, proximal muscle weakness – 60%, wide purple striae – 50%) was present in 90% of the patients. Other features supporting the diagnosis were acne (26%), hyperpigmentation (30%), hirsutism and menstrual irregularities.

Conclusion: The possibility of CS should be considered in patients with unexplained hypokalemia even in the absence of cushingoid features. Proper examination for the presence of highly discriminatory clinical features is helpful to know the pretest probability of CS.

Abstract citation ID: lvag096.1467

EP1222 - ECE_2023 - Multifocal paraganglioma in Von Hippel-Lindau syndrome: a diagnostic conundrum unfolded through multimodal investigation

Maimoona Nawaz, Rachel Brindle, Waseem Majeed and Adhithya Sankar
Manchester, United Kingdom

Introduction: We present a diagnostically complex case of multifocal phaeochromocytoma and paraganglioma (PPGL), initially suggestive of metastatic disease. Further evaluation revealed a unifying diagnosis of Von Hippel-Lindau (VHL) syndrome.

Case Presentation: A 42-year-old female with no personal or family history of PPGL presented with flank pain and urinary symptoms. CT imaging revealed a 4.3 cm atypical right adrenal lesion. Endocrinology review noted episodic hypertension, sweating, and palpitations. Biochemistry showed elevated plasma normetadrenaline (5.51 nmol/L) and metadrenaline (0.34 nmol/L). Alpha blockade with doxazosin was initiated.

Functional imaging (MIBG, FDG PET, somatostatin receptor scintigraphy) confirmed pheochromocytoma. Additional lesions included a 1 cm left para-aortic mass, a non-avid left adrenal nodule (likely adenoma), and a right retrothyroidal neck lesion—all showing uptake on functional imaging. Thyroid ultrasound revealed a U5 lesion, raising concern for metastatic PPGL.

Cytology of the neck lesion confirmed a head and neck paraganglioma. Further imaging identified benign liver haemangioma and bilateral renal parapelvic cysts, prompting genetic testing. Genetic analysis revealed a heterozygous pathogenic VHL mutation: NM_000551.3:c.250G>A; p.(Val84Met), confirming the diagnosis of VHL syndrome. A heterozygous pathogenic VHL mutation was found, making multifocal PPGL more likely. However, the distribution of neuroendocrine lesions was still concerning for metastatic PPGL. Patient underwent uncomplicated laparoscopic right

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

adrenalectomy. Histology confirmed pheochromocytoma with classic Zellballen architecture, chromogranin and synaptophysin positivity, and a low Ki-67 index (<2%), consistent with benign behaviour. Persistently elevated normetanephrines led to excision of the left para-aortic lesion, with histology confirming paraganglioma and biochemical normalization. Surveillance imaging remains unremarkable, excluding metastatic disease.

Discussion: VHL syndrome is a rare autosomal dominant disorder associated with multifocal neuroendocrine tumours. Though sporadic VHL mutations are rare, clinical awareness can aid diagnosis. PPGL in VHL mostly presents as benign multifocal disease but in rare cases can be metastatic.

Abstract citation ID: lvag096.1468

EP1223 - ECE_2110 - An endocrine double act: a double-edged neuroendocrine tumour—insulinoma with ectopic ACTH secretion

Theingi Zaw[1] and Aye Nyunt[2,3]
[1]Diabetes and Endocrine Department, Glan Clwyd Hospital, Rhyl, United Kingdom; [2]Diabetes and Endocrinology, Rhyl LL18 5UJ, United Kingdom; [3]Endocrinology, Glan Clwyd Hospital, Rhyl, United Kingdom

Introduction: The global incidence of neuroendocrine tumours (NETs) is increasing. Among these, pancreatic neuroendocrine tumours (pNETs) are one of the most common subtypes, with an estimated incidence of approximately 1 per 100 000 population.[1] Insulinomas, although rare, are the most common functional pNETs, with an annual incidence of 1-4 cases per million.[2] We describe a unique case of a previously diagnosed metastatic insulinoma that later developed ectopic ACTH secretion, highlighting the dynamic hormonal behaviour and heterogeneity of NETs.

Case: A 58-year-old man was diagnosed in 2021 with a non-resectable, metastatic, well-differentiated grade 1 pancreatic NET with liver metastases, functioning as an insulinoma. He received four cycles of peptide receptor radionuclide therapy (PRRT), followed by lanreotide and Everolimus due to disease progression.

In early 2024, approximately 4 months prior to hospital admission, he developed bilateral legs oedema accompanied by an unexpected improvement in hypoglycaemic symptoms. He subsequently presented with persistent hypokalaemia, hypocalcaemia and acute psychosis, complicated by type 1 respiratory failure secondary to resistant to intravenous correction of electrolytes requiring intensive care unit admission.

Biochemical evaluation revealed severe hypokalaemia with severe metabolic alkalosis. These findings raised suspicion for hypercortisolism as the underlying cause of the electrolyte disturbance.

Serum cortisol was profoundly elevated at 2951 nmol/L, with a concomitantly high ACTH level of 389 ng/L. CT imaging of the head demonstrated a normal pituitary gland. Additional findings showed markedly elevated calcitonin level of 9290 ng/L.

Given the background of metastatic pancreatic NET and the absence of pituitary pathology, the unsuppressed ACTH secretion was most consistent with ectopic ACTH production. The patient was commenced on metyrapone following multidisciplinary discussion with the NET team. This resulted in significant improvement in hypokalaemia and neuropsychiatric symptoms, allowing successful discharge. He is currently maintained on a block-and-replace regimen with metyrapone and hydrocortisone.

Discussion: The majority of pancreatic NETs produce a single hormone and present with a corresponding hormonal syndrome. However, a minority of tumours may develop secondary hormone secretion at a later stage. Emerging evidence suggests that NETs may demonstrate hormonal plasticity, with the potential to alter or acquire new hormone-secreting profiles as the disease progresses.[3]

This case underscores the importance of recognising the heterogeneity of neuroendocrine tumours and maintaining a high index of suspicion for new or evolving hormonal syndromes, particularly in the context of disease progression. Hormonal co-secretion or phenotypic switching can occur at any stage. It is significantly associated with increased mortality.

Abstract citation ID: lvag096.1469

EP1224 - ECE_3614 - Everolimus in lung neuroendocrine tumors: statin-associated myopathy risk and potential PFS benefit of concomitant lipid-lowering therapy

Maurizio Martiradonna, Flaminia Russo, Virginia Zamponi, Rossella Mazzilli and Antongiulio Faggiano
Endocrinology Unit, Department of Clinical and Molecular Medicine, Sant'Andrea Hospital, ENETS Center of Excellence, Sapienza University of Rome, Rome, Italy

Everolimus, an oral mTOR inhibitor approved for progressive lung neuroendocrine tumors (RADIANT-4), frequently induces metabolic effects such as hyperglycaemia and dyslipidaemia. In transplant medicine, coadministration of statins with mTOR and/or calcineurin inhibitors is known to increase the risk of statin-associated muscle toxicity due to pharmacokinetic interactions involving CYP3A4, P-glycoprotein and hepatic OATP1B1, which raise systemic statin exposure. However, evidence in oncology is scarce.

We report preliminary data from a retrospective study of patients with lung neuroendocrine tumors (NET) on chronic statin therapy who started antitumor everolimus therapy. Five patients have been included: four treated with everolimus at standard dose of 10 mg daily, who were receiving rosuvastatin 10 mg (n.3) and atorvastatin 40 mg (n.1), and one treated with low-dose everolimus 5 mg daily who was receiving rosuvastatin 5 mg. Among the four patients on standard doses, all had normal baseline CK (median 85 U/L; range 77-123; ULN 168). CK elevations occurred in all patients within 1-3 months. Two exceeded clinically relevant thresholds: one on rosuvastatin increased from 123 to 730 U/L at 1 month (4.3× ULN); one on atorvastatin rose from 110 to 311 U/L at 3 months (1.9× ULN) and, after dose escalation to 80 mg for LDL control, reached 903 U/L at 6 months (5.4× ULN). The remaining two patients showed milder increases (<4× ULN: 77→234 U/L and 85→217 U/L) and were prophylactically switched to non-statin lipid-lowering agents (ezetimibe, bempedoic acid). Notably, the fifth patient on low doses maintained CK within normal limits, suggesting a possible dose-dependent interaction. In addition, progression-free survival (PFS) was compared in 10 patients with lung NET treated with everolimus, divided according to concomitant use of lipid-lowering therapy (statin or non-statin; $n = 5$) versus no lipid-lowering therapy ($n = 5$). Median PFS was higher in the lipid-lowering therapy group (12 months) than in the no lipid-lowering therapy group (6 months), with a statistically significant difference ($P = .03$).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Although limited by small numbers, these preliminary findings suggest that everolimus may potentiate statin-associated myopathy in lung NET patients, complicating dyslipidaemia management. At the same time, lipid-lowering therapy in patients with lung NET treated with everolimus appears to be associated with superior PFS, suggesting a possible favourable role in oncological outcomes.

Abstract citation ID: lvag096.1470

EP1225 - ECE_1606 - Early-stage Cushing's disease in adolescence revealed by progressive loss of circadian ACTH and cortisol regulation

Data Kekutia[1,2], Shota Janjgava[1,3] and Elen Giorgadze[1,3]
[1]National Institute of Endocrinology, Tbilisi, Georgia; [2]Tbilisi State University, Tbilisi, Georgia; [3]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

Introduction: Cushing's disease is relatively rare in adolescence and often presents with slowly progressive and subtle changes in biochemical parameters. Interestingly, there is not always marked hypercorticism or convincing imaging findings in the early stages of the disease.

Case Presentation: A 16-year-old boy presented with progressive fatigue, headache, insomnia (with inversion of the sleep-wake cycle), mood swings, constipation, dry skin, mild weight gain, and purple striae on the shoulders. There was a history of childhood inflammatory disease of the spinal cord, during which systemic glucocorticoid therapy was administered. Mild signs of Cushingoid physiology were detected, without significant growth retardation.

Investigations: Hormonal studies demonstrated a disruption of the circadian rhythm of the hypothalamic-pituitary-adrenal axis, as manifested by a disproportionately elevated nocturnal level of adrenocorticotropic hormone (ACTH) (~35 pg/mL; reference: <19 pg/mL) and significant nocturnal secretion of cortisol. The presence of endogenous hypercorticism was confirmed by an elevated level of free cortisol in 24-hour urine, determined by the LC-MS/MS method (~103 μg/24 h; normal: 11-70). Serial laboratory studies over a year showed a progressive increase in ACTH levels from the upper limit of normal to a markedly elevated morning level (~84 pg/mL), with suppression of the nocturnal level, accompanied by loss of diurnal variation in cortisol and elevated cortisol levels. These changes were accompanied by mild but persistent hyperprolactinemia and hypergonadotropinemia (LH and FSH), suggesting multihormonal hypersecretion of the pituitary gland. Electrolytes were within normal limits. Abdominal imaging showed normal adrenal anatomy without focal lesions, ruling out adrenal-dependent Cushing's syndrome. High-resolution magnetic resonance imaging of the pituitary gland with dynamic contrast revealed heterogeneous hypersecretion of the adenohypophysis and a small hypovascular lesion measuring 1.5 mm in the left lobe, suggesting a microadenoma, although the reliability of the result was limited due to motion artifact.

Management and Follow-up: The patient underwent detailed endocrinological monitoring and pharmacological therapy. Dynamic changes in biochemical data allowed the diagnosis of pituitary-induced ACTH-dependent Cushing's syndrome, which is consistent with Cushing's disease.

Conclusion: The present case demonstrates that Cushing's disease in childhood can occur against the background of initially normal cortisol levels, with progressive disruption of circadian rhythms and increased ACTH. This emphasizes the need for cyclical hormonal analysis, the most accurate assessment of urinary cortisol, and detailed pituitary examination to differentiate Cushing's disease from pseudo-Cushing's conditions.

Abstract citation ID: lvag096.1471

EP1227 - ECE_2032 - Clinical characteristics and therapeutic outcomes of patients with acromegaly in Alexandria—Egypt: a retrospective study

Ahmed Abdelhameed Osman[1], Eman Zaky Ahmed Abdelaziz Azzam[1], Mahmoud Aly Abbassy[2] and Asmaa Abdelsalam Elsherbiny[1]
[1]Endocrinology Unit, Department of Internal Medicine, Alexandria Faculty of Medicine, Alexandria, Egypt; [2]Faculty of Medicine, Department of neurosurgery, Alexandria University, Alexandria, Egypt

Introduction: Acromegaly, though a rare disease is a debilitating disease with variable outcomes when it comes to different therapeutic modalities. We conducted a retrospective study of 22 patients with acromegaly attending Endocrinology outpatient clinic at the Alexandria main university hospital with the aim of characterizing different clinical presentations, therapeutic modalities and outcome.

Results: The study population had a mean age of 35 years at the time of diagnosis, with a slight male predominance (54.5%). The most common primary presentations were headache (68.2%) and acral enlargement (63.6%). Significant comorbidities included hypertension (45.5%), obstructive sleep apnea (45.5%), and hyperprolactinemia (40.9%). Patients needed a mean of 2.91 doctors to establish the diagnosis of acromegaly. Most patients (95.5%) underwent transsphenoidal surgery (TSS) as a primary treatment.

Following treatment, there was a significant reduction in median GH levels from 17.25 ng/mL at baseline to 2.26 ng/mL at 6 months ($P < 0.001$). Similarly, IGF-1 levels decreased from a median of 691.0 ng/mL to 276.0 ng/mL over the same period ($P < .001$). MRI findings showed a significant reduction in mean lesion size from 3.01 cm at baseline to 2.20 cm at 6 months ($P < .001$). By the end of the study, 22.7% of patients were considered cured, while 77.3% remained ongoing treatment.

Conclusion: Therapeutic interventions, primarily surgical, significantly improved biochemical markers (GH and IGF-1) and reduced tumor size in this study. However, a high percentage of patients required multi-modal second and third-line therapies to manage residual disease. The findings emphasize the need for early diagnosis and a comprehensive, long-term management strategy to address persistent comorbidities and improve clinical outcomes for acromegalic patients.

Abstract citation ID: lvag096.1472

EP1228 - ECE_3748 - Tamoxifen in combination with low dose pasireotide improves both acromegaly control and glucose metabolism

Klaus Badenhoop and Jürgen Reusch
Endocrinology, Deutsches Endokrinologisches Versorgungszentrum, DEVZ, Frankfurt/Main, Germany

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

A now 70-year old female patient was diagnosed with acromegaly due to a STH secretinng macroadenoma in 2002. Neurosurgical removal did not correct STH hypersecretion and led to partial hypopituitarism. The patient was not amenable to further operation nor to radiotherapy. Conservative management was undertaken with pegvisomant which normalised IGF-1 levels, while hydrocortisone and L-thyroxine were supplemented for adequate adrenal and thyroid function. Since the patient was reluctant to inject pegvisomant daily for further long periods of her life she was offered monthly treatment with pasireotide. This new treatment was partially successful for reducing but not normalising IGF-1. However the patient developed type 2 diabetes mellitus (HbA1C 7.8%) under the dose of pasireotide 40 mg/month. After consulting another endocrinologist she was offered treatment with tamoxifen as an off-label drug. The tamoxifen dose was started with 20 mg/d. The combination with pasireotide gradually reduced IGF-1, allowing a dose reduction of pasireotide after IGF-1 had normalised. Due to vertigo attacks and falls the tamoxifen dose had to be reduced to 10 mg/d. Under this daily dose the patient is now without vertigo. Pasireotide (10 mg) is injected at bimonthly intervals with normalised IGF-1. Diabetes control is optimal with a last HbA1C of 6.3% under metformin 500 mg twice daily.

The case illustrates the potential of tamoxifen adjunct therapy in treatment resistant acromegaly. An individualised combination regimen lowers untoward side effects of pasireotide while safeguarding endocrine stability

Abstract citation ID: lvag096.1473

EP1229 - ECE_3684 - Sex-related differences in Cushing's syndrome: a single-center cohort study

Elena Sofia Blanca[1], Giordana Siracusano[1], Carla Paola Costa[1], Ylenia Alessi[2], Angela Alibrandi[3], Salvatore Cannavò[4] and Francesco Ferraù[4]
[1]Endocrine Unit, University Hospital of Messina, Messina, Italy; [2]Department of Biomedical, Dental and Morphological and Functional Imaging Sciences, University of Messina, Messina, Italy; [3]Sant'Agata di Militello (ME), Italy; [4]Department of Human Pathology of Adulthood and Childhood, University of Messina, Messina, Italy

Introduction: Cushing's syndrome (CS) is a rare, debilitating endocrine disorder caused by chronic glucocorticoid excess, predominantly affecting women, leading to multisystem morbidity. Evidence highlights sexual dimorphism in tumor behavior and genetic background, possibly influencing disease onset, severity and outcomes. Nevertheless, the influence of gender on clinical presentation and prognosis remains debated. This study investigated, within a single-center cohort, sex-related differences in phenotypic, anthropometric, clinical-biochemical features, at diagnosis (D) and at last follow-up in patients undergone remission (R).

Methods: Seventy-nine patients with CS (55 females; mean age 39.41 ± 15.7 years; female-to-male ratio 2.3:1) were followed for 71.1 ± 6.7 months. Data collected included clinical features, anthropometrics, biochemical parameters (urinary free cortisol [UFC, expressed as multiples of the upper limit of normal, ULN], serum cortisol after a 1-mg overnight dexamethasone suppression test [DST], serum midnight cortisol (μg/dl), adrenocorticotropic hormone [ACTH], glucose levels, HbA1c, electrolytes, IGF-1 (standard deviation score)), comorbidities (hypertension, diabetes mellitus [DM], dyslipidemia, osteopenia/osteoporosis, vertebral fractures [VF], psychiatric disorders, cardiovascular [CV] events, central hypothyroidism/hypogonadism, growth hormone [GH] deficiency). Data were stratified and compared by gender.

Results: In the group of patients evaluated at D, 61 patients had Cushing's disease (CD), 12 adrenal adenomas, and 6 ectopic CS. Males more frequently presented diabetes (40% vs12.7%, $P = .009$) and CV events (22.2% vs 2.3%, $P = .010$). Central hypothyroidism was more common in women (18.0% vs 0.0%, $P = .037$), while easy bruising showed a trend toward female predominance (85.7% vs 40.0%, $P = .059$). Remission was achieved more frequently in women (94.5% vs 75.0%, $P = .033$).

In R group, men showed more frequently proximal myopathy (14.3% vs 0.0%, $P = .024$), diabetes, dyslipidemia, and cardiovascular events (42.9% vs 11.8%, $P = .016$; 85.7% vs 33.3%, $P = .001$; 15.4% vs 0.0%, $P = .044$, respectively).

In the comparison between group D and R, BMI ($P = .01$), waist circumference ($P = .063$) and moon facies ($P = .031$) improved in men. Conversely, women showed significant reductions in BMI ($P = .015$), waist circumference ($P = .011$) and HbA1c ($P = .005$).

Conclusion: This study highlights significant sex-related differences in Cushing's syndrome. Men presented with more severe features, including higher rates of diabetes, and cardiovascular complications, while women had a greater prevalence of central hypothyroidism. At last follow-up, women experienced higher remission rates, both genders showed improvements in anthropometric parameters, with women also demonstrating reductions in glycated hemoglobin, whereas men faced increased risks of myopathy and cardiometabolic issues. Recognizing sex-specific patterns can improve diagnostic accuracy and support personalized management.

Abstract citation ID: lvag096.1474

EP1230 - ECE_1244 - Pituitary stalk interruption syndrome (case report)

Maria Chrysoula Tatarida Palla, Marika Kokkorou, Andreas Bampilis, Galateia Stathori, Michalis Magklis, Myrsini Chamakioti, Agapi Karkampouna, Mina Koutrouli, Eleni Papanikolaou and George Chrousos
Endocrine Unit, National and Kapodistrian University of Athens, Athens, Greece

Background: Pituitary Stalk interruption syndrome (PSIS) is a rare congenital disorder defined by the MRI triad of a thinned or absent pituitary stalk, underdevelopment of the anterior pituitary gland, and an ectopic or non-visualized posterior pituitary. Clinical presentation varies, and although most cases manifest in early childhood, later onset of pituitary hormone deficiencies has been described.

Case Presentation: A 35-year-old male presented with long-standing fatigue. His medical history was notable for late-onset pituitary insufficiency diagnosed at age 10. Prior to that time, growth and developmental milestones were normal. Shortly after a tonsillectomy, he developed high fever (up to 40 °C), followed by a comatose state that required hospitalization. Endocrine evaluation revealed combined anterior pituitary hormone deficiencies, and replacement therapy with hydrocortisone, levothyroxine, and testosterone was initiated. At age 14, growth hormone (GH) therapy was added and continued for six years, resulting in attainment of mid-parental target height.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

MRI of the sellar region demonstrated a hypoplastic anterior pituitary gland, a thin and right-displaced pituitary stalk, and an ectopic posterior pituitary located beneath the hypothalamus—findings characteristic of pituitary stalk interruption syndrome.

Recent laboratory assessment reconfirmed combined anterior pituitary hormone deficiencies, including growth hormone (GH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), adrenocorticotropic hormone (ACTH), and thyroid-stimulating hormone (TSH). Hyperprolactinemia was also identified, consistent with reduced hypothalamic dopaminergic inhibition. Posterior pituitary function has remained intact. Bone mineral density testing revealed osteopenia.

The patient had experienced inadequate symptom control on conventional doses of hydrocortisone, prompting transition to modified-release hydrocortisone (Efmody®), which resulted in improved biochemical stability. GH therapy was also reinitiated after a period of discontinuation by patient preference. Following these adjustments, the patient demonstrated marked improvement in clinical symptoms as well as overall quality of life.

Conclusion: This case highlights a rare presentation of late-onset congenital hypopituitarism due to PSIS, underscoring the need for clinical vigilance in children with acute decompensation after physiological stress and the importance of long-term endocrine follow-up into adulthood. Efmody replacement contributed to improved sense of wellbeing.

Abstract citation ID: lvag096.1475

EP1231 - ECE_2301 - High stress on the frontline: psychological impact and HPA axis changes in intensive care unit workers during COVID-19

Emre Durcan[1], Serdar Sahin[1], Hande Mefkure Ozkaya[1], Senol Turan[2], Oktay Demirkıran[3], Dildar Konukoglu[4], Fahrettin Kelestimur[5] and Mustafa Sait Gonen[1]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Cerrahpaşa Faculty of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Turkey; [2]Department of Psychiatry, Cerrahpaşa Faculty of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Turkey; [3]Department of Anesthesiology and Resuscitation, Cerrahpaşa Faculty of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Turkey; [4]Department of Medical Biochemistry, Cerrahpaşa Faculty of Medicine, Istanbul University-Cerrahpaşa, Istanbul, Turkey; [5]Department of Endocrinology, Yeditepe University, Medical School, Istanbul, Turkey, Istanbul, Turkey

Objective: During the COVID-19 pandemic, healthcare workers faced intense psychological stressors, including increased workload, fear of transmitting the virus to family members, and social isolation. These stressors were especially pronounced among intensive care unit (ICU) workers due to continuous close contact with infected patients, potentially affecting the hypothalamic–pituitary–adrenal (HPA) axis. This study aimed to evaluate the psychological impact of pandemic-related stress and associated HPA axis changes among ICU workers.

Materials and Methods: This prospective, single-center study included ICU healthcare workers caring for COVID-19 patients, ICU workers with no contact with COVID-19 patients, and healthy controls. Sociodemographic characteristics, job position, working hours, and ICU experience were recorded. Psychological status was assessed using the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and PTSD Checklist-5 (PCL-5). Vital signs were measured, and morning blood samples were collected for pituitary hormone analysis. A 1-μg low-dose ACTH stimulation test was performed in all participants.

Results: A total of 106 participants were included: 43 COVID ICU workers, 35 non-COVID ICU workers, and 28 healthy controls. Groups were comparable regarding COVID-19 exposure risk, ICU working hours, and prior ICU experience. COVID ICU workers had a higher pulse rate than non-COVID ICU workers, while blood pressure was similar. Total psychological scale scores showed no significant differences between ICU workers caring for COVID-19 patients and those who did not. However, based on the PCL-5 cutoff, PTSD prevalence was higher among COVID ICU workers (51.7% vs 24%, $P = .035$), whereas depression and anxiety prevalence did not differ by BDI or BAI cutoffs. Basal and peak cortisol levels following ACTH stimulation were similar across groups. Using the minimum peak cortisol level of healthy controls as reference, adrenal insufficiency was more frequent in COVID ICU workers than in non-COVID ICU workers (14% vs 2.9%, $P = .038$). Morning cortisol was never below 3 μg/dL but fell below 5 μg/dL in two COVID ICU workers with inadequate ACTH responses. Psychological scale scores did not differ between participants with and without adrenal insufficiency.

Conclusion: ICU healthcare workers caring for COVID-19 patients had a higher prevalence of PTSD and adrenal insufficiency compared with non-COVID ICU workers, despite similar depression, anxiety, and cortisol responses. These findings indicate that prolonged pandemic-related stress may contribute to both psychological vulnerability and subtle HPA axis dysfunction. Regular psychological screening and endocrine monitoring may help identify at-risk ICU workers during extended public health crises.

Abstract citation ID: lvag096.1476

EP1232 - ECE_2342 - Clinical characteristics and outcomes of endoscopic treatment of pituitary adenomas with Pit-1 and SF-1 coexpression

Barbara Buchalska[1], Maria Maksymowicz[2], Mateusz Bujko[3], Julia Rymuza[3] and Jacek Kunicki[1]

[1]Department of Neurosurgery, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [2]Warsaw, Poland; [3]Department of Molecular and Translational Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Background: Pituitary adenomas arise from three lineages of cells expressing different transcription factors: Pit-1 (somatotroph, lactotroph, thyrotroph, mixed), TPIT (corticotroph), and SF-1 (gonadotroph). Typically, pituitary adenomas express only one of these transcription factors; however, in some cases, tumor cells show expression of several. Coexpression of Pit-1 and SF-1 is particularly common in densely granulated somatotroph adenomas.

Purpose: The aim of this study was to describe the outcomes of endoscopic treatment of pituitary adenomas with Pit-1 and SF-1 coexpression.

Methodology: This was a retrospective analysis of 26 patients (15 women and 11 men) treated between 2020 and 2024 with endoscopic transsphenoidal resections for pituitary adenomas showing Pit-1 and SF-1 coexpression. The mean age of patients was 53 years (range 26-79), and the mean follow-up was 2.4 years.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: The main clinical manifestation was acromegaly ($n = 25$; 96.2%). Five patients had visual disturbances (19.2%), and one patient presented with headaches (4.4%). Most patients had macroadenomas ($n = 23$; 88.5%), with an average size of 16 mm. According to the Knosp classification, 3 patients (11.5%) had grade 3 adenomas and 2 patients (7.7%) had grade 4 adenomas. Gross total resection was achieved in most cases ($n = 24$; 92.3%). Immunohistochemistry confirmed positive staining for growth hormone in all patients, for α-subunit in 23 patients, for prolactin in 16, for luteinizing hormone in 6, and for follicle-stimulating hormone in 1. Remission of acromegaly was achieved in 93.8% of patients.

Conclusion: The main clinical manifestation in patients with pituitary adenomas showing Pit-1 and SF-1 coexpression is acromegaly, which can be effectively treated with endoscopic transsphenoidal resection. This method is safe and associated with a low risk of complications.

Abstract citation ID: lvag096.1477

EP1234 - ECE_1063 - A rare case of autoimmune infundibulo-hypophysitis and arginine vasopressin deficiency following mild traumatic brain injuries

Tamar Kvaratskhelia
New Vision University, New Vision Univeristy Hospital, Internal, Tbilisi, Georgia

Introduction: Infundibulo-hypophysitis is a rare condition, and its pathogenesis in the setting of mild head trauma is seldom described. Traumatic brain injury (TBI) is increasingly recognized to cause hypopituitarism, even many years post-injury. Fatih Tanriverdi et al. demonstrated antipituitary antibodies (APAs) in 44.8% of patients three years after TBI, with a significantly higher rate of pituitary dysfunction in APA-positive patients compared with APA-negative patients (46.2% vs 12.5%) (2). These findings suggest that autoimmune mechanisms may contribute to post-traumatic pituitary injury rather than mechanical or ischemic damage alone.

Case Presentation: This report describes a rare case of a 16-year-old female who developed polyuria, polydipsia (>8 L/day), nocturia, headache, and a 7 kg weight loss. Her medical history was notable for a mild TBI (concussion) at age 8 and a recent mild TBI (concussion) while skating, occurring three months prior to symptom onset; both events were managed on an outpatient basis. Initial laboratory evaluation revealed hypernatremia, elevated plasma osmolality, inappropriately low urine osmolality, low copeptin, and low morning cortisol, consistent with arginine vasopressin deficiency and possible secondary hypocortisolism. Anterior pituitary hormones were otherwise within normal limits. MRI findings were consistent with infundibulo-neurohypophysitis, suggestive of autoimmune etiology.

Follow-Up: The patient was started on desmopressin (10 µg/day) and prednisolone (40 mg/day). At 3.5-month follow-up, she reported reduced polyuria and polydipsia (~3 L/day), weight gain of 3 kg, and improved energy and mood. Laboratory parameters, including anterior pituitary functional tests, were within normal limits. Prednisolone was tapered and discontinued gradually. Serial MRI demonstrated positive radiologic changes, with reduction of pituitary and infundibulum hypertrophy following three months of glucocorticoid therapy.

Conclusion: This case highlights a rare instance of autoimmune infundibulo-hypophysitis with arginine vasopressin deficiency following childhood TBI, with clinical exacerbation after a recent TBI. It underscores the importance of considering autoimmune mechanisms in post-traumatic pituitary dysfunction and the need for early diagnosis, appropriate therapy, and longitudinal hormonal and radiologic monitoring.

Keywords autoimmune infundibulo-hypophysitis, traumatic brain injury, arginine vasopressin deficiency

Abstract citation ID: lvag096.1478

EP1235 - ECE_1389 - Uncontrolled diabetes mellitus revealing underlying acromegaly

Mirjana Bojic[1], Anja Stanic[1], Tamara Dojcinovic[1,2], Ivona Risovic[1,2] and Aleksandra Markovic[1,2]
[1]*University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina;* [2]*Faculty of Medicine, University of Banja Luka, Banja Luka, Bosnia and Herzegovina*

Acromegaly most often occurs as a result of somatotropic cell adenoma, with hypersecretion of growth hormone. Elevated GH levels stimulate increased hepatic production of insulin-like growth factor 1 (IGF-1). The clinical manifestations of GH and IGF-1 hypersecretion are numerous and often slowly develop over time. Growth hormone, unlike other hormones of the adenohypophysis, has effect on all organs and tissues. In addition, GH has a pronounced diabetogenic effect: it increases blood glucose levels, reduces peripheral glucose uptake, and stimulates insulin secretion, ultimately contributing to the development of diabetes mellitus.

We present the case of a 48-year-old patient who was hospitalized due to unsatisfactory glycoregulation. The diagnosis of type 2 diabetes was established in 2016. Due to the clinically visible acromegaloid habitus, an extensive endocrinological evaluation was performed, and it revealed elevated basal values of IGF1 (1225 ng/mL) with a paradoxical GH rise in the oral glucose load test (OGTT). No abnormalities were detected in the lactotrophic or thyrotrophic axes, while hypogonadotropic hypogonadism was present. Pituitary MRI confirmed a 16-mm pituitary macroadenoma with extension into the cavernous sinus. Neurosurgical consultation was obtained, and surgical treatment via a transsphenoidal approach was indicated. During hospitalization, optimization of the therapeutic regimen resulted in satisfactory glycemic control, achieved with a long-acting insulin analog in combination with metformin, a DPP-4 inhibitor, and dietary measures for diabetes. Follow up after operation revealed residual and still active tumor, so long acting somatostatin analogue was introduced in 4-week intervals leading to better disease control.

Diabetes, as a complication of acromegaly, occurs in about 30% of patients and has a significant impact on the prognosis of the disease. Patients with overt diabetes have a 60% higher overall mortality and twice the risk of cardiovascular mortality compared to those without diabetes. The goal of treatment is to stop the hypersecretion of GH and IGF-1, stop tumor growth, remove comorbidities and preserve pituitary gland function, thereby reducing the risk of disease complications.

Keywords acromegaly, diabetes mellitus, hyperglycemia

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1479

EP1236 - ECE_2710 - Ectopic ACTH syndrome associated with Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia (DIPNECH): the first reported case in Asia

Wei-Lin Huang and Chia-Hung Lin
Department of internal medicine, Division of metabolism and endocrinology, National Taiwan University Hospital, Taipei City, Taiwan

Introduction: Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare preinvasive pulmonary condition characterized by diffuse proliferation of pulmonary neuroendocrine cells, with or without associated tumorlets. Owing to neuroendocrine cell-mediated constrictive bronchiolitis, DIPNECH is frequently misdiagnosed as adult-onset asthma. Although DIPNECH is a known precursor of pulmonary neuroendocrine tumors, its presentation as ectopic adrenocorticotropic hormone (ACTH) syndrome (EAS) is extremely rare, particularly in Asian populations. We report a case of EAS associated with DIPNECH in an Asian woman with long-standing asthma-like symptoms.

Case Presentation: A 62-year-old woman presented with a 5-month history of progressive proximal muscle weakness, Cushingoid appearance, pitting edema and hypertension. Her medical history was notable for "long-standing asthma" treated with inhaled glucocorticoids for several years. Laboratory evaluation revealed hypokalemia, hyperglycemia, high urinary free cortisol, non-suppressible cortisol on the low-dose dexamethasone suppression test, and elevated ACTH, suggesting ACTH-dependent Cushing's syndrome.

Pituitary MRI identified a 3 mm hypo-enhancing lesion, initially raising suspicion for Cushing's disease. However, bilateral inferior petrosal sinus sampling (BIPSS) revealed no central-to-peripheral ACTH gradient, confirming an ectopic source of ACTH. High-resolution chest CT subsequently identified a right middle lobe nodule accompanied by background mosaic attenuation and scattered nodules. Video-assisted thoracoscopic surgery (VATS) confirmed a typical carcinoid tumor arising within a background of diffuse neuroendocrine cell hyperplasia, consistent with DIPNECH. Post-operatively, the patient's symptoms, including muscle weakness and pitting edema, resolved significantly. In addition, her plasma ACTH and cortisol levels normalized rapidly, and her hyperglycemia and hypertension completely resolved without further medication use.

Discussion: This case represents the first reported Asian patient with DIPNECH-associated EAS. Ectopic ACTH secretion from pulmonary neuroendocrine tumors often follows an indolent course, closely resembling Cushing's disease and frequently complicated by incidental pituitary lesions and discordant biochemical testing. In this context, BIPSS remains the definitive diagnostic tool to confirm the origin of ACTH secretion and prevent unnecessary pituitary surgery.

DIPNECH is characterized by diffuse pulmonary neuroendocrine cell proliferation with secretion of bioactive peptides, leading to constrictive bronchiolitis and fixed airflow obstruction that clinically mimics refractory asthma. Therefore, recognition of mosaic attenuation and multiple small pulmonary nodules on high-resolution CT is essential for distinguishing DIPNECH from common bronchial asthma.

Conclusion: This case highlights the diagnostic challenges in ACTH-dependent Cushing's syndrome, underscoring that BIPSS is the gold standard for accurate localization of ACTH excess. DIPNECH should be considered in older non-smoking women with refractory asthma, particularly when accompanied by Cushing's syndrome.

Abstract citation ID: lvag096.1480

EP1237 - ECE_2215 - Refractory cerebral salt wasting after traumatic brain injury: a case highlighting severe natriuresis and the role of combined sodium and mineralocorticoid therapy

Marjeta Kermaj, Ursina Hajdini, Violeta Hoxha, Klodi Poshi and Agron Ylli
Endocrinology, University Hospital Center "Mother Tereza", Tirana, Albania

Background: Hyponatremia is a common electrolyte abnormality following traumatic brain injury (TBI), most frequently attributed to the syndrome of inappropriate antidiuretic hormone secretion (SIADH) or cerebral salt wasting (CSW). Differentiation between these entities is critical, as therapeutic strategies differ substantially. Although CSW has traditionally been considered rare, recent literature suggests a highly variable incidence, indicating that it may be under-recognized in clinical practice.

Case Presentation: We report a 70-year-old male who developed progressive and refractory hyponatremia after cranial trauma with occipital fracture and frontal contusion. Despite treatment with isotonic and hypertonic saline, serum sodium levels continued to decline. The patient exhibited marked polyuria (up to 3.5 L/day), extreme urinary sodium excretion (570 mmol/24 h), hypouricemia, and absence of edema or cardiac dysfunction. Endocrine evaluation, including thyroid and adrenal function, was normal, and repeat neuroimaging revealed no new acute intracranial pathology. Persistent natriuresis despite aggressive intravenous sodium replacement prompted the addition of high-dose oral sodium supplementation (up to 9 g/day). Ongoing sodium loss suggested an active renal salt-wasting process rather than inadequate replacement. Adjunctive mineralocorticoid therapy with fludrocortisone (initially 100 µg/day, subsequently tapered) was introduced, resulting in gradual stabilization of serum sodium and full clinical recovery.

Conclusion: This case illustrates a severe and refractory form of CSW following TBI, characterized by extreme natriuresis and resistance to conventional saline-based therapy alone. It highlights the importance of recognizing renal sodium wasting as a dynamic process and supports a combined therapeutic approach using intravenous fluids, high-dose oral sodium supplementation, and mineralocorticoid therapy. Early identification and targeted treatment of CSW are essential to prevent prolonged hyponatremia and its associated complications.

Abstract citation ID: lvag096.1481

EP1238 - ECE_3483 - Pituitary apoplexy after peripheral thrombolysis: a rare cause of acute neuro-ophthalmological deficits and adrenal crisis

Kornel Witek[1], Tomasz Wieczorkiewicz[1], Joanna Sobolewska[2], Lukasz Dzialach[2], Aleksandra Dubiel[3], Jakub Stępień[4] and Przemysław Witek[2]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Medical University of Warsaw, Warsaw, Poland; [2]Department of Internal Medicine, Endocrinology and Diabetes, Medical University of Warsaw, Warsaw, Poland; [3]Department of Internal Medicine, Mazowiecki Szpital Bródnowski, Warsaw, Poland; [4]Department of Neurosurgery, Mazowiecki Szpital Bródnowski, Warsaw, Poland

Background: Pituitary apoplexy is a medical emergency caused by acute haemorrhage or infarction within a pituitary adenoma, resulting in rapid tumour expansion, mass effect, and potentially life-threatening hypopituitarism. Although apoplexy is well recognised in several clinical settings, its occurrence following thrombolytic therapy remains rare. We report haemorrhagic infarction of a previously undiagnosed pituitary macroadenoma temporally associated with peripheral thrombolysis, complicated by neuro-ophthalmological deficits and secondary adrenal insufficiency.

Case Report: A 72-year-old man was admitted to the Vascular Surgery Department due to exacerbation of chronic lower limb ischaemia. He underwent angioplasty followed by targeted thrombolysis of a stenotic popliteal artery. In the early postoperative period, he developed acute bilateral ptosis and ophthalmoplegia. Urgent head computed tomography revealed a sellar mass with parasellar extension. Dedicated pituitary MRI confirmed a pituitary macroadenoma with bilateral cavernous sinus invasion, suprasellar extension with optic chiasm elevation, and optic nerve compression, consistent with pituitary apoplexy.

During hospitalisation, the patient became haemodynamically unstable with hypotension (79/50 mmHg). Immediate intravenous hydrocortisone replacement resulted in rapid clinical improvement. After exclusion of other acute causes, the deterioration was attributed to secondary adrenal insufficiency due to corticotropic axis failure (adrenal crisis). The patient was transferred to the Endocrinology Department, stabilised under glucocorticoid coverage, and subsequently underwent planned subtotal transsphenoidal resection of the pituitary tumor. Postoperative recovery was uneventful, with no further impairment of pituitary axes. The patient remains under long-term endocrine follow-up.

Conclusions: Pituitary apoplexy following thrombolytic therapy is a rare but potentially fatal complication. Acute neuro-ophthalmological deficits and/or haemodynamic deterioration in patients receiving anticoagulants or thrombolytics should prompt urgent sellar imaging and immediate administration of stress-dose hydrocortisone, alongside interdisciplinary management.

Abstract citation ID: lvag096.1482

EP1239 - ECE_3637 - Comprehensive clinical, biochemical and long-term outcome analysis of patients with hypopituitarism

Naciye Guduk Sirvan[1], Polat Ercan[2], Selin Tekin[2], Nergis Basmacı[2], Alperen Onur Işler[2], Suleyman Nahit Sendur[2], Selcuk Dagdelen[2] and Tomris Erbas[2]
[1]Internal Medicine, Hacettepe University Hospital, Ankara, Turkey; [2]Endocrinology, Hacettepe University Hospital, Ankara, Turkey

Background: Hypopituitarism is a severe endocrine disorder characterized by combined anterior and, in some cases, posterior pituitary hormone deficiencies, leading to widespread systemic consequences. Its presentation is often subtle and nonspecific, resulting in delayed diagnosis and preventable morbidity, including adrenal crises and long-term metabolic and cardiovascular complications. This study aimed to comprehensively evaluate the etiological spectrum, clinical features, hormonal profiles, comorbidities, and long-term outcomes of patients with hypopituitarism in a real-world tertiary care setting.

Methods: We conducted a retrospective observational study of 56 patients diagnosed with hypopituitarism between 2000 and 2025 at Hacettepe University School of Medicine. Demographic, clinical, laboratory, imaging, and etiological data were systematically collected, and treatment modalities including hormone replacement, surgery, and radiotherapy were recorded.

Results: A total of 56 patients (27 F/29 M) were analyzed, with a mean age at diagnosis of 34.5 (16-53) years. The leading etiologies were non-adenoma tumor (54.8%), pituitary adenoma (33.3%), autoimmune (4.8%), histiocytosis (4.8%), hereditary (2.4%). The patients were followed for a median of 10 (4-17) years. The median diagnostic delay was 4-6 months. Most patients were diagnosed shortly after the onset of acute symptoms, whereas one patient was diagnosed nearly 35 years after the initial manifestation of symptoms. The most frequent presenting complaints were fatigue (84.1%), weight changes (38.6%), hyponatremia (9.5%), hypotension (2.3%), and reproductive or sexual dysfunction (20.6%). During follow-up, 1.7% of patients experienced at least one adrenal crisis, while 25.8% of the patients required recurrent hospitalizations. The prevalence of major comorbidities—including MASLD, osteoporosis, and cardiovascular disease—was 20.4%, 20.5%, and 10.0%, respectively. The median [IQR] Hepatic Steatosis Index, FIB-4, NAFLD Fibrosis Score, BARD, and APRI scores of 39 patients (69.6%) were 23.2 [10.1-37.1], 0.86 [0.25-1.69], −4.31 [−5.30 to −2.94], 2.0 [2.0-3.0], and 0.18 [0.13-0.33], respectively. Among the patients, 8.9% had cancer, 12.5% had anemia (including 5.4% anemia of chronic disease and 7.1% iron deficiency anemia), and 3.6% had cerebrovascular events (1.8% hemorrhagic and 1.8% ischemic). Mortality during follow-up was 5.4%, with 3.6% due to myocardial infarction and 1.8% due to aspiration.

Conclusion: Hypopituitarism presents with heterogeneous etiologies and nonspecific symptoms, yet is associated with a substantial burden of long-term metabolic, skeletal, and cardiovascular comorbidities. Our findings highlight the need for early recognition and structured, lifelong multidisciplinary follow-up to reduce preventable morbidity and improve long-term outcomes.

Abstract citation ID: lvag096.1483

EP1240 - ECE_1609 - Early hypocortisolism with persistent remission following osilodrostat therapy in a patient with long-standing Cushing disease

Liat Sasson[1,2] and Ilan Shimon[1,2]
[1]Endocrinology, Institute of Endocrinology, Rabin Medical Center, Petah Tikva, Israel; [2]Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel

Background: Cushing syndrome is a disorder of endogenous hypercortisolism associated with increased morbidity and mortality, requiring effective long-term control of cortisol excess. When pituitary surgery is not feasible or unsuccessful, medical therapy targeting either adrenocorticotropic hormone (ACTH) secretion or adrenal steroidogenesis is commonly employed. Osilodrostat, a potent oral 11β-hydroxylase inhibitor, has emerged as an effective treatment.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Case Presentation: We present a 70-year-old woman with ACTH-dependent Cushing disease due to a pituitary macroadenoma (15 mm), diagnosed in 2008. The patient declined surgery and was managed medically for many years with pasireotide, resulting in marked tumor shrinkage (<4 mm), and later combination therapy with metyrapone due to persistent hypercortisolism. Despite partial biochemical control, urinary free cortisol (UFC) remained elevated, prompting initiation of osilodrostat (2 mg twice daily) in February 2024, with discontinuation of metyrapone.

Within ten days of treatment initiation, the patient developed fatigue, nausea and hypotension. Morning serum cortisol was markedly low (76 nmol/L), consistent with adrenal insufficiency. Osilodrostat was immediately discontinued, and physiologic glucocorticoid replacement was initiated, with rapid clinical improvement.

Outcome and Follow-Up: Despite minimal exposure to osilodrostat, the patient developed sustained cortisol suppression. UFC normalized within approximately five weeks and remained within the normal range throughout nearly two years of follow-up without further Cushing-directed therapy. Morning cortisol levels demonstrated slow and incomplete recovery. A follow-up ACTH measurement revealed elevated ACTH in the presence of low-normal cortisol, suggesting impaired adrenal responsiveness after prolonged ACTH suppression. Clinically, the patient experienced substantial metabolic improvement, including a 16.5-kg weight loss and marked improvement in glycemic control, allowing discontinuation of insulin and GLP-1 receptor agonist therapy.

Conclusion: This is among the earliest documented cases of osilodrostat-induced hypocortisolism with long sustained hormonal remission after treatment discontinuation. It highlights the importance of early monitoring and awareness that prolonged remission may occur in select patients after brief adrenal steroidogenesis inhibition.

Abstract citation ID: lvag096.1484

EP1241 - ECE_1679 - Association of iodine status and sex with sleep duration in adults: an analysis of NHANES 2005-2020

Stella Proikaki[1], Eleni Kouroglou[1], Efthymia Kallistrou[1], Dimitra Ragia[1], Dimitra Motsiou[1], Vasiliki Tsiama[1], Konstantinos Belis[1], Ioannis Ilias[1], Athanasios Tselebis[2], Lina Zabuliene[3] and Christos Savvidis[1]

[1]Department of Endocrinology, Hippocration General Hospital of Athens, Athens, Greece; [2]Department of Psychiatry, Sotiria Hospital, Athens, Greece; [3]Faculty of Medicine, Vilnius University, Vilnius LT-03101, Lithuania

Introduction: Sleep duration changes with age and differs by sex, impacting metabolic and cognitive health. Iodine, essential for thyroid hormone synthesis, may influence sleep regulation, but its interaction with age in relation to sleep duration is not well studied.

Aim: To examine whether iodine status modifies the relationship between age and sleep duration in adults, and to assess the roles of sex and iodine status.

Materials and Methods: Data from adults (≥18 years) with urinary iodine concentration (UIC) and self-reported sleep duration from NHANES 2005-2020 were analyzed. UIC was categorized as ≤150 µg/L or >150 µg/L. ANCOVA was conducted with sleep duration (hours) as the dependent variable, iodine status and sex as fixed factors, age as a covariate, and interaction terms for iodine status × age and iodine status × sex included to evaluate moderation effects.

Results: Data from 17 564 adults (mean age 47.5 ± 17.3 years, 51.3% female) were analyzed. Females reported longer sleep duration than males ($P < .001$). Iodine status alone was not associated with differences in mean sleep duration ($P = .922$). Critically, a significant interaction was found between iodine status and age ($P < .001$), indicating that the relationship between age and sleep duration differed between iodine status categories: Among individuals with UIC ≤150 µg/L, sleep duration showed a different trajectory across age compared to those with UIC >150 µg/L ($P < .001$). No significant interaction between iodine status and sex was observed ($P = .290$).

Discussion: While iodine status does not affect overall sleep duration, it significantly alters how sleep duration changes with age. This may reflect the role of iodine-dependent thyroid function in age-related sleep regulation, with iodine sufficiency potentially buffering or modifying age-associated sleep changes.

Abstract citation ID: lvag096.1485

EP1242 - ECE_2473 - Telemedicine-based management of an ophthalmic emergency caused by a non-functioning pituitary macroadenoma in a satellite charity clinic during war and displacement

Hessa Albanki[1], Mohammed Al Mutasim[2], Waiel Bashari[3] and Azmi Mohammed[1]

[1]Department of Endocrinology and Metabolism, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia; [2]Sudan Pituitary Foundation, Khartoum, Sudan; [3]Addenbrooks Memory Clinic, Cambridge, United Kingdom

Background: Armed conflict and population displacement severely disrupt access to specialist endocrine and neurosurgical care. Pituitary macroadenomas presenting with acute or progressive visual compromise constitute ophthalmic emergencies requiring timely multidisciplinary intervention. Telemedicine may provide a critical bridge in such settings.

Case: We report the case of a 54-year-old displaced Sudanese man presenting to a satellite charity clinic during continuing hostilities with progressive visual field loss. Remote assessment identified bitemporal hemianopia with reduced visual acuity, confirmed on formal automated perimetry. Hormonal evaluation demonstrated partial anterior hypopituitarism with preserved hypothalamic–pituitary–adrenal axis and normal prolactin. MRI revealed a large (≈4 cm) non-functioning pituitary macroadenoma causing chiasmal compression with sphenoid sinus invasion and no significant cavernous sinus involvement.

Using a telemedicine-based model, input from endocrinology, ophthalmology, neuroradiology, and neurosurgery was coordinated across borders. Urgent referral for transsphenoidal surgery was facilitated despite displacement and healthcare system fragmentation. The patient underwent a successful transsphenoidal resection. Histopathology confirmed a pituitary neuroendocrine tumour (adenoma), NOS, with negative pituitary hormone immunostaining and a low proliferative index (Ki-67 ≈2%). Postoperative MRI demonstrated no residual or recurrent tumour with decompression of the optic chiasm. Visual and neurological outcomes stabilized postoperatively.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusion: This case illustrates how telemedicine-enabled multidisciplinary collaboration can successfully manage ophthalmic endocrine emergencies in conflict zones. Structured remote triage, data sharing, and international referral pathways can lessen delays, preserve vision, and deliver specialist care under extreme healthcare disruption. Such models have wider significance for endocrine emergency care in humanitarian settings.

*The Sudan Pituitary Foundation is a charitable, not-for-profit organization registered in Sudan, dedicated to the management and support of Sudanese patients with pituitary disorders. The Foundation primarily utilises telemedicine technologies and a multidisciplinary model of care to deliver specialized healthcare services and comprehensive support to individuals affected by pituitary diseases.

Abstract citation ID: lvag096.1486

EP1243 - ECE_1263 - Giant prolactinoma with central hypopituitarism: dramatic biochemical and clinical response to dopamine agonist therapy

Andrew Gerges[1], Suresha Muniyappa[2] and Paula Marchetti[2]
[1]*Sheffield teaching hospitals NHS trust, Sheffield, United Kingdom;* [2]*Doncaster Royal Infirmary, Doncaster, United Kingdom*

Background: Prolactinomas are the most common hormone secreting pituitary tumours and account for up to 40% of pituitary adenomas. They are categorised by size into microprolactinomas (<10 mm), macroprolactinomas (≥10 mm) and giant prolactinomas (≥40 mm). Giant prolactinomas are uncommon and characteristically invasive, frequently presenting with a combination of markedly elevated prolactin levels, mass effect symptoms and varying degrees of hypopituitarism. Current European guidelines recommend dopamine agonists as first line therapy regardless of tumour size, with surgery reserved for visual compromise not improving with medical treatment, dopamine agonist resistance or intolerance, or in cases of apoplexy. We describe a giant prolactinoma presenting with central hypothyroidism and hypogonadism, demonstrating a significant biochemical and clinical response to medical therapy.

Case Report: A 45-year-old man was evaluated for ejaculatory dysfunction. Initial testing showed profound hyperprolactinaemia (220 948 mU/L), central hypogonadism (testosterone 1.70 nmol/L with low LH and FSH), central hypothyroidism (free T4 7.5 pmol/L with inappropriately normal TSH) and no biochemical evidence of adrenal insufficiency. He reported fatigue, headaches, visual blurring, dizziness, low libido and generalised aches. He denied galactorrhoea, rhinorrhoea or erectile dysfunction. Past medical history included repaired atrial septal defect, pulmonary valve stenosis and chronic hepatitis B.

MRI revealed a more than 4 cm invasive pituitary macroadenoma remodelling the clivus, displacing the optic chiasm, encasing the left internal carotid artery and extending into both cavernous sinuses. The patient had no symptoms of cerebrospinal fluid (CSF) leak. Visual fields were normal on confrontation, but formal perimetry demonstrated gross bilateral field depression, leading to advice not to drive. Baseline echocardiography was stable.

Cabergoline was initiated at 250 µg twice weekly and escalated, with the patient later stabilised on 500 µg twice weekly. After one month, prolactin fell to 19 526 mU/L, and on subsequent review decreased further to 476 mU/L, representing a more than 99% reduction from baseline. Due to persistently low free T4 and testosterone levels, the patient was established on levothyroxine and testosterone replacement. He is currently awaiting repeat MRI to evaluate tumour shrinkage and guide ongoing management.

Conclusion: This case highlights the potential for marked prolactin reduction, hormonal stabilisation and clinical improvement in giant prolactinomas managed with dopamine agonist therapy alone. Even in large, invasive tumours, effective medical therapy may delay or avoid the need for surgery. Multidisciplinary coordination remains essential to optimise tumour control, visual outcomes and endocrine replacement.

Abstract citation ID: lvag096.1487

EP1244 - ECE_2800 - Incidental sellar region lipoma: a case highlighting the importance of comprehensive evaluation in sellar region lesions

Elene Dophidze[1,2], Nino Gabidzashvili[1], Nana Nakaidze[1], Kristine Ambriashvili[1], Nana Iorashvili[1], Tamara Antia[3], George Gegia[4], Elena Bezhentseva[4], Ketevani Jakhtanidze[4], Giorgi Katchakhidze[4], Tina Iordanishvili[1] and Ketevan Ghibradze[1]
[1]*Department of Endocrinology, American Hospital Tbilisi, Tbilisi, Georgia;* [2]*American Hospital Tbilisi, Tbilisi, Georgia;* [3]*Department of Radiology, "American Hospital Tbilisi", Tbilisi, Georgia;* [4]*Neurosurgery, "American Hospital Tbilisi", Tbilisi, Georgia*

Introduction: Intracranial lipomas are rare congenital malformations with an autopsy incidence ranging from 0.08% to 0.46%, resulting from persistence and abnormal differentiation of the meninx primitiva during development of the subarachnoid cisterns. These benign fatty lesions are typically asymptomatic and discovered incidentally on neuroimaging performed for unrelated indications. In the sellar region, lipomas typically occur in the suprasellar cistern, accounting for approximately 10%-15% of all intracranial lipomas. Conservative management is standard given their benign nature and the technical challenges of surgical resection due to adherence to neurovascular structures.

Case Presentation: We present a case of a 22 year old man with an incidentally discovered intra-suprasellar lipoma. The patient initially developed uncontrollable upper eyelid movements in May 2025, followed by difficulty speaking and uncontrollable movements of the left upper extremity and left great toe in September 2025. These symptoms gradually improved spontaneously over time. Brain MRI, performed during workup of these neurological symptoms, revealed an intrasellar lesion with suprasellar extension, measuring 26 mm at its greatest dimension. The lesion demonstrated characteristic T1 hyperintensity with complete signal suppression on fat-saturated sequences, consistent with a lipoma.

Surgery was initially considered given the lesion size. However, comprehensive endocrine evaluation revealed no evidence of hypopituitarism. Visual field perimetry showed no defects, and visual acuity was normal. Neurological examination revealed no focal deficits, and the presenting symptoms showed no anatomical correlation with the sellar lesion location. The lipoma was therefore determined to be an incidental finding unrelated

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

to the patient's neurological symptoms. Given the benign nature of the lipoma, absence of hormonal dysfunction, normal visual function, and lack of mass effect symptoms, conservative management with clinical and radiological surveillance was chosen.

Conclusion: This case highlights the importance of comprehensive endocrine evaluation in managing sellar region lesions. Despite considerable size, asymptomatic intra-suprasellar lipomas can be safely managed conservatively, avoiding unnecessary surgical intervention. Clinicians should recognize that incidental sellar findings should not be automatically attributed to presenting symptoms without clear anatomical and physiological correlation. This approach emphasizes patient-centered care and careful use of surgical resources.

Abstract citation ID: lvag096.1488

EP1246 - ECE_1571 - Clinical spectrum of benign pituitary tumors: a five-year retrospective analysis

Aleksandra Markovic[1,2], Tamara Dojcinovic[1,2], Ivona Risovic[1,2], Jelena Malinovic Pancic[1,2], Valentina Soldat Stankovic[1,2], Suzana Savic[2,3] and Tamara Popovic Peric[2,4,5]

[1]University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina; [2]Faculty of Medicine, University of Banja Luka, Banja Luka, Bosnia and Herzegovina; [3]Faculty of Medicine, University of East Sarajevo, East Sarajevo, Bosnia and Herzegovina; [4]PHI Hospital "Sveti Vračevi", Bijeljina, Bosnia and Herzegovina; [5]Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia

Introduction: Benign pituitary tumors are predominantly slow-growing lesions with variable clinical presentation. Their manifestations depend on hormonal activity, tumor size, and local mass effects, resulting in a spectrum ranging from incidental findings to clinically significant endocrine and neurological disturbances. Although histologically benign, these tumors may be associated with considerable morbidity due to hormonal hypersecretion, hypopituitarism, or compression of adjacent structures. Epidemiological data suggest that pituitary adenomas are relatively common, yet their clinical behavior remains heterogeneous. A comprehensive evaluation of clinical, endocrine, and radiological characteristics is essential for accurate diagnosis and optimal management. This study aimed to characterize the clinical spectrum of benign pituitary tumors, with emphasis on demographic features, hormonal activity, and tumor size in a tertiary care setting.

Methods: This retrospective cohort study included patients diagnosed with benign pituitary tumors and treated at a tertiary referral center between 2019 and 2023. All patients underwent standardized clinical assessment, hormonal evaluation, and pituitary magnetic resonance imaging. Demographic data, endocrine profiles, and radiological characteristics were collected from medical records. Tumor size and invasiveness were determined based on MRI findings. Tumors were classified as functioning or non-functioning according to biochemical evidence of hormonal hypersecretion. Statistical analyses assessed associations between clinical characteristics and tumor features.

Results: The study population included patients aged 20-85 years, with a mean age of 48.61 years (SD = 17.60). Among 53 patients with available hormonal data, functioning adenomas were identified in 79.2% of cases, with prolactin-secreting tumors being the most frequent subtype (64.1%). Macroadenomas were present in 58.0% of patients, while radiological evidence of invasive growth was observed in 22.4%. A subset of patients ($n = 21$) required surgical treatment, most commonly via a transsphenoidal approach (76.2%). Complete tumor resection was achieved in 17.7% of cases, and biochemical remission was documented in 5.9% of patients.

Conclusions: Benign pituitary tumors in this cohort were predominantly functioning and frequently diagnosed as macroadenomas, underscoring the need for early recognition and structured endocrine evaluation. Timely radiological assessment and management in specialized centers may improve therapeutic outcomes and reduce disease-related morbidity.

Keywords pituitary tumors, benign pituitary adenomas, hormonal activity, macroadenomas, clinical characteristics, magnetic resonance imaging

Abstract citation ID: lvag096.1489

EP1247 - ECE_3606 - ACTH-dependent Cushing's syndrome: diagnostic pitfalls and personalised treatment strategies: a case series

Tiberiu Gabriel Manole[1], Ionela Baciu[1,2], Anda Dumitrascu[1] and Catalina Poiana[1]

[1]C I Parhon National Institute of Endocrinology, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Introduction: Cushing's syndrome (CS) is caused by increased cortisol production from the adrenals or by ACTH secretion from a pituitary tumour (Cushing disease – CD) or non-pituitary tumour (ectopic secretion), leading to increased morbidity and mortality. The first line of treatment is surgery, but medical treatment, radiation or bilateral adrenalectomy are needed for recurrences or inoperable lesions.

Objective and Methods: To present the therapeutic challenges and individualised treatment options in 3 patients with ACTH-dependent CS, treated in a tertiary centre.

Results: The first patient is a 61-year-old female with a microprolactinoma (responsive to low-dose cabergoline), who developed CD due to a second pituitary microadenoma 10 years later, complicated with obesity, hypertension, diabetes mellitus, dyslipidaemia. Inferior petrosal sinus sampling was not available for the lateralisation of the ACTH secretion – she underwent selective neurosurgery on the biggest lesion followed by a second surgery due to persistent hypercortisolism, with a resolution of the CD and the metabolic syndrome. Three years later, CD relapsed, without identifiable pituitary or ectopic lesions on imaging. Low-dose pasireotide was initiated, with biochemical control and favourable metabolic evolution.

The second patient is a 51-year-old woman with an invasive non-functioning pituitary macrodenoma, who underwent 2 partial adenomectomies and radiotherapy. Thirteen years later tumour progression was accompanied by the development of CD and metabolic complications – she underwent a third surgery, with persistent hypercortisolism. Pasireotide achieved cortisol control, but the diabetes worsened, therefore she was switched to ketoconazole, with a good biochemical and metabolic response.

The third patient is a 67-year-old woman with a florid Cushing phenotype, weight loss, hypokalaemia, markedly elevated

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

cortisol, ACTH and DHEAS levels. Extensive imagery (pituitary, chest and abdomen) came back negative, with the exception of a small indeterminate renal lesion. The somatostatin receptor scintigraphy and the inferior petrosal sinus sampling also failed to localise the ACTH source. She was initially started on ketoconazole, with a partial biochemical response, therefore she was switched to osilodrostat with a good clinical and hormonal evolution. She was referred to Nephrology for a renal biopsy, given the severe initial clinical and biochemical profile, suggesting a possible ectopic ACTH secretion (even though the scintigraphy was negative).

Conclusion: ACTH-dependent CS remains a complex condition with significant challenges, particularly in recurrent disease, aggressive pituitary tumours or occult ectopic ACTH secretion. These cases underscore the importance of a personalised approach and demonstrate the expanding role of medical therapies when surgical cure is not attainable.

Abstract citation ID: lvag096.1490

EP1248 - ECE_1820 - An aggressive prolactin-secreting pituitary adenoma resistant to multimodal therapy: a case report

Daniela-Georgiana Amzar[1], Mihaela Maria Vlad[1], Melania Balas[1], Ioana Golu[1], Stoian Dana[1], Oriana Pelineagră[1] and Laura Cotoi[2]
[1]*Endocrinology, Spitalul Clinic Județean de Urgență Timișoara, Timișoara, Romania;* [2]*Endocrinology, Centre Hospitalier de Luxembourg, Luxembourg, Luxembourg*

Introduction: Pituitary adenomas are the most common cause of sellar masses from the third decade on, accounting for up to 10% of all intracranial neoplasms. The pituitary tumor transforming gene is overexpressed in most lactotroph adenomas. It also appears to play a role in tumor invasiveness since expression is increased in tumors that invade the sphenoid bone.

Case Presentation: We report the case of a 47-year old male patient, diagnosed in 2013 with a prolactin secreting adenoma. At presentation, the patient exhibited optic field defects, which was subsequently confirmed by magnetic resonance imaging (MRI) to be caused by a large sellar mass compressing the optic chiasm and extending into the third ventricle (4.3/3.2/4 cm).

At diagnosis, the patient's serum prolactin was 4319 ng/mL. Medical treatment with dopamine agonists (Cabergoline) was initiated at a dose of 0.5 mg and later increased to 1.5 mg weekly. Biochemical response was achieved with afore-mentioned dosage with prolactin levels maintained below 100 ng/mL until 2016.

Reimaging by MRI was performed in 2016 as prolactin levels suddenly increased. Rapid growth of the adenoma was observed on serial imaging, as well as important prolactin elevation above 2000 ng/mL. Prolactin levels remained elevated despite medical treatment and transsphenoidal surgery was advised in 2019. Postoperative prolactin levels remained over 2000 ng/mL, when a second surgery was performed in 2020, followed by external radiotherapy without any regression in tumor size or prolactin levels.

After a multidisciplinary approach, combined therapy with Cabergoline (6 mg weekly) and Temozolomide (100 mg 5 tablets weekly) was initiated.

At the most recent follow-up, a favourable biochemical response was noted with prolactin levels decreasing to near-normal levels (75 ng/mL), although radiologic control of the pituitary mass has not yet been achieved.

Conclusion: Temozolomide has been documented as valuable for the treatment of aggressive pituitary adenomas and carcinomas. No significant complications have been attributed to temozolomide therapy. Thus, temozolomide is an effective treatment for most aggressive adenomas and carcinomas.

Abstract citation ID: lvag096.1491

EP1249 - ECE_2494 - Acromegaly with multisystem manifestations in a patient with hypothyroidism and multinodular goiter

Mariam Orjonikidze[1], Nino Zavrashvili[1] and Ia Kavtiashvili[2]
[1]*Endocrinology, Tbilisi Institute of Medicine (TIM), Tbilisi, Georgia;* [2]*Tbilisi Institute of Medicine (TIM), Tbilisi, Georgia*

Background: Acromegaly is a rare endocrine disorder caused by chronic growth hormone (GH) excess, most commonly due to a pituitary adenoma. Its insidious onset often leads to delayed diagnosis and significant multisystem involvement. Coexisting thyroid disorders may further obscure the clinical picture.

Case Presentation: A postmenopausal woman presented with a 2-3-year history of progressive acral enlargement, soft tissue swelling of the hands and feet, arthralgia, hyperhidrosis, tachycardia, and episodic hypertension. She reported an increase in shoe size and inability to wear rings. Her medical history was notable for **hypothyroidism associated with multinodular non-toxic goiter**, diagnosed in 2021 and treated with **levothyroxine**.

Biochemical evaluation demonstrated markedly elevated insulin-like growth factor-1 (IGF-1: 742 µg/L). Thyroid function tests were within reference range under levothyroxine therapy, and thyroid autoantibodies were negative. Pituitary magnetic resonance imaging revealed a $3.0 \times 2.6 \times 2.1$ cm intra-, infra- and suprasellar pituitary macroadenoma with mild parasellar extension and pituitary stalk deviation, without optic chiasm compression.

The patient underwent transsphenoidal transnasal pituitary adenomectomy in December 2024. Following surgery, she experienced significant clinical improvement, including resolution of hypertension and snoring, reduction of acral and facial edema, and improvement in arthralgia and skin texture. Postoperative hormonal assessment confirmed biochemical remission (IGF-1: 111 µg/L; GH: 1 ng/mL). Mild postoperative adrenal insufficiency was suspected and managed with low-dose hydrocortisone, resulting in improved energy levels.

Conclusion: This case highlights the diagnostic challenges of acromegaly in the presence of coexisting hypothyroidism and multinodular goiter. Awareness of progressive somatic changes and careful hormonal evaluation are essential for timely diagnosis. Surgical management can achieve biochemical remission and marked clinical improvement, while long-term follow-up remains crucial to monitor pituitary function and associated comorbidities.

Abstract citation ID: lvag096.1492

EP1250 - ECE_3051 - The role of surgical expertise in achieving durable outcomes after transsphenoidal surgery for acromegaly

Mariam Pailodze[1,2], Salome Kalandadze[1,3], Nino Pailodze[2] and Zviad Malazonia[1]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Caucasus Medical Centre, Tbilisi, Georgia; [2]David Tvildiani Medical University, Tbilisi, Georgia; [3]Endocrinology, Caucasus Medical Center, Tbilisi, Georgia

Background: Pituitary macroadenomas causing acromegaly represent a considerable therapeutic challenge because of their size, excessive hormone secretion, and the potential risk of postoperative hypopituitarism. Transsphenoidal surgery remains the preferred approach for achieving rapid tumor reduction and hormonal control; however, long-term outcomes and preservation of pituitary function remain key indicators of treatment success.

Case Presentation: 60-year-old female diagnosed with a pituitary macroadenoma causing acromegaly who underwent endoscopic transnasal transsphenoidal surgery performed by an experienced neurosurgeon. Preoperatively, insulin-like growth factor-1 (IGF-1) was markedly elevated at 418.05 ng/mL (reference range 17-323). Early postoperative evaluation demonstrated preserved pituitary function, with normal prolactin, thyroid, adrenal, and growth hormone levels.

During follow-up, serial biochemical assessments remained within normal ranges. At two months postoperatively, IGF-1 decreased to 154 ng/mL, with normal PRL, cortisol, TSH, FT4, electrolytes, and glucose. At three months, oral glucose suppression testing confirmed biochemical remission, with GH decreasing from 1.56 ng/mL at baseline to 0.47 ng/mLtwo hours after 75 g glucose. MRI demonstrated postoperative sellar changes without evidence of residual or recurrent adenoma, later evolving into secondary empty sella.

MRI performed three years postoperatively showed stable postoperative sellar anatomy with secondary empty sella formation and no radiological evidence of adenoma recurrence. The pituitary stalk was midline, and the optic apparatus was preserved. No additional hormonal abnormalities were identified during subsequent follow-up evaluations.

Conclusion: This case highlights that successful management of large pituitary macroadenomas extends beyond biochemical remission. Surgical expertise is a key determinant of outcome**,** as experienced transsphenoidal surgeons can achieve effective tumor debulking while preserving pituitary function, leading to durable radiological control and excellent long-term endocrine outcomes.

Abstract citation ID: lvag096.1493

EP1251 - ECE_3468 - Recurrent craniopharyngioma—between the benign nature of the case and clinical aggressiveness

Diana Taifas[1], Ionela Baciu[1], Camelia Procopiuc[2] and Catalina Poiana[1]

[1]C.I.Parhon National Institute of Endocrinology, Bucharest, Romania; [2]Pediatric Endocrinology, C.I. Parhon National Institute of Endocrinology, Bucharest, Romania

Introduction: Craniopharyngioma is a rare epithelial tumor arising from embryological remnants of the pituitary gland, with an estimated incidence of 0.5-2 cases/million/year. Although histologically benign, it demonstrates a distinctive and often aggressive clinical behavior due to its location near critical hypothalamic–pituitary structures and its pronounced tendency to recur. Consequently, craniopharyngioma is associated with significant long-term morbidity, particularly in pediatric patients, affecting growth, endocrine function, metabolism, and overall quality of life. Management remains complex and requires a multidisciplinary approach integrating neurosurgery, radiotherapy, endocrinology, and nutritional support.

Case: We report the case of a 22-year-old male patient who was initially diagnosed with craniopharyngioma at the age of five. The patient underwent two transsphenoidal surgical resections at five and six years of age. In 2015, imaging revealed a left frontal recurrence, which was treated with surgical resection followed by adjuvant proton beam therapy consisting of thirty sessions, completed in 2016. In 2021, radiological findings raised suspicion of another recurrence, which progressed requiring an additional surgical intervention in August 2025. This prolonged clinical course illustrates the particularly aggressive and recurrent nature of the disease.

Following repeated surgical procedures, the patient developed permanent global hypopituitarism, necessitating lifelong hormone replacement therapy. Central diabetes insipidus secondary to vasopressin deficiency was also diagnosed and is currently treated with desmopressin. A major associated complication is severe obesity of mixed etiology, resulting from hypothalamic damage and increased caloric intake, present since childhood and difficult to manage. Despite persistently low insulin-like growth factor 1 levels and unfavorable metabolic consequences, stature was in accordance with genetic target height and growth hormone replacement therapy has not been initiated due to concerns related to the history of multiple tumor recurrences.

Conclusions: This case highlights the substantial challenges in the management of recurrent craniopharyngioma. Despite its benign histological appearance, the tumor may behave in a clinically aggressive manner, requiring repeated surgical interventions and radiotherapy. Long-term endocrine and metabolic complications represent a burden comparable to local tumor control. A coordinated, individualized, and multidisciplinary long-term strategy is essential to improve survival outcomes and preserve quality of life in affected patients. Early recognition of recurrence, careful endocrine monitoring, and patient-centered follow-up are crucial for minimizing morbidity, guiding therapeutic decisions, and supporting long-term psychosocial adaptation in young adults living with this chronic condition after childhood onset and treatment.

Abstract citation ID: lvag096.1494

EP1252 - ECE_2649 - Silent but significant: a rare case of a dopamine-secreting carotid body tumour

Muhammad Sohail Akhtar[1,2], Kushaa Vohra[1], Ann Francis[1] and Cornelius Fernandez James[1]

[1]Diabetes & Endocrine, Pilgrim Hospital Boston(United Lincolnshire Hospitals NHS Trust), Boston, United Kingdom; [2]Endocrine &diabetes, Pilgrim Hospital Boston, Boston, United Kingdom

Introduction: Carotid body tumours are a rare paraganglioma (prevalence 1 in 100 000), originating from the chemoreceptive carotid body at the carotid bifurcation. While most are non-secretory, a minority (4%) secrete dopamine or its metabolite 3-methoxy tyramine. We present a case of a rare asymptomatic non-malignant dopamine-secreting carotid body tumour.

Case Presentation: A 68-year-old lady presented with a six-month history of a painless, left-sided neck swelling. Examination revealed a soft, non-tender, non-pulsatile 3 cm

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

mass in the left cervical region. Ultrasound neck: 29 × 26 × 23 mm solid hypervascular mass, suggesting carotid body tumour. A non-contrast MRI neck revealed a 33 × 26 × 24 mm carotid body tumour, further characterised by contrast-enhanced CT neck and thorax: 33 × 24 mm hypervascular soft-tissue density mass at the bifurcation of the left common carotid artery with characteristic displacement and splaying of internal and external carotid arteries, consistent with a carotid body tumour. CT abdomen and pelvis: no other paraganglioma.

Biochemistry revealed consistently raised plasma 3-methoxytyramine (3-4-fold) at 749, 640, and 590 pmol/L (reference range 0-180), with normal metanephrine/normetanephrine levels confirming the diagnosis of dopamine-secreting carotid body paraganglioma. Patient remained asymptomatic and normotensive with no features of catecholamine excess. Genetic testing for hereditary paraganglioma syndromes did not identify any pathogenic variants. Following multidisciplinary input from ENT and vascular surgery, surgical resection was agreed. The patient is currently awaiting surgery.

Discussion: Dopamine is the neurotransmitter of carotid body cells. Hence, a carotid body tumour could potentially secrete dopamine. However, these tumour cells are well-differentiated maintaining vesicular storage/efficient dopamine reuptake, so dopamine is not usually secreted into the bloodstream. Our case is peculiar as this is a dopamine-secreting carotid body tumour.

Carotid body paraganglioma is the most common (60%) "Head and Neck paraganglioma" (HNPGL), others being vagal (10%), middle ear (30%) and laryngeal (very rare) paragangliomas. HNPGLs constitute only 0.6% of all head and neck neoplasms. Carotid body tumours typically affect women (F: M 2:1) aged 50-60 years, often asymptomatic (painless neck lump) and unilateral (bilateral 10%-25%).

Nearly one-third (33%-40%) of carotid body tumours are hereditary secondary to *SDHx* mutation, and only 3-10% present with metastasis. Surgery is the definitive treatment, though it carries risks of bleeding, stroke and lower cranial nerve palsy. Pre-operative angiography and a multidisciplinary approach are necessary.

Conclusion: A high index of suspicion, appropriate imaging, hormonal workup and multidisciplinary approach remain paramount for optimal management of carotid body paragangliomas.

Abstract citation ID: lvag096.1495

EP1255 - ECE_1780 - A teenager with central diabetes insipidus and puberty arrest: current status a decade after initial diagnosis

Eleni Palioura[1], Maria Rigana[2], Maria Katsafyloudi[2], Alexandros Konidaris[2] and Andromahi Vryonidou[2]
[1]*Hellenic Red Cross Hospital, Athens, Greece;* [2]*Department of Endocrinology and Diabetes Center, Hellenic Red Cross Hospital, Athens, Greece*

Introduction: Central diabetes insipidus (CDI) is a rare clinical entity caused by deficiency in the secretion of arginine vasopressin (AVP) from the posterior pituitary gland. In children and adolescents, its presence may be indicative of underlying pathology including intracranial tumors, granulomatous or infiltrative disorders with hypothalamic and/or pituitary involvement or inflammatory/autoimmune conditions affecting pituitary. As the diagnosis and course of these diseases may not be clear, systematic follow-up of young patients is imperative.

Case Report: We present the case of a $16^{8/12}$–year-old teenager, who was referred to our department with symptoms of polyuria/nocturia and polydipsia since the age of 12, leading to consumption of almost ten liters of liquids daily. Pediatric history was remarkable for a decline in height charts from the 50th to 3th percentile since the age of 12, in parallel with puberty arrest at Tanner stage III (testicular volume of 12 mL) when symptoms started.

The CDI diagnosis was established through water deprivation testing. Anterior pituitary function tests revealed low testosterone levels for Tanner stage (Testo = 0.961 ng/mL, normal range:2-8.5), with inappropriately low gonadotropin levels (FSH = 2.23 mIU/mL and LH = 3.03 mIU/mL), a finding indicative of gonadotropic cells deficiency. IGF-1 levels (196 ng/mL) were at the lower-normal range for patient's age and Tanner stage. Magnetic resonance imaging (MRI) revealed a relatively small for patient's age adenohypophysis (dmax = 4.5 mm), with absence of high signal intensity in the posterior pituitary gland and a focal pituitary stalk thickness (4 mm). An extensive laboratory and imaging workup revealed no coexisting pathology, making hypophysitis in remission the most likely diagnosis, with possible onset at 12 years of age.

Therapeutically, patient started desmopressin (60 mcg, 3 times/daily) and transdermal testosterone 10 mgT/day, gradually titrated to 30 mgT/day. Over the subsequent three years, he gained 9.5 cm in height, reaching the 20th percentile on growth charts (final height = 172 cm) and secondary sexual characteristics continued to develop. Four years after initial presentation, complete recovery of hypothalamic-pituitary-gonadal axis was observed, leading to discontinuation of testosterone therapy, with normal testosterone (6.7 ng/mL) and FSH/LH (4.7/3.6 mIU/mL) levels and bilateral testicular size of 20 mL. IGF-1 levels were also normal (264 ng/mL). Notably, no differences were observed in annual MRI findings over the follow-up period. Ten years since initial presentation, our patient is a thriving young adult with CDI well-regulated on desmopressin and no other emerging pathology.

Discussion: Adolescents with CDI but without confirmed diagnosis at initial evaluation, require long-term neuroimaging and endocrine follow-up to exclude any underlying etiology.

Abstract citation ID: lvag096.1496

EP1258 - ECE_2893 - Pancreatic neuroendocrine neoplasms in association with MEN-1 syndrome- particularities in two clinical cases

Stanca Oana Stefania[1], Andreea-Alexandra Grosu[2], Beatrice Cristea[2] and Corin Badiu[2]
[1]*Thyroid Disorders IV, National Institute of Endocrinology C.I.Parhon, Bucharest, Romania;* [2]*National Institute of Endocrinology C.I.Parhon, Bucharest, Romania*

Background: Pancreatic NENs tend to be less aggressive when arising in the setting of MEN-1 compared to sporadic pancreatic NENs. There have been very important improvements over the past years in both genotyping, genetic counselling and family screening.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Materials and Method: We followed the clinical and biological evolution of two patients diagnosed at the National Institute of Endocrinology "C.I.Parhon", Bucharest, Romania, with pancreatic NENs and secondary determinations, associated with MEN-1 syndrome. In both cases, family genetic testing was performed and they underwent treatment with peptide receptor radionuclide therapy (PRRT).

Results: Case 1. A 59-year-old patient, with a 41-year history of an operated bronchial carcinoid tumor G2 and primary hyperparathyroidism treated surgically at age 43, as well as a macroprolactinoma managed with dopaminergic agonists, has presented since 2012 with two pancreatic lesions, non-invasive with total size 58/31 mm. These lesions were accompanied by elevated chromogranin A and serotonin levels. Genetic analysis identified a synonyumus heterozygous mutation in p.Ala213 aminoacid, classified as likely pathogenic. The mutation was also positive in 5 other cases from his family. The patient was among the first in our department to receive PRRT with 177-Lutetium-DOTATOC in Basel. This treatment yielded initially a partial response per RECIST 1.1 criteria, however, by 2024, the patient experienced tumor progression leading to referral for surgery in June 2025. A laparoscopic corporeocaudal splenopancreatectomy was performed, with histopathological and immunohistochemical analysis confirming a well-differentiated pancreatic NEN G2. Postoperative recovery was favourable, with a decline in tumor marker levels.

Case 2. A 43-year-old patient diagnosed at 41 with pancreatic G1-NET, with secondary lymphnode determinations and primary hyperparathyroidism twice operated. Genetic testing revealed a heterozygous deletion in exon 7 of the *MEN1 gene* (pPro320 del), classified as pathogenic, a mutation also present in one of his two sons. In addition to treatment with somatostatin analogues and chemotherapy, the patient also benefited from PRRT, in the same center as the patient in the previous case. One year after, the patient presented a decrease in biochemical markers and partial response according to RECIST1.1 criteria.

Conclusions: Alongside genetic screening development, medical, surgical and radionuclide treatments have improved morbidity and quality of life in many patients. Despite this progress, there is still space for improving into the geneticf actors in relation to the biological mechanisms determining NENs as part of MEN-1.

Abstract citation ID: lvag096.1497

EP1259 - ECE_2406 - Epidemiology of somatotropic pituitary adenomas in the city of Oran

Khadra Faraoun[1] and Chentli Farida[2]
[1]*Faculté de Médecine d'Oran, Endocrinology, Clinique Larribere d'Endocrinologie, Oran, Algeria;* [2]*Université Alger, Alger, Algeria*

Introduction/Objectives: Somatotroph pituitary adenomas (SPAs) are tumors that develop from pituitary somatotroph cells. Our objective is to evaluate their prevalence and incidence rates in Oran, Algeria.

Subjects and Methods: Our study is observational, multicenter, with prospective and retrospective data collection. Data entry and analysis were performed using CDC (USA) EPI Info version 6 software, SPSS 20, Statistica 10, MedCalc 12 and Join Point Regression Program 4.6.0.0.

Results: We collected data on 90 cases of Somatotroph pituitary adenomas (SPAs), representing 18.9% of all endocrine pituitary tumors. Of these, 52 (57.8%) were in males and 38 (42.2%) in females, resulting in a male-to-female ratio of 1.36. This difference was not statistically significant. The age-standardized prevalence and incidence rates of SPAs compared to the WHO population were 11.2% (12.9% in men, 9.7% in women, male-to-female ratio 1.32) and 1.92%, respectively, with a peak between 25 and 30 years of age. The mean age at diagnosis was 40.3 ± 14.7 (14-71) years: 40.9 ± 15.1 years (15-67) in men versus 39.5 ± 14.5 years (14-71) in women. This difference was not statistically significant. The mean time to consultation was 25.3 ± 30.6 months. The frequency was higher in macrolesions (≥1 cm) at 85.5% vs 14.5% ($P < .001$). Microadenomas were discovered at the same age as macroadenomas: 41.3 ± 20.4 years vs 41.7 ± 13.7 years for microadenomas ($P = .94$).

Conclusion: Somatotroph pituitary adenomas are predominantly found in males, with a higher frequency of macroadenomas. Their prevalence ranks them third after prolactinomas and nonfunctional adenomas. The time to consultation remains long, hence the importance of raising awareness for earlier diagnosis.

Abstract citation ID: lvag096.1498

EP1260 - ECE_2669 - Tumour shrinkage secondary to pre-operative somatostatin analogue in acromegaly: a role for deferring pituitary surgery

Amy Mach[1], Khaled Ahmed[1], Trevor Tam[1,2], Hani J. Marcus[3,4] and Rupa Ahluwalia[1]
[1]*Endocrinology & Diabetes, Norfolk & Norwich University Hospital, Norwich, United Kingdom;* [2]*University of East Anglia, Norwich, United Kingdom;* [3]*Neurosurgery, National Hospital for Neurology & Neurosurgery, London, United Kingdom;* [4]*Neurosurgery, University College London, London, United Kingdom*

Background: Biochemical remission following transsphenoidal surgery for acromegaly is challenging in patients with invasive pituitary macroadenomas. Pre-operative somatostatin analogues (SSAs) are sometimes used to control hormone excess and reduce tumour volume, although practice varies. We present a case of acromegaly due to an invasive macroadenoma demonstrating marked tumour shrinkage following a single pre-operative octreotide injection, leading to deferral of planned surgery.

Case Presentation: A 42-year-old woman presented with progressive acral enlargement and coarsening of facial features over several years, alongside neuropathy, arthralgia, amenorrhoea and hyperhidrosis. Biochemistry showed elevated IGF-1 (78.6 nmol/L), hyperprolactinaemia (1454 mIU/L) and low morning cortisol (185 nmol/L). Failure of GH suppression on oral glucose tolerance testing confirmed acromegaly (nadir GH 24.9 µg/L at 60 minutes).

Pituitary MRI demonstrated a 21×14 mm invasive macroadenoma with left cavernous sinus invasion (Knosp grade IV) and optic chiasmal compression. Visual fields and echocardiography were normal and adrenal reserve was confirmed on short Synacthen testing. While awaiting surgery, she received a single dose of long-acting octreotide 30 mg.

Repeat MRI one month later showed marked tumour shrinkage with resolution of chiasmal compression, prompting deferral of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

surgery to reassess disease control. Repeat GH suppression testing after a six-week SSA washout confirmed persistent active disease (nadir GH 11.2 µg/L), although follow-up MRI demonstrated sustained volume reduction (16.5 × 10 mm). She reported symptomatic improvement with no further acral enlargement and return of menses.

Given persistent hormone excess but significant radiological response, monthly octreotide 60 mg was commenced with plans for interval reassessment prior to considering surgery. Genetic testing (R217 panel) has been sent.

Discussion: This case illustrates rapid and clinically meaningful tumour shrinkage following a single dose of SSA in an invasive macroadenoma. In this context, the usual surgical indications were reconsidered. The diagnosis was already established biochemically, and resolution of chiasmal compression removed the need for urgent decompression. Given extensive cavernous sinus invasion, complete surgical remission was unlikely, and surgery would primarily have achieved partial debulking with ongoing need for medical therapy.

Pre-operative SSAs may therefore allow selected patients to avoid or defer surgery when mass effect resolves and biochemical control approaches remission. While predictors of response have been described, including MRI signal characteristics and receptor expression, further data are needed to guide personalised decision-making.

This case supports an individualised approach to pre-operative SSA use and highlights the need for longer-term outcome data in acromegaly patients managed with deferred surgery.

Abstract citation ID: lvag096.1499

EP1261 - ECE_1854 - A non-functioning pituitary macroadenoma presenting with systemic inflammatory and autoimmune-like features: a six-year diagnostic challenge

Cristina Ene
"Dr Victor Babes" Foundation, Bucuresti, Romania

Background: Non-functioning pituitary adenomas can remain asymptomatic for long periods, while progressive hypopituitarism may present with vague and misleading systemic symptoms. Chronic inflammation and autoimmune-like presentations can further mask endocrine disorders, mainly when glucocorticoid therapy conceals hormonal deficiencies. This case illustrates the diagnostic challenges of hypopituitarism secondary to an invasive pituitary adenoma.

Case Presentation: A 56-year-old woman was referred for endocrine evaluation due to persistently low free thyroxine (FT4) levels with normal thyroid-stimulating hormone (TSH) levels. Her clinical history spanned six years, marked by systemic symptoms and menopause at 49 years. Following menopause, she developed fasting hyperglycemia, obesity, and hypertension, initially managed with lifestyle changes and metformin, resulting in over 30 kg of weight loss over two years, along with gastrointestinal symptoms and fatigue attributed to the treatment.

Two years after amenorrhoea onset, the patient developed pleural and pericardial effusions and underwent extensive multidisciplinary evaluation for infectious and autoimmune causes—positive antinuclear antibodies (ANA), anti-Ro/SSA, and anti-La/SSB antibodies suggesting a systemic inflammatory disorder. Treatment with colchicine, followed by hydroxychloroquine and prolonged glucocorticoid therapy, led to partial symptom control and subsequent weight regain. Over time, the patient noticed the appearance of new symptoms—musculoskeletal pain—despite treatment. Attempts to taper glucocorticoids resulted in recurrence of nausea, vomiting, and profound asthenia.

Endocrine evaluation showed central hypothyroidism, hypogonadotropic hypogonadism, normal prolactin, and preserved electrolyte balance under glucocorticoid therapy. Magnetic resonance imaging revealed a large invasive macroadenoma with suprasellar extension and deviation of the pituitary stalk; visual field was preserved. The diagnosis of a non-functioning invasive pituitary macroadenoma leading to hormonal insufficiencies was established.

The patient underwent transsphenoidal hypophysectomy, with histopathological and immunohistochemical analysis confirming a gonadotroph adenoma. Postoperatively, hormone replacement with levothyroxine and hydrocortisone was initiated, leading to successful glucocorticoid withdrawal and favorable recovery of the hypothalamic–pituitary–adrenal axis, one year after surgery.

Conclusion: This case highlights the diagnostic complexity of a pituitary macroadenoma presenting with systemic inflammatory symptoms and autoimmune-like features. Persistently low FT4 levels with normal TSH in postmenopausal women warrant early pituitary imaging, despite positive autoimmune tests. A thorough evaluation is essential, as endocrine and autoimmune disorders may coexist, and awareness of glucocorticoid effects is crucial to avoid diagnostic delays and ensure timely management.

Abstract citation ID: lvag096.1500

EP1262 - ECE_1894 - Cyclic Cushing's syndrome, a challenging clinical case

Varvava Chalmantzi[1], Vasiliki Siampanopoulou[1], Alexandros Lafioniatis[1], Georgia Tsirou[1], Despoina Tsopouzidou[1], Miltiadis Gravvanis[2], Danai Georgakopoulou[3], Paschalia Bekiaridou[1], Eleni Memi[1], Athina Markou[3] and Anna Angelousi[1]
[1]Endocrinology Unit, First Department of Internal Medicine, European Reference Network on Rare Endocrine Conditions (ENDO-ERN), Laikon General Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece; [2]Radiology Department, G. Gennimatas' General Hospital of Athens, Athens, Greece; [3]Unit of Endocrinology and Diabetes Center, G. Gennimatas' General Hospital of Athens, Athens, Greece

Introduction: Cyclic Cushing's Syndrome is a rare entity characterized by intermittent hypercortisolemia with periods of normal or even low cortisol lasting from days to months.

Case Presentation: A 63-year-old woman with a medical history of breast cancer and thyroid cancer was referred to our Endocrinology Outpatient Clinic for evaluation of osteopenia. Her past medical history also included type 2 diabetes mellitus, dyslipidemia and a left adrenal adenoma. On clinical examination, the patient exhibited facial hirsutism, cervical fat accumulation, and centripetal obesity, without striae, facial plethora, or proximal muscle weakness.

Initial laboratory investigations revealed ACTH-dependent hypercortisolism, with a baseline ACTH level of 24.1 pg/mL (normal

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

range: 7-63), elevated serum cortisol following a 1-mg overnight dexamethasone suppression test (ODST) (160 nmol/L), and increased midnight salivary cortisol (18.84 nmol/L; normal <5.79). Loss of the normal circadian rhythm of cortisol secretion was also documented. Twenty-four–hour urinary free cortisol (UFC) was within the normal range (2275.8 nmol/L; normal range: 317.24-2813.7).

Pituitary MRI demonstrated heterogeneity in the posterior region of the adenohypophysis, without evidence of a discrete lesion. A desmopressin stimulation test showed a >20% increase in cortisol and a >50% increase in ACTH. 18-FDG-PET/CT was performed and demonstrated no abnormal FDG uptake. Two months later, remission of hypercortisolism was confirmed by a repeat 1-mg ODST (cortisol: 61.69 nmol/L), and a subsequent pituitary MRI showed no abnormalities.

At the 1-year follow-up, hypercortisolism recurred, with elevated UFC (3666.2 nmol/L) and increased midnight salivary cortisol (12.469 nmol/L; normal <5.79). A desmopressin stimulation test performed after a low-dose dexamethasone suppression test again demonstrated a >20% increase in cortisol and a >50% increase in ACTH. A high-dose (8-mg overnight) dexamethasone suppression test resulted in a >50% reduction in cortisol levels, consistent with Cushing's disease.

Based on these findings, a diagnosis of cyclic Cushing's syndrome was assumed. The patient subsequently underwent bilateral inferior petrosal sinus sampling (BIPSS), which revealed a basal central-to-peripheral ACTH ratio: 1.24 (<2) and a post-stimulation ratio at 5 min: 7.8 (>3) confirming a pituitary origin of ACTH excess. She was referred to an experienced neurosurgeon for exploratory transsphenoidal surgery (TSS), which is currently being scheduled.

Conclusion: Cyclic Cushing's syndrome remains a significant diagnostic and therapeutic challenge. Accurate diagnosis often requires repeated and thorough evaluations to document intermittent hypercortisolism. Increased clinical awareness is essential, particularly in patients with adrenal adenomas and a constellation of comorbidities suggestive of cortisol excess.

Abstract citation ID: lvag096.1501

EP1263 - ECE_2011 - Beyond the breast: a gonadotropinoma presenting with suspicious gynecomastia in a male patient

Stefania-Alexandra Bunceanu[1], Bena Andreea[2], Roxana Pui[1], Monica Latia[1] and Stoian Dana[2]

[1]*Department of Doctoral Studies, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania;* [2]*Timisoara, Romania*

Background: Gynecomastia in older men requires a careful evaluation because it may conceal breast malignancy or reflect underlying endocrine disorders. Functional gonadotroph pituitary adenomas are uncommon and frequently overlooked, as many gonadotroph tumors are clinically "silent." Conversely, in the rare situations where FSH/LH hypersecretion is clinically relevant, a comprehensive assessment is necessary to identify co-secretion, define the endocrine phenotype, and address associated gonadal and systemic comorbidities.

Case Presentation: We report the case of a 68-year-old man, with no significant chronic medication, who presented with gynecomastia and suspected breast pathology. Initial breast ultrasonography revealed bilateral fibrocystic mastopathy (BI-RADS 3), followed by the detection of a solid parenchymal lesion, markedly hypoechoic, ill-defined, with spiculated margins (BI-RADS 4). Immediate core needle biopsy for histopathological assessment was performed, with benignity confirmation afterwards. Comprehensive endocrine evaluation was assesed in order to identify the etiology of gynecomastia, which demonstrated repeatedly marked hyperprolactinemia (267-323 ng/mL) and mildly elevated gonadotropins (LH 9.33 IU/L, FSH 21.7 IU/L), with total testosterone and estradiol within the reference range. The patient denied galactorrhea but reported associated sexual dysfunction. IGF-1 values were mildly increased, but growth hormone was appropriately suppressed during the oral glucose tolerance test, excluding acromegaly. Thyroid and adrenal axes were within normal limits. Given the persistent elevation of prolactin, contrast-enhanced pituitary MRI was performed and revealed a sellar mass with typical features of a pituitary macroadenoma, measuring approximately $11.7 \times 11 \times 15.5$ mm. Cabergoline therapy was initiated at 1 mg twice weekly, leading to normalization of prolactin levels, while LH and FSH increased further on follow-up (LH 11.87 IU/L, FSH 29.41 IU/L), raising suspicion of a mixed pituitary secretion profile of prolactin and gonadotropins. Testicular ultrasonography showed normal gonadal size and morphology. In addition, α-subunit levels were elevated, further supporting the suspicion of a plurihormonal secretory pituitary macroadenoma.

Conclusion: This case highlights the importance of a comprehensive endocrine assessment when gynecomastia and breast lesions are identified in a male patient. In our case, marked hyperprolactinemia and the detection of a pituitary macroadenoma represented the first significant endocrine abnormalities. However, after initiation of cabergoline therapy and normalization of prolactin levels, the magnitude of FSH and LH hypersecretion became evident, while elevated α-subunit levels further supported the diagnosis of plurihormonal pituitary secretion, with prolactin co-secreted alongside gonadotropins. Although such cases are exceptionally rare, their recognition is essential to ensure accurate diagnosis and timely, appropriate management.

Abstract citation ID: lvag096.1502

EP1264 - ECE_3479 - Where is the end of Cushing's disease?

Dominika Ondruskova, Jana Leskova, Igor Durmek and Peter Vanuga

V.internal clinic of the Faculty of Medicine of Comenius University, National Institute of Endocrinology and Diabetology in Lubochna, Bratislava, Slovakia

Introduction: Cushing's disease is an endocrine disorder caused by excessive secretion of ACTH from the pituitary gland, leading to increased cortisol production. Diagnosis and treatment are challenging due to nonspecific symptoms and the difficulty of localizing small adenomas. Despite a wide range of therapeutic options, persistence or recurrence of the disease is common, emphasizing the need for long-term patient follow-up.

Case Report: A 32-year-old woman with Cushing's disease due to an ACTH-producing pituitary adenoma had been followed since 2017. Pharmacotherapy with pasireotide and osilodrostat was not tolerated. After two transsphenoidal adenomectomy (in 2017 and 2020), following a total hypophysectomy (in 2025),

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

we did not achieve suppression of ACTH production by pathological tissue. Three months after hypophysectomy, central hypocorticism developed, but ACTH levels were still slightly elevated. The patient required Hydrocortisone replacement therapy. Two months later, the patient experiences a clinical relapse of hypercorticism, manifested by hirsutism, the appearance of new stretch marks, fluid retention and tachycardia. We partially reduce the dosage of Hydrocortisone and assume the presence of residual ACTH-producing pituitary adenoma tissue. After consulting the radiosurgery department, we found a potential source of ACTH and planned therapy with Leksel's gamma knife.

Conclusion: Cushing's disease remains a challenging condition to manage despite advances in diagnostic and therapeutic options. Even after multiple surgical interventions, including total hypophysectomy, persistent ACTH secretion can occur due to residual ACTH secreting tissue. This case highlights the complexity of treatment and the necessity of a multidisciplinary approach, continuous hormonal monitoring, and individualized long-term management to achieve disease control and improve patient outcomes. Long-term, multidisciplinary follow-up is essential to tailor therapy and minimize metabolic and cardiovascular complications associated with fluctuating cortisol levels.

Abstract citation ID: lvag096.1503

EP1265 - ECE_2329 - When the source remains hidden-diagnostic dilemmas in ACTH-dependent Cushing's syndrome

Christina Lymniati[1], Eleni Statiri[1], Georgia Ntali[2], Phivi Rontogianni[3], Anastasios Chatzinikolaou[1], Anastasia Tsolakidou[1], Anastasia Filippidou[1] and Charalampos Tsentidis[1]

[1]*Endocrinology, Diabetes Mellitus and Metabolism Department, General Hospital of Nikaia Piraeus "AG. PANTELEIMON", Piraeus, Greece;* [2]*Department of Endocrinology "D.Ikkos"—Diabetes Center, Endo-ERN, General Hospital EVANGELISMOS, Athens, Greece;* [3]*Nuclear Medicine and PET/CT Department, Evanggelismos General Hospital, Athens, Greece*

Aim: To analyze the diagnostic challenges in ACTH-dependent Cushing's syndrome when no causative lesion is initially identified, with emphasis on the differentiation between pituitary and ectopic sources of ACTH excess, and on the role of medical therapy during prolonged diagnostic evaluation.

Summary/Methods: A 23-year-old male presented with progressive clinical features of Cushing's syndrome (CS), including rapid weight gain, central obesity, proximal muscle weakness, moon facies, erythroviolaceous striae, buffalo hump and acanthosis nigricans. He also had arterial hypertension, diabetes mellitus and dyslipidaemia. Biochemical evaluation confirmed endogenous ACTH-dependent hypercortisolism. Initial pituitary magnetic resonance imaging (MRI) showed no identifiable lesion.

Given the absence of a visible pituitary adenoma, a structured diagnostic approach was undertaken to localize the source of ACTH excess. Differential diagnostic considerations included pituitary Cushing's disease (CD) and ectopic ACTH secretion (EAS). Cross-sectional thoracic imaging and extensive functional nuclear medicine studies, including 68Ga-DOTATOC PET/CT, 18F-FDG PET/CT and 18F-DOPA PET/CT, failed to identify an ectopic ACTH-producing tumor.

Inferior petrosal sinus sampling (IPSS) was performed to further differentiate between pituitary and ectopic ACTH secretion. However, the procedure was non-diagnostic due to incomplete bilateral catheterization, precluding definitive exclusion of a pituitary source. Repeated hormonal assessments demonstrated marked fluctuations in ACTH and cortisol concentrations during follow-up, complicating the interpretation of dynamic testing and the overall diagnostic process.

Results: Medical therapy with the 11β-hydroxylase inhibitor osilodrostat was initiated to control hypercortisolism while diagnostic evaluation continued. Treatment resulted in effective biochemical control and substantial clinical improvement. Glycemic parameters normalized, blood pressure and lipid profile improved, and classical manifestations of CS regressed, including recovery of muscle strength.

Following treatment initiation, a paradoxical transient decrease in ACTH levels was observed. Several pathophysiological mechanisms were considered, including cyclic ACTH secretion, partial tumor cell dysfunction, and complex feedback effects related to the accumulation of steroid precursors with residual glucocorticoid or mineralocorticoid activity. These observations underscore the non-linear and dynamic regulation of the ACTH–cortisol axis in ACTH-dependent CS under medical therapy.

Subsequent repeat pituitary MRI revealed a subtle hypointense lesion measuring <4 mm, supporting a normotopic ACTH source and favoring a diagnosis of pituitary Cushing's disease despite initially negative imaging.

Abstract citation ID: lvag096.1504

EP1267 - ECE_3153 - Neonatal septo-optic dysplasia: a case report

Daniel Duarte[1], Miguel Marques[1], Marta Almeida[1], H. Francisca[1], Ana Quítalo[1], Marta Andrade[2], David Barbosa[1], Sara Franco[1] and Maria Carlos Cordeiro[1]

[1]*Unidade Local de Saúde de Almada-Seixal, Almada, Portugal;* [2]*Unidade Local de Saúde Santa Maria, Lisbon, Portugal*

Introduction: Septo-optic dysplasia (SOD) is a rare congenital condition characterized by midline brain abnormalities, optic nerve hypoplasia and hypothalamic-pituitary dysfunction, affecting 1 in every 50 000 births.[1] Its exact etiology remains unclear.[1] We present a case of neonatal SOD causing panhypopituitarism.

Case Report: A newborn infant male was admitted to the Neonatology Intermediate Care ward for difficulty breastfeeding and persistent hypoglycemia (20-35 mg/dL) in his first 48 hours of life. His parents had no relevant medical history. The pregnancy had been followed since the 2nd trimester, with no diagnosis of gestational diabetes. Born at 40 weeks and 1 day by vaginal delivery, with an Apgar index of 9/10, initial physical examination revealed right cryptorchidism and micropenis.

Biochemical evaluation revealed hypoglycemia (43 mg/dL), hyponatremia (129 mmol/L), hyperkalemia (5.8 mmol/L), central adrenal insufficiency (0.64 µg/dL cortisol [RR 15.3 ± 7.9], 5.2 pg/mL ACTH [RR 83.9 ± 38]), hypogonadotrophic hypogonadism (LH <0.3 UI/L; FSH <0.3 UI/L; total testosterone <3.0 ng/dL 8.16 µg/dL), central hypothyroidism (TSH 6.52 mUI/L [RR 6.5 ± 2.4], free T4 1.27 ng/dL [RR 2.8 ± 0.61 ng/dL]) and low 1.2 ng/mL GH (RR > 5.0). 17-OH-progesterone was normal (7.11 ng/mL [RR 8.05 ± 2.73]).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Cranial MRI revealed pituitary stalk agenesia, ectopic neurohypophysis at the infundibular recess of the third ventricle and marked right optic nerve and optic chiasm hypoplasia. Ophthalmological examination was consistent with right optic nerve hypoplasia.

The infant was started on hydrocortisone 12 mg/m^2/day on day 3, followed by levothyroxine 25 mcg/day on day 12 and subcutaneous somatotropin 22 mcg/kg/day on day 20, with sustained normoglycemia, normalization of electrolyte disturbances and acquisition of feeding autonomy. He was discharged on day 37, with referral to Neuropediatrics, Pediatric Ophtalmology and Pediatric Endocrinology appointments.

At 6-month follow-up, adequate psychomotor development, weight gain and linear growth have been maintained under hydrocortisone, levothyroxine and somatotropin. Gonadotrophins and total testosterone remain untraceable.

Conclusion: The differential diagnosis of neonatal hypoglycemia must exclude adrenal insufficiency. In the face of panhypopituitarism, prompt MRI evaluation allowed an early diagnosis of septo-optic dysplasia and adequate treatment, with improved metabolic outcomes.

Reference

1. Mouhcine Y, Beyyato S, Ouazzani H, et al. Septo-optic dysplasia: a case report and systematic literature review. *Med Rep*. 2025;14:100357. https://doi.org/10.1016/j.hmedic.2025.100357

Abstract citation ID: lvag096.1505

EP1269 - ECE_3182 - Where is the source of Cushing's syndrome?

Dominika Ondruskova, Jana Leskova, Igor Durmek and Peter Vanuga
V.internal clinic of the Faculty of Medicine of Comenius University, National Institute of Endocrinology and Diabetology in Lubochna, Bratislava, Slovakia

Introduction: Cushing's syndrome remains a significant diagnostic challenge, particularly in cases with ambiguous or inconclusive imaging findings. Bilateral adrenal abnormalities may suggest a adrenal etiology of disease. However, comprehensive endocrine evaluation, including invasive diagnostic procedures, is essential for accurate localization of the source of inappropriate hormonal overproduction. Correct identification of the underlying pathology is crucial for targeted treatment and optimal long-term outcomes.

Case Report: We present the case of a female patient with clinical and biochemical features of hypercortisolism in whom initial imaging revealed bilateral adrenal lesions, raising suspicion of adrenal type of Cushing's syndrome. Despite this finding, hormonal evaluation supported an ACTH-dependent etiology. To clarify the source of ACTH secretion, bilateral inferior petrosal sinus sampling was performed, which conclusively demonstrated pituitary ACTH overproduction. Subsequent expert re-assessment of pituitary MRI subsequently identified a previously unrecognized microadenoma. Based on these findings, the patient was referred for stereotactic radiosurgical treatment using the Leksell Gamma Knife. Radiosurgical treatment resulted in gradual biochemical improvement and clinical stabilization.

Conclusion: This case highlights the importance of a systematic and multidisciplinary diagnostic approach in patients with Cushing's syndrome, especially when imaging findings and laboratory results are discordant.. Bilateral adrenal abnormalities do not necessarily represent the primary cause of hypercortisolism and may obscure a central ACTH-secreting source. Inferior petrosal sinus sampling plays a pivotal role in accurately localizing ACTH secretion and enables definitive, targeted therapy, including stereotactic radiosurgery. Long-term, multidisciplinary follow-up is essential to achieve sustained disease control and minimize complications.

Abstract citation ID: lvag096.1506

EP1271 - ECE_2058 - Crooke cell pituitary neuroendocrine tumor (PitNET) masquerading as ectopic ACTH syndrome: a diagnostic challenge of an aggressive variant

Yi-Hsuan Lai and Wan-Chen Wu
Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

Background: Crooke cell pituitary neuroendocrine tumors (PitNETs) are rare, aggressive variants of corticotroph adenomas characterized by extensive cytoplasmic hyaline change. These tumors are notorious for their clinically invasive behavior, higher recurrence rates, and potentially lower rates of biochemical remission compared to typical corticotroph tumors.

Case Presentation: A 65-year-old woman presented with progressive weakness and 15-kg weight loss within two months, and severe refractory hypokalemia (2.1 mmol/L). Laboratory evaluation confirmed ACTH-dependent hypercortisolism with ACTH 404.5 pg/mL, cortisol 55.7 μg/dL and loss of diurnal rhythm. High-dose dexamethasone suppression test yielded <50% cortisol suppression, initially raising suspicion of ectopic ACTH syndrome (EAS). Pituitary MRI identified a 1.2-cm adenoma, however, due to the severe clinical presentation, a systemic search for EAS was performed. Extensive imaging, including Ga-68-DOTATOC PET/CT, was negative for an ectopic source. Bilateral inferior petrosal sinus sampling (BIPSS) demonstrated a central-to-peripheral ACTH gradient, confirming a pituitary source.

Hypercortisolism showed poor response to high-dose fluconazole (up to 1200 mg daily), subsequently, pre-operative cortisol control was achieved using a combination of etomidate infusion and pasireotide. Staged transsphenoidal surgery was performed due to significant intraoperative hemorrhage. Histopathology confirmed a Crooke cell T-PIT lineage PitNET, displaying characteristic ring-like CAM5.2 staining (hyaline change), weak ACTH staining limited to cell periphery, and Ki-67 index <1%. Postoperatively, the patient achieved biochemical remission (ACTH 2.75 pg/mL, cortisol 14.60 μg/dL on physiological prednisolone replacement), though the course was further complicated by septic shock and acute kidney injury requiring intensive management.

Conclusion: This case highlights the diagnostic dilemma of Crooke cell tumors, which can closely mimic EAS due to extreme hypercortisolism and poor dexamethasone suppressibility. BIPSS remains the gold standard for localization when clinical and biochemical features are atypical, even in the presence of a pituitary mass. Despite a low proliferative index (Ki-67 <1%),

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Crooke cell adenomas often exhibit aggressive clinical behavior and high recurrence risk (up to 60%). Rigorous long-term surveillance is imperative for this aggressive subtype.

Abstract citation ID: lvag096.1507

EP1275 - ECE_1172 - Hypernatremia as the first manifestation of arginine vasopressin deficiency secondary to hypothalamic–pituitary disease: a case report

Sona Maghakyan, Sofiya Khachaturyan and Hovhannes Tumanian
Mikaelyan University Hospital, Yerevan, Armenia

Hypernatremia, defined as serum sodium >145 mmol/L, reflects a deficit of free water relative to sodium and is associated with significant morbidity and mortality if unrecognized. It usually results from inadequate water intake, excessive water loss, or sodium overload.

Neuroendocrine causes are uncommon but clinically significant, including central diabetes insipidus (CDI)-recently redefined as arginine vasopressin deficiency (AVP-D)-and hypothalamic disorders affecting thirst or osmoreceptor function. AVP-D arises from impaired synthesis or secretion of vasopressin and manifests as polyuria, polydipsia, and, in severe cases, hypernatremia. It may be congenital or acquired, typically secondary to pituitary or hypothalamic lesions, trauma, surgery, or autoimmune inflammation.

We report a case of severe hypernatremia as the first clinical manifestation of AVP-D caused by a hypothalamic-pituitary lesion, underscoring the diagnostic importance of copeptin and MRI in such presentations.

Case Presentation: A 71-year-old man was admitted with a five-month history of general weakness, dry mouth, polyuria (up to 5 L/day), headaches, weight loss (3-4 kg), and constipation. Symptoms began after a short febrile illness with diarrhea. He had no previous medical history.

Initial evaluation revealed severe hypernatremia (166 mmol/L). A CT scan showed a right adrenal incidentaloma and prostatic hyperplasia. Laboratory workup (renin, aldosterone, ACTH, TSH, HbA1c, glucose, PSA, plasma metanephrines, and urinary cortisol) was normal. Notable abnormalities were prolactin 30.5 ng/mL (normal: 4.0-15.2) and urine specific gravity 1.005. Given the symptoms of diabetes insipidus, copeptin was measured at <2.7 pmol/L with plasma osmolality 344 mOsm/kg, confirming AVP-D. MRI of the pituitary showed an endo- and suprasellar lesion suggestive of adenoma.

A diagnosis of AVP-D, hypernatremia, hyperprolactinemia, and right adrenal incidentaloma was made. The patient received 5% glucose infusions and intranasal desmopressin (one drop nightly for two days, then two drops twice daily), along with cabergoline 0.25 mg twice weekly. Within three days, polyuria and polydipsia subsided, serum sodium normalized (145 mmol/L), and urine specific gravity rose to 1.011.

Five months later, the patient developed headaches and behavioral changes. Repeat MRI revealed hypothalamic and optic tract edema, consistent with infundibulo-hypophysitis or hypothalamitis. Neurosurgery recommended conservative management with continued desmopressin and dexamethasone 4 mg daily, which stabilized symptoms.

Conclusion: Hypernatremia accompanied by polyuria and low urine osmolality should prompt evaluation for AVP-D. Integrating biochemical, radiological, and clinical data is essential to distinguish adenomatous from inflammatory causes of hypothalamic-pituitary dysfunction. Early diagnosis and appropriate hormone replacement can prevent complications and improve long-term outcomes.

Abstract citation ID: lvag096.1508

EP1277 - ECE_2996 - An incidental case of lymphocytic hypophysistis following traumatic brain injury

Teodora Puscas[1], Elena-Maria Pavel[1], Claudiu Zaharia[1], Diana Stanciu[2], Mihaela Stanciu[1,2] and Codruta Lebada[1,2]
[1]Medias, Romania; [2]Department of Endocrinology, Lucian Blaga University of Sibiu, Sibiu, Romania

Introduction: Lymphocytic hypophysitis is a rare autoimmune disease, characterized by lymphocityc infiltration of the pitutary tissue, leading to inflammation of the pitutary gland and/or infundibulum. Initially considered a condition predominantly affecting pregnant or postpartum women, recent studies have demonstrated a wider distribution across genders and age groups, with frequent associations with other autoimmune diseases. Clinical presentation is nonspecific and may mimic other pituitary disorders, such as pituitary adenomas. Diagnosis is primarily one of exclusion, based on pituitary MRI findings and biochemical evaluation, which typically reveals varying degrees of hypopituitarism. Management of this disease focuses on hormone replacement, antiinflamatory treatment and selective surgical intervention for mass efects.

Case Report: We present the case of a 64-year-old male patient who suffered an occupational traumatic brain injury in 2001 and subsequently presented for medical evaluation complaining of headache and vertigo. Cranial CT imaging raised the suspicion of lymphocytic hypophysitis, based on pituitary morphological changes, describing an enlarged anterior pituitary gland with inhomogeneous appearance on both native and post-contrast images, as well as pituitary stalk thickening. Hormonal evaluation confirmed plurihormonal anterior hypopituitarism, involving corticotropic, thyrotropic, and gonadotropic deficiencies. Hormone replacement therapy was initiated, consisting initially of Prednisone 5 mg/day, Levothyroxine 125 µg/day and Testosterone gel 16.2 mg/day, with subsequent dose adjustments according to follow-up assessments, leading to a favorable clinical evolution. The patient was also diagnosed with concomitant chronic autoimmune thyroiditis. However, 24 years after the initial diagnosis, MRI examination showed an area occupying a large portion of the glandular tissue, hypointense on T2-weighted images and hyperintense on T1-weighted images, showing no contrast enhancement, measuring 7/12.8 /7.3 mm, interpreted as a necrotic area. This finding will be subject to longitudinal imaging follow-up.

Conclusions: This case highlights that lymphocytic hypophysitis may present with heterogeneous clinical and radiological features at diagnosis and can be asymptomatic at disease onset. Early recognition is crucial, as hormonal deficiencies, particularly corticotropic insufficiency, is a life-threatening condition if left untreated. The association with chronic autoimmune thyroiditis further supports an autoimmune background and underscores the need to actively screen for concomitant autoimmune disorders. Lifelong follow-up is essential for appropiate adjustment of hormone replacement therapy and for the prevention or limitation of long-term complications.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1509

EP1278 - ECE_1372 - From prolactinoma to mixed pituitary tumor with thyroid autoimmune shift: a diagnostic and therapeutic challenge

Tea Shehu Kolnikaj[1,2], Maren Ruka[3], Jetmira Kerxhaliu[3], Doris Laçej[4], Mirel Grada[5], Klajdi Tarko[6] and Florian Toti[7]

[1]Endocrinology, American Hospital 3, Tirana, Albania; [2]Department of Clinical and Molecular Medicine, Sapienza University of Rome, Rome, Italy; [3]Neurosurgery, University Hospital Centre "Mother Teresa", Tirana, Albania; [4]Department of Pharmaceutical Sciences, Sapienza University of Rome, Rome, Italy; [5]Neurosurgery, American Hospital 3, Tirana, Albania; [6]Laboratory, University Hospital Centre "Mother Teresa", Tirana, Albania; [7]Endocrinology, University Hospital Centre "Mother Teresa", Tirana, Albania

Background: Mixed hormone-producing pituitary tumors are rare and may present diagnostic challenges, particularly when one hormonal component is clinically silent at presentation. Moreover, the coexistence of autoimmune thyroid disease further complicates both diagnosis and follow-up, especially in the context of shifts in thyroid autoimmunity.

Case Presentation: We report the case of a 31-year-old man referred for persistent headache and decreased libido. Initial evaluation revealed central hypogonadism, hypothyroidism with positive anti-TPO antibodies and low TSH, and markedly elevated prolactin levels. Adrenal and growth hormone (GH) axes were preserved. Pituitary MRI demonstrated a 2 cm macroadenoma. Medical therapy with cabergoline (up to 3 mg/week) and levothyroxine led to significant prolactin reduction and mild tumor shrinkage over one year.

However, despite stable imaging findings, a progressive increase in IGF-1 levels was observed during follow-up, raising suspicion of a mixed or evolving secretory phenotype. Therefore, transsphenoidal surgery was performed.

Results: Histopathological examination revealed a PIT-1–positive mixed mammo-somatotroph adenoma, predominantly prolactin-secreting, with co-expression of GH, Ki-67 index of 2%, absent mitoses, and negative p53, consistent with a low-grade tumor (Trouillas grade 2a). Postoperatively, IGF-1 normalized and prolactin levels improved. However, low-dose cabergoline was still required. Gonadal axis recovered and there was no evidence of adrenal insufficiency or diabetes insipidus. Postoperatively, a shift in thyroid autoimmunity was observed, from hypothyroidism to hyperthyroidism due to Graves' disease. Methimazole therapy was started. The patient remains under close endocrinological follow-up. Genetic testing is planned.

Conclusion: Mixed hormone–producing pituitary tumors may present diagnostic and therapeutic challenges, as they may initially present with predominant secretion of a single hormonal component. This case emphasizes the need for continuous reassessment of pituitary hormonal profiles, even in the presence of apparent treatment response. The development and shift of thyroid autoimmune disease during follow-up further highlights the importance of integrated endocrine surveillance.

Keywords prolactinoma, mammo-somatotroph tumor, pituitary surgery, thyroid autoimmunity, Graves' disease

Abstract citation ID: lvag096.1510

EP1279 - ECE_3122 - Pituitary incidentaloma unmasking subtle acromegaly: a macroadenoma case report

Muhammad Haroon Riasat[1], Samraiz Nafees[2], Khurram Qayyum[1], Muhammad Masroor Amjad[1], Najeeb Shah[1], Rehmat Karim[1] and Shiva Mongolu[1]

[1]Hull Royal Infirmary, Hull, United Kingdom; [2]Scarborough General Hospital, Scarborough, United Kingdom

Background: Acromegaly often develops insidiously and may first be suspected only when a pituitary lesion is detected incidentally on neuroimaging. Clinical features can be subtle despite established biochemical disease, particularly in patients with common comorbidities such as type 2 diabetes and hypertension. This case describes the journey from an incidental pituitary macroadenoma to a confirmed diagnosis of acromegaly, highlighting the importance of systematic endocrine evaluation and multidisciplinary management.

Case Report: A middle-aged man with type 2 diabetes (on metformin) and recently diagnosed hypertension (on lisinopril) underwent CT head imaging, which incidentally revealed a pituitary lesion. Subsequent pituitary MRI confirmed a 15-17 mm macroadenoma with suprasellar extension but no optic chiasm compression. Over the preceding year he had developed increasing tiredness and intermittent light-headedness, and more recently a persistent central pressure-type headache. He denied visual disturbance but reported an increase in shoe size from 10.5 to 11.5 and a perception that his hands were enlarging. Examination showed mildly coarse facial features, a widened nasal bridge, subtle prognathism and broadened digits, without obvious frontal bossing or macroglossia. Initial pituitary profile demonstrated elevated age-adjusted insulin-like growth factor-1 (IGF-1 ≈90 nmol/L) with growth hormone (GH) around 2 µg/L, normal thyroid function, low-normal testosterone with low sex hormone-binding globulin, normal gonadotrophins, mildly raised prolactin and borderline-low morning cortisol. A subsequent short synacthen test confirmed an adequate adrenal reserve. Repeat IGF-1 remained elevated and an oral glucose tolerance test showed failure of GH suppression, with values persistently 1.9-2.3 µg/L and a nadir around 1.9 µg/L, confirming acromegaly. Formal visual field testing was normal, concordant with the absence of chiasmal compression on imaging. The case was discussed at the pituitary multidisciplinary team meeting, which recommended transsphenoidal surgery as first-line treatment.

Conclusion: This case illustrates how a pituitary incidentaloma can unveil clinically important acromegaly when subtle phenotypic changes and cardiometabolic comorbidities are actively sought. It emphasises the need for high clinical suspicion, structured biochemical assessment and early multidisciplinary input, even in the absence of visual field defects, to enable timely surgical management and reduce long-term complication risk.

Abstract citation ID: lvag096.1511

EP1280 - ECE_1869 - Clinical profile of Cushing's syndrome patients attending a tertiary endocrine center in Nepal

Ansumali Joshi[1,2], Srijana Karmacharya[1], Puspa Dahal[1], Smriti Khadka[1], Radhika Tuladhar[1] and Sapana Yadav[1]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Kathmandu Diabetes and Thyroid Center, Lalitpur, Nepal; [2]Kathmandu Diabetes and Thyroid Centre, Kathmandu, Nepal

Cushing's syndrome patients' data in Nepal is lacking. We retrospectively reviewed data of all our Cushing's syndrome patients from 2010 to 2024. There were 33 patients. The mean age was 38.24 ± 13.37 years. Males were 6(18.18%) and females 27(81.82%) with M:F ratio 0.22:1. Mean weight was 72.93 ± 13.735 kg and BMI 30.78 ± 5.6 kg/m^2. ACTH dependent Cushing syndrome patients were 16(48.48%), ACTH independent syndrome 7(21.21%), iatrogenic Cushing syndrome 10(30.30%), Ectopic ACTH syndrome was 1. Common symptoms and signs were weight gain in 30(90.91%) patients, moon face 30(90.91%) patients, buffalo hump 28(84.85%), red abdominal stretch marks in 23(69.70%) patients, proximal weakness in 14(42.42%) patients. Hypertension was seen in 21(63.64%) patients and diabetes in 12(36.36%). Mean ONDST was 24.23 ± 16.20 µg/dl, LDDST was 21.61 ± 14.39 µg/dl and Mean ACTH level was 74.69 ± 19.08 pg/mL in ACTH dependent Cushing syndrome. Mean ONDST was 22.52 ± 10.44 µg/dl, LDDST was 27.90 ± 8.56 µg/dl and ACTH level was 5.66 ± 2.30 pg/mL in ACTH independent Cushing syndrome. In ACTH dependent Cushing syndrome, pituitary microadenoma was seen in 6 patients(37.5%) and macroadenoma in 5 patients(31.25%). In ACTH independent Cushing Syndrome, adrenal adenoma was seen in the right side in 4 patients (57.14%) and in 2 patients(28.57%)in the left side. For ACTH dependent Cushing syndrome, TNTS was done in 6 patients(37.5%) and SLTS in 1 patient(6.25%). For ACTH independent Cushing syndrome, Laparoscopic adrenalectomy was done in all 6 patients**.** For the patient with Ectopic ACTH syndrome, medical treatment with Ketoconazole was given and later on, bilateral adrenalectomy was done. For ACTH dependent Cushing syndrome, remission was seen in 10 patients(62.5%). Those who did not go into remission, medical treatment with Ketoconazole was done in 4 patients(66.66%) and bilateral adrenalectomy in 2 patients (33.33%). For ACTH independent Cushing syndrome, remission was seen in all 7 patients(100%).

Abstract citation ID: lvag096.1512

EP1281 - ECE_2436 - The role of Tolvaptan in an outpatient setting

Hafsah Hussain[1], Bhavini Bhatt[1], Furhana Hussein[1], Mohamed Baalawi[1], Aylin Can[1], Ilias Ibrahim[1] and Gideon Mlawa[1,2]
[1]Barking Havering and Redbridge Hospitals NHS Trust, London, United Kingdom; [2]Diabetes and Endocrinology, Queen's Hospital, Queen's Hospital Diabetes and Endocrinology Centre, London, United Kingdom

Introduction: Tolvaptan is a vasopressin-V2 antagonist, used in the treatment of hyponatremia. It functions through targeting type-2 receptors in the distal renal tubules, inhibiting the action of the hormone vasopressin. As a result, water reabsorption is reduced and excretion is increased, thus correcting the dilutional hyponatremia and balancing serum sodium levels.

Currently, Tolvaptan is most used for short-term, inpatient treatment. Due to its mechanism, Tolvaptan presents a high risk of rapid, overcorrection of serum sodium levels. Maximal change occurs within the first 24 hours, and it is therefore recommended that sodium levels are closely monitored during this period to prevent adverse events. However, there has been recent discussion into potential efficacy of this drug in the outpatient setting. We have explored a patient case where Tolvaptan was successfully provided as a longer-term treatment for symptomatic hyponatremia.

Case Report: A 72-year-old patient with a background of SIADH and left-sided adrenal adenoma had recurrent admissions to hospital since January 2023, due to acute confusion and vacant episodes secondary to euvolemic hyponatraemia (lowest Na: 119). This symptomatic hyponatraemia was treated in hospital and the patient was advised to fluid restrict to 750 mL and take demeclocycline and oral sodium tablets. However, it failed to correct the sodium and has led to multiple admissions, with some requiring intensive care support. On one admission, the patient was started on Tolvaptan as an inpatient, to which she showed a good response. She was discharged with 3.75 mg of Tolvaptan to be taken once a day as an outpatient, which has corrected her sodium (most recent Na: 134) and led to fewer admissions in hospital.

Discussion/Conclusion: This case illustrates the potential role of Tolvaptan in the management of hyponatraemia in an outpatient setting. Tolvaptan offers a targeted approach by antagonising vasopressin receptors, thus promoting free water excretion without affecting sodium retention. This treatment may be particularly beneficial for patients with recurrent, symptomatic hyponatremia who fail to respond to conventional therapies. This patient's successful management with Tolvaptan suggests that it can be a valuable therapeutic option in the outpatient care of patients with SIADH, leading to better sodium control and fewer hospitalisation episodes. Further studies are needed to better define its long-term efficacy and safety in this context.

Abstract citation ID: lvag096.1513

EP1283 - ECE_1288 - From neurology to endocrinology: subclinical Cushing's syndrome diagnosed in a patient with nonfunctioning pituitary macroadenoma

Sona Maghakyan and Sofiya Khachaturyan
Mikaelyan University Hospital, Yerevan, Armenia

Many endocrine diseases have neurological manifestations, and sometimes these manifestations appear at first. We would like to present a case of subclinical Cushing's syndrome.

Case Report: A 46-year-old man presented to a neurologist with the following complaints: feelings of anxiety, restlessness, insomnia, pronounced weakness in the upper and lower extremities, difficulty swallowing, unusual fatigue, decreased work capacity, pain in the lumbar region. The neurologist suspected myasthenia gravis (disproof) and referred for electroneuromyography and brain MRI examination. Brain MRI showed a pituitary macroadenoma. The patient was referred to an endocrinologist. During the examination, it was found that the patient had erectile dysfunction for about a month, the patient was overweight (BMI 27.5) and did not have diabetes or arterial hypertension.

Laboratory tests were performed: FSH, LH, Prolactin, ACTH, IGF-1, TSH, FT4 and free testosterone were within the normal range, 24-hour urine cortisol was 246.1 (N 11.5-102.0). 1 mg Dexamethasone test result was cortisol-60,84 (N <50).

Abdominal CT scan result: in the left adrenal gland, a round tissue formation measuring 4.0 * 3.3 * 3.5 cm.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Subclinical Cushing's syndrome diagnosis was made and decided to make left adrenalectomy after preparation for surgery. The patient underwent laparoscopic adrenalectomy. The histopathology result was adrenal adenoma. He was discharged on oral hydrocortisone 10 mg in the morning.

Conclusion: Cushing syndrome is caused by prolonged exposure to elevated levels of either endogenous glucocorticoids or exogenous glucocorticoids. It is a rare disorder and the estimated prevalence of Cushing's syndrome, considering all causes, ranges from 57 to 79 cases per million individuals. It has a lot of various clinical manifestations, including neurological. Patients may experience emotional liability, fatigue, and depression. In our case these complains make the patient to go to a neurologist and ACTH-independent Cushing syndrome with adrenal adenoma and nonfunctioning pituitary adenoma was diagnosed, which is a rare occurrence.

Abstract citation ID: lvag096.1514

EP1285 - ECE_3430 - Hypercalcitoninemia and large-cell neuroendocrine carcinoma of the lung: a diagnostic challenge

Leandro Augusto Silva[1], Bárbara Jesus[2], Joana Reis Guiomar[2], Mariana Lavrador[2], Daniela Guelho[2], Dírcea Rodrigues[2], Carla Baptista[2], Ana Margarida Novo[2], Vânia Almeida[2], Lina Carvalho[2] and Leonor Gomes[2]
[1]Endocrinology Department, Portuguese Institute of Oncology of Coimbra, Coimbra, Portugal; [2]Local Health Unit of Coimbra, Coimbra, Portugal

Introduction: Calcitonin-secreting neuroendocrine neoplasms (NENs) of the lung are rare, with a particularly difficult diagnosis due to their overlapping cytomorphologic and immunohistochemical features with medullary thyroid carcinoma (MTC). Although markedly elevated serum calcitonin strongly suggests MTC, it is not pathognomonic and may reflect ectopic secretion.

Clinical Case: 50-year-old female patient, presenting with a 3-month history of headache. Cranial CT identified a 2 cm left parietal lesion suggestive of primary brain tumour. Evaluated by Neurosurgery; cranial MRI demonstrated enlargement of the lesion and appearance of additional intracranial lesions, raising suspicion for metastatic disease. Surgical resection of the lesion was performed, and histopathological analysis was consistent with neuroendocrine neoplasm metastasis. Referred to Endocrinology with a 2-month history of cervical swelling and dysphonia. Physical examination revealed palpable masses consistent with cervical lymphadenopathy. Neck ultrasound showed a 3.7 cm right thyroid lobe nodule, EU-TIRADS-5, with fine-needle aspiration cytology suggestive of MTC/undifferentiated carcinoma. Calcitonin in needle washout of lateral cervical lymphadenopathy was 1164 pg/mL. Labs revealed calcitonin 2050 pg/mL (<5.0), CEA 6.2 ng/mL (<5.4), CgA 411 ng/mL(<85.0) and NSE 89 ng/mL(<15.0). Histological revision of the brain metastasis demonstrated positive immunohistochemical staining for calcitonin. Given the suspicion of metastatic MTC, germline *RET* testing was performed (no pathogenic variants identified). CT-CAP revealed a 43 × 29 mm lesion contiguous with the right thyroid lobe, suggestive of a nodal conglomerate. Lung imaging revealed a 28 × 21 mm irregular, heterogeneous lingular nodule suspicious for a primary pulmonary lesion. Additionally, bilateral adrenal metastatic involvement. Differential diagnosis included metastatic MTC (however, the presence of a solitary pulmonary metastasis and absence of hepatic metastases is less likely given the overall disease burden) VS primary lung malignancy VS two synchronous primary neoplasms. Biopsy of the lung lesion was performed with histopathological diagnosis of calcitonin-expressing large-cell neuroendocrine carcinoma of the lung, Ki-67 80%, PD-L1 expression in 60%. Somatic NGS in lung cancer did not identify actionable variants. After multidisciplinary discussion, systemic treatment with carboplatin and etoposide and whole-brain radiotherapy were proposed. The patient died following the first cycle of chemotherapy due to an infectious complication.

Discussion/Conclusions: This case highlights the diagnostic complexity of hypercalcitoninemia, particularly the challenge of distinguishing MTC from extrathyroidal calcitonin-secreting NENs, especially in patients with concurrent thyroid nodules or cervical disease, where metastatic MTC may be falsely assumed. This distinction is crucial because management and prognosis differ significantly, and misdiagnosis may lead to unnecessary interventions, including inappropriate thyroidectomy. Accurate diagnosis requires integrating clinical evaluation, histopathology/immunochemistry and targeted imaging to determine primary tumour origin.

Abstract citation ID: lvag096.1515

EP1286 - ECE_1531 - Pituitary apoplexy, the endocrinologycal stroke code: a case report

Belen del Arco Romualdo, Maria Jose Vallejo Herrera and Veronica Vallejo Herrera
Endocrinology, Hospital Regional Universitario de Málaga, Málaga, Spain

Introduction: Pituitary apoplexy is a rare but potentially life-threatening endocrine emergency, characterized by acute hemorrhage or infarction of the pituitary gland, most often occurring in the context of a pre-existing adenoma. Clinical presentation is highly variable and may mimic other neurological emergencies, frequently leading to diagnostic delay.

Case Presentation: We report the case of a 79-year-old man with arterial hypertension as his only relevant past medical history, who presented to the Emergency Department with severe headache exacerbated by Valsalva maneuvers and associated vomiting of 24 hours' duration. An initial non-contrast cranial computed tomography (CT) scan suggested a possible anterior communicating artery aneurysm versus a pituitary adenoma. Subsequent CT angiography ruled out vascular pathology, and conservative symptomatic management was initiated, with outpatient referral to Neurosurgery and Endocrinology.

Forty-eight hours later, the patient re-presented to the Emergency Department with syncope and worsening, refractory headache. A repeat non-contrast cranial CT scan revealed a hyperdense lesion consistent with intracranial hemorrhage in the sellar region, raising suspicion of pituitary apoplexy. A stroke code was activated, and the patient was transferred to a tertiary referral center.

On admission, neurological examination demonstrated new-onset diplopia and left temporal hemianopsia. Urgent laboratory evaluation, including biochemical profile, coagulation studies,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and pituitary hormonal assessment, revealed panhypopituitarism with secondary adrenal insufficiency. High-dose intravenous corticosteroid therapy was promptly initiated. Given initial neurological stability, a conservative approach with close neurological monitoring was chosen following neurosurgical evaluation.

Magnetic resonance imaging (MRI) performed 48 hours after admission confirmed the diagnosis of pituitary apoplexy. Although initial clinical improvement was observed, persistence of a left-sided visual field defect (quadrantanopsia) was noted after seven days of hospitalization. After multidisciplinary discussion, transsphenoidal surgical decompression was performed.

In the early postoperative period, the patient developed central diabetes insipidus requiring desmopressin therapy. Reassessment of pituitary function at 72 hours post-surgery confirmed persistent panhypopituitarism. The patient was discharged with replacement therapy including levothyroxine, hydrocortisone, and nocturnal desmopressin, with outpatient follow-up by Neurosurgery and Endocrinology.

Conclusion: This case highlights the diagnostic complexity of pituitary apoplexy and underscores the importance of early endocrine evaluation in patients presenting with acute neurological symptoms. A multidisciplinary approach is essential to optimize neurological and endocrine outcomes, and timely surgical intervention should be considered in cases with persistent visual impairment.

Abstract citation ID: lvag096.1516

EP1288 - ECE_3254 - Recurrence of ACTH-dependent Cushing's disease after pregnancy: clinical case

Khiuaz Ali, Anna Bazarova and Malika Kozhemzharova
Astana, Kazakhstan

Introduction: ACTH-dependent Cushing's disease (CD) is a rare endocrine disorder associated with significant morbidity. Transsphenoidal surgery (TSS) is the first-line therapy for an ACTH-secreting pituitary adenoma. However, even after surgical resection, recurrence may develop in up to half of cases.

Aim: To present and analyze a clinical case of recurrent ACTH-dependent CD with onset and relapse temporally associated with pregnancy and biochemical recurrence despite inconclusive pituitary imaging.

Methods: We retrospectively analyzed clinical history, biochemical data, pituitary imaging, inferior petrosal sinus sampling (IPSS), surgical findings, and histopathology of a patient with recurrent CD and 3 pregnancies with live births at term.

Case Presentation: A forty-three-year-old woman presented with biochemical relapse of ACTH-dependent CD. Initial manifestations appeared at age 24 years after the first pregnancy and included secondary amenorrhea, weight gain, central obesity, hirsutism, mood disturbances, and headaches. Low-dose dexamethasone suppression test showed lack of cortisol suppression, high-dose dexamethasone suppressed cortisol, twenty-four-hour urinary free cortisol was elevated, and CRH stimulation increased ACTH. Pituitary MRI revealed an adenoma with suprasellar extension.

The patient underwent TSS with histological confirmation of an ACTH-secreting pituitary adenoma. Remission persisted during 5 years. Two subsequent pregnancies occurred without complications. However, after the third pregnancy, symptoms of hypercorticism appeared and began to increase. ACTH levels gradually increased with weight gain and hypertension. Dopamine agonist therapy (cabergoline) provided partial control and was discontinued due to adverse effects.

IPSS with CRH stimulation confirmed pituitary ACTH hypersecretion. Repeat TSS yielded histologically confirmed ACTH-secreting adenoma. Postoperatively, adrenal insufficiency requiring glucocorticoid replacement, and transient diabetes insipidus requiring desmopressin. Within 2 years, the clinical picture of hypopituitarism resolved, and the following 2 years show no signs of hypercorticism. Follow-up MRI showed an empty sella with a small contrast- enhancing area suggestive of residual adenoma. Biochemical relapse occurred in late two thousand twenty-five and was confirmed on repeat testing. Currently, the patient is raising 3 children. No biochemical and clinical signs of CD were present at last follow-up.

Conclusion: Pregnancy may trigger onset and recurrence of ACTH-dependent CD. Biochemical relapse may precede radiological evidence, especially in empty sella. Long-term multidisciplinary surveillance with sensitive biochemical testing is essential for timely diagnosis and management. A rare case for Kazakhstan of successful management of a patient with ACTH-dependent CD and 3 pregnancies with live births at term is presented.

Abstract citation ID: lvag096.1517

EP1291 - ECE_3704 - A case of cyclic ectopic Cushing's syndrome

Emma Capparelli[1], Elisabetta Sciarroni[1], Maurizio Carbonari[1], Chiara Bologna[1], Giulia Marconcini[1], Filomena Cetani[2], Alessio Basolo[1], Claudio Urbani[1], Isabella Lupi[1], Ferruccio Santini[1] and Luca Manetti[1]
[1]*Department of Clinical and Experimental Medicine, Unit of Endocrinology 1, Pisa University Hospital, Pisa, Italy;* [2]*Rende (CS), Italy*

Background: Cyclic Cushing's syndrome (CCS) is a rare condition characterized by alternating phases of hypercortisolism and biochemical remission. Approximately 54% of CCS cases are pituitary-related, 26% results from ectopic ACTH secretion, and 11% are adrenal. Diagnosis is particularly challenging, as it requires biochemical assessment during active disease phases.

Case Presentation: A 58-year-old patient presented with recurrent episodes of generalized edema and arterial hypertension over a 4-year period, partially responsive to diuretics and antihypertensive therapy. Laboratory findings revealed neutrophilic leukocytosis and hypokalemia. In October 2022, a neuroendocrine tumor of the pancreatic body–tail was detected. In June 2024, referral to our Center confirmed radiological stability of the lesion and significant uptake on ^68Ga-DOTATOC PET/CT, consistent with a pancreatic neuroendocrine tumor; serum neuroendocrine tumor markers were negative.

Secondary causes of hypertension were investigated: catecholamine excess was excluded and mineralocorticoid function was preserved. An overnight 1-mg dexamethasone suppression test suggested hypercortisolism (serum cortisol 10.9 μg/dL). In July 2024, the patient developed a new episode of generalized

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

edema associated with markedly elevated ACTH (310 pg/mL) and serum cortisol (80.3 µg/dL), confirming cyclic ACTH-dependent hypercortisolism. Monthly urinary free cortisol monitoring was initiated, and the patient was admitted for further differential diagnosis and surgical evaluation.

During hospitalization, severe hypercortisolism with elevated ACTH levels, loss of circadian cortisol rhythm, and lack of suppression following both low- and high-dose dexamethasone suppression tests were documented. Pituitary MRI with gadolinium showed no pituitary abnormalities. Following multidisciplinary discussion, surgical resection of the pancreatic lesion was indicated, and adrenolytic therapy with metyrapone was initiated as a bridge to surgery.

In April 2025, the patient underwent robotic left pancreatectomy. Histopathology revealed a well-differentiated G2 neuroendocrine tumor (Ki-67 index 3%), positive for chromogranin A, synaptophysin, ACTH, and somatostatin receptor subtype 2 (SSTR2), with pancreatic parenchymal invasion and posterior margin involvement (pT1 N0 G2 R1). Postoperatively, glucocorticoid replacement therapy with cortisone acetate (37.5 mg/day) was initiated. One month after surgery, ACTH levels normalized; however, an inadequate cortisol response to the Synacthen test indicated secondary adrenal insufficiency, and glucocorticoid replacement therapy was therefore continued. Disease restaging was planned.

Conclusion:: This case highlights the diagnostic complexity of ACTH-dependent CCS and the risk of delayed diagnosis despite significant clinical manifestations. Identification of a resectable ectopic ACTH-secreting pancreatic neuroendocrine tumor enabled timely surgical treatment, the first-line treatmentfor ectopic Cushing's syndrome. Given the histological features and margin involvement, strict long-term follow-up is warranted due to the increased risk of persistence or recurrence disease

Abstract citation ID: lvag096.1518

EP1292 - ECE_3773 - Occult ectopic ACTH secretion in cyclic Cushing syndrome: a prolonged diagnostic and therapeutic challenge

Alina-Elena Șchiopu[1,2], Anca Matei[1,2], Georgiana Constantinescu[2], Viviana Adam[2], Alexandru Florescu[1,2], Stefana Bilha[1,2], Maria-Christina Ungureanu[1,2] and Cristina Preda[1,2]
[1]*Endocrinology, Saint Spiridon County Hospital, Iași, Romania;* [2]*University of Medicine and Pharmacy "Gr. T. Popa", Iasi, Romania*

Introduction: ACTH-dependent Cushing syndrome represents a major diagnostic and therapeutic challenge when the source of ACTH secretion remains elusive despite extensive investigations. Identifying ectopic ACTH-secreting tumors is particularly difficult in cyclic forms, where fluctuating biochemical activity may delay or preclude tumor localization. Severe hypercortisolism with intermittent remission further complicates diagnostic assessment, treatment monitoring, and long-term management.

Case Presentation: We report the case of a 61-year-old woman with a history of papillary thyroid microcarcinoma treated surgically in 2005. In 2016, she presented with progressive neuro-ophthalmic symptoms. Pituitary magnetic resonance imaging revealed a large sellar mass (23 × 35 × 29 mm) with optic chiasm compression. Incomplete transsphenoidal resection was performed. Histopathology confirmed a pituitary adenoma (Ki-67 index 4%), initially immunonegative for ACTH. At that time, pituitary hormonal work-up, including assessment of cortisol secretion, came back normal.

Later the same year, the patient developed severe ACTH-dependent hypercortisolism with hypokalemia. While patient history data from that period are scarce, abdominal imaging studies were performed, showing two left sided adrenal adenomas and bilateral adrenal hyperplasia, which led to the surgical removal of the left adrenal gland. Due to persistent diagnostic uncertainty, a second transsphenoidal surgery was subsequently undertaken, with immunohistochemistry demonstrating ACTH positivity. Follow-up pituitary MRI showed an empty sella.

Despite these interventions, the disease course was characterized by recurrent episodes of ACTH-dependent hypercortisolism with hypokalemia, profound muscle weakness, and diabetes mellitus, alternating with periods of biochemical remission, consistent with cyclic Cushing syndrome.

Further evaluation identified a large cephalo-isthmic pancreatic lesion, which was surgically resected; however, histopathological examination and subsequent clinical evolution excluded the pancreas as the source of ACTH secretion. During follow-up, a pulmonary nodule with progressive dimensional increase was detected, raising suspicion for an ectopic ACTH-secreting tumor. Functional imaging with 99mTc-tektrotyd SPECT/CT didn't show pathological tracer uptake. Because of severe complications related to prolonged hypercortisolism—including recurrent infections, respiratory failure, and major metabolic disturbances—definitive surgical or invasive diagnostic procedures were repeatedly deferred.

Medical treatment with steroidogenesis inhibitors was initiated. Given the cyclic disease pattern, a block-and-replace strategy combining ketoconazole with glucocorticoid replacement was adopted, allowing partial biochemical control. The condition was ultimately classified as occult ectopic ACTH secretion with cyclic activity.

Conclusions: This case underscores the complexity of ACTH-dependent Cushing syndrome when the source of ACTH secretion cannot be localized. Cyclic hypercortisolism, intermittent spontaneous remission, and limited interventional options substantially hinder diagnostic confirmation and disease monitoring, emphasizing the need for prolonged, individualized, multidisciplinary management.

Abstract citation ID: lvag096.1519

EP1293 - ECE_2138 - Clinical case of repid successful medical treatment of invasive prolactinoma in a man

Mykhailo Kyryliuk[1,2,3]
[1]*Endocrinology, Academic Medical Centre, Kyiv, Ukraine;* [2]*Academic Medical Centre, Kyiv;* [3]*Endocrinology, Kharkiv National Medical University, Kyiv, Ukraine*

Prolactin-secreting adenomas (prolactinomas) are the most common secreting pituitary neuroendocrine tumors (PitNETs \2017) (27.2%-40%) Invasive giant prolactinomas (IGPs) are a rare subtype of PitNETs (0.5%-4.4%). Their criteria include a maximum tumor diameter >40 mm, serum prolactin concentration >200 ng/mL, and tumor invasion into the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

cavernous sinus. IGPs are more common in young men due to its late diagnosis.[1] Biochemical and instrumental control of tumor growth is a current problem in neuroendocrinology due to its aggressive clinical course.[2] Dopamine agonists (DA) are used in the first-line treatment of prolactinomas.[3] However, their effectiveness in the treatment of IGPs is discussed.[4]

The successful treatment by AD cabergoline of IGP, incidentally detected on MRI after a car accident of a man aged 38 years, is presented. MRI was showed: The sella turcica is dilated, there is an invasion of bulky mass (measuring 26 × 24 × 25 mm) into sinus cavernous, which is tightly adjacents to the right internal carotid artery with deviation of the pituitary infundibulum to the left and back. After treatment of the injury, further blood examination was prescribed. Laboratory data showed the following results: serum PRL 1415.94 ng/mL (ref. 2.64-13.13), big-big PRL <1%, TSH 1.614 μIU/mL (0.4-4.85), morning cortisol 8.49 μg/dl (4.82-19.5), somatomedine C1 (IGF-1) 121 ng/mL (58-219), LH 2.04 mIU/mL (0.57-12.07), FSH 2.18 mIU/mL (0.95-11.95), testosterone total 12.39 nmol/l (8.33-30.19). It was prescribed cabergoline (dosage 0.5 mg per week). After 1 months from the start of medical treatment PRL concentration decreased to 2.67 ng/mL, and after 4 months – down to 1.53 ng/mL, tumor volume decreased by 19.74%, LH level increased up to 3.68 mIU/mL, FSH level – to 3.93 mIU/mL, testosterone total concentration – to 17.05 nmol/l.

Conclusion: Thus, the results of drug treatment showed a very good tumor sensitivity to cabergoline without side effects with an improvement of pituitary gonadotropic function, which predetermines further positive dynamics of tumor size reduction.

Keywords invasive prolactinoma, cabergoline

References

1. Schaller B. Gender-related differences in prolactinomas. A clinicopathological study. *Neuro Endocrinol Lett*. 2005;26(2): 152-159.
2. Shrivastava RK, Arginteanu MS, King WA, Post KD. Giant prolactinomas: clinical management andlong-term follow up. *J Neurosurg*. 2002;97(2):299-306. https://doi.org/10.3171/jns.2002.97.2.0299
3. Melmed S, Casanueva FF, Hoffman AR, et al. Diagnosis and treatment of hyperprolactinemia: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96(2): 273-288. https://doi.org/10.1210/jc.2010-1692
4. Maiter D, Delgrange E. Therapy of endocrine disease: the challenges in managing giant prolactinomas. *Eur J Endocrinol*. 2014;170(6):R213-R227. https://doi.org/10.1530/EJE-14-0013

Abstract citation ID: lvag096.1520

EP1294 - ECE_1300 - Recurrent colonic diverticular bleeding in acromegaly: improvement after surgical remission

Naotetsu Kanamoto[1,2], Yuki Minamoto[1], Yui Yamashita[1], Yumiko Sasai[1], Keiko Yamagami[1] and Kenichi Ishibashi[3]
[1]Department of Endocrinology, Osaka City General Hospital, Osaka, Japan; [2]Department of Endocrinology and Metabolism, National Hospital Organization Kyoto Medical Center, Kyoto, Japan; [3]Department of Neurosurgery, Osaka City General Hospital, Osaka, Japan

Background: Acromegaly is associated with various gastrointestinal complications, particularly colorectal neoplasms. However, non-neoplastic colonic disorders, including diverticular disease and diverticular bleeding, have been less well characterized.

Case Presentation: A 64-year-old woman had experienced recurrent episodes of hematochezia for two years, which were suspected to be due to colonic diverticular bleeding. During the same period, she developed progressive snoring and noticed enlargement of her fingers, such that rings no longer fit. Four months prior to referral, she was hospitalized for sigmoid colon diverticular bleeding, and acromegaly was suspected based on her characteristic facial features. Endocrinological evaluation revealed insufficient suppression of growth hormone (GH) during a 75-g oral glucose tolerance test (OGTT), elevated insulin-like growth factor-1 (IGF-1), and mild hyperprolactinemia. A paradoxical GH response to thyrotropin-releasing hormone (TRH) stimulation was observed. GH suppression with octreotide was insufficient, while bromocriptine markedly suppressed both GH and prolactin (PRL). Pituitary MRI revealed a 5-mm tumor. The patient underwent endoscopic endonasal transsphenoidal surgery. Histopathological examination demonstrated tumor cells positive for Pit-1, GH, and PRL, with perinuclear CAM5.2 staining. Co-expression of GH and PRL within the same tumor cells led to a diagnosis of mammosomatotroph pituitary neuroendocrine tumor. Postoperatively, IGF-1 normalized, GH was adequately suppressed during OGTT, the paradoxical TRH-induced GH response disappeared, and PRL levels and responsiveness improved.

Outcome and Discussion: Although episodes of diverticular bleeding persisted after surgery, their frequency remarkably decreased during a 44-month follow-up period. Previous studies have reported a higher prevalence of colonic diverticula in patients with acromegaly, which is associated with disease duration and GH-related colonic morphological changes, such as colonic elongation. In addition, endothelial dysfunction in small vessels has been described in active acromegaly and may contribute to diverticular bleeding. Improvement in GH/IGF-1 excess might ameliorate these pathological changes and may be associated with a reduced risk of diverticular bleeding.

Conclusion: This case suggests that acromegaly may contribute to recurrent colonic diverticular bleeding. Biochemical remission may be associated with a reduction in bleeding frequency. Clinicians should consider non-neoplastic colorectal complications in patients with acromegaly, in addition to surveillance for colorectal neoplasms.

Abstract citation ID: lvag096.1521

EP1295 - ECE_3618 - Clinical, biochemical, and radiological outcomes of persistent acromegaly: insights from a small case series

Mariam Bulashvili, Nino Zavrashvili and Mariam Orjonikidze
Tbilisi Institute of Medicine, Tbilisi, Georgia

Background: Acromegaly is a rare condition caused by a growth hormone (GH)-secreting pituitary adenoma driving excess

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

secretion of insulin-like growth factor-1 (IGF-1). In addition to the somatic features, uncontrolled acromegaly is associated with a number of complications and excess mortality. Transsphenoidal pituitary surgery is generally first-line treatment. Residual disease after surgery remains a major challenge in the management of acromegaly. Treatment options for persistent acromegaly include radiotherapy or medical therapies.

Methods: We retrospectively reviewed five patients with acromegaly who underwent transsphenoidal surgery. Clinical features, comorbidities, postoperative MRI findings, serum IGF-1 levels, and subsequent management strategies were analyzed.

Results: All patients presented with acral enlargement, maxillofacial changes, and hyperhidrosis (100%). Metabolic comorbidities were common, with dyslipidemia in 40%, hypertension in 25%, and diabetes mellitus in 20% of patients. Postoperative MRI revealed residual pituitary tissue in four patients. Residual disease was associated with persistent elevation of IGF-1 levels and clinical symptoms, necessitating adjuvant therapy, including Gamma-Knife radiosurgery and treatment with somatostatin analogs and/or dopamine agonists. Improvement in biochemical markers was accompanied by symptom improvement during follow-up. One patient achieved biochemical and radiological remission following surgery alone.

Conclusion: Postoperative residual tissue in acromegaly correlates with persistent biochemical activity and symptom burden. Integrated clinical, biochemical, and radiological assessment is essential to guide individualized postoperative management.

Patient	Pre-op IGF-1/GH & MRI	Post-op IGF-1/GH & MRI	Follow-up / Treatment
42-year-old male	IGF-1 1500 mcg/L; MRI: Hypodense adenoma 23 × 20 × 25 mm	IGF-1 500 mcg/L; MRI: Residual tissue 10 × 11 × 12 mm	Gamma Knife radiosurgery; IGF-1 323 mcg/L Octreotide 20 mg initiated;
27-year-old female	IGF-1 850 mcg/L, GH 3.95 ng/mL; MRI: Hypodense adenoma 13-14 mm (densely granulated)	IGF-1 700 mcg/L; MRI: Residual tissue 9 × 12 × 9 mm	Gamma Knife radiosurgery; IGF-1 504 mcg/L Octreotide 20 mg + Cabergoline initiated;
31-year-old female	IGF-1 875 mcg/L, GH 15.2 ng/mL; MRI: Hypodese macroadenoma	MRI: Residual tissue 4.1 × 7.6 × 7.6 mm; After repeat TSS - IGF-1 361 mcg/L	Declined somatostatin analogs; Cabergoline initiated. Current IGF-1 239 mcg/L; MRI: no residual tissue
58-year-old female	IGF1 890 mcg/L; MRI – Adenoma 30 × 34 × 31 mm;	MRI: Residual tissue; IGF-1 796 mcg/L	Octreotide 20 mg initiated;
57-year-old female	IGF-1 742 mcg/L; MRI: Adenoma 30 × 26 × 21 mm	IGF-1 111 mcg/L; MRI: No residual tissue	No adjuvant therapy; IGF-1 normalized

Abstract citation ID: lvag096.1522

EP1296 - ECE_2225 - Cortisol normalization with osilodrostat reduces sleeping metabolic rate and protein oxidation in Cushing's disease: a case report

Alessio Basolo[1], Isabella Lupi[1], Claudio Urbani[1], Luca Manetti[1], Paolo Piaggi[2], Alberto Landi[2] and Ferruccio Santini[1]
[1]Endocrinology Unit, University Hospital of Pisa, Pisa, Italy; [2]Department of Information Engineering, University of Pisa, Pisa, Italy

Chronic hypercortisolism causes major metabolic disturbances that adversely affect whole-body energy metabolism, leading to central adiposity, and progressive skeletal muscle loss. We have recently shown that severity of hypercortisolism is positively associated with 24-h energy expenditure (24hEE) and protein oxidation (Protox). However, whether cortisol normalization with medical therapies such as osilodrostat, an oral 11β-hydroxylase inhibitor, can affect body composition and 24hEE, sleeping metabolic rate (SMR) and Protox has not been investigated.

A 45-year-old woman with ACTH-dependent hypercortisolism due to a pituitary adenoma experienced multiple disease recurrences despite 3 trans-sphenoidal pituitary surgeries.

In 2024 disease recurrence with characteristic clinical features of hypercortisolism was demonstrated by elevated 24-hour urinary free cortisol levels (mean UFC: 228-119 μg/24 h, normal values: 11-70). Pituitary MRI did not identify a clearly detectable adenoma. Treatment with osilodrostat was started at 1 mg once daily and up-titrated to 1 mg twice daily leading to a UFC normalization (mean UFC: 24-30 μg/24 h), accompanied by an overall clinical improvement.

To explore metabolic effects beyond conventional biochemical endpoints, body composition and 24-hour energy metabolism were assessed both during active hypercortisolism and following cortisol normalization, 12 months after osilodrostat initiation.

Body composition was evaluated by dual-energy X-ray absorptiometry (DXA), while 24-h energy metabolism was assessed using whole-room indirect calorimetry, the gold-standard method for measuring 24-h energy metabolism and macronutrient oxidation.

Lean soft tissue was unchanged (33.3 kg at baseline vs 33.9 kg at follow-up). 24-h EE was reduced (1252 kcal/d at baseline vs 1154 kcal/d at follow-up), as well as SMR (815 kcal/d at baseline vs 663 kcal/d at follow-up) and Protox (431 kcal/d at baseline vs 194 kcal/d at follow-up). This combined reduction in 24-h EE, SMR and Protox occurring in the absence of changes in lean mass, may reflect restoration of a more physiological cortisol rhythm and improved metabolic regulation.

In a patient with refractory Cushing's disease, osilodrostat achieved biochemical control. While lean soft tissue had not yet

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

recovered, treatment was associated with a reduction in 24hEE, SMR and Protox, supporting the hypothesis that effective medical control of hypercortisolism may contribute to the restoration of metabolic physiology. These observations warrant confirmation in larger, prospective studies.

Abstract citation ID: lvag096.1523

EP1298 - ECE_1416 - Pituitary apoplexy in a patient with diabetic foot: a case report

Kader Ugur[1], Dilek Kılınç Candemir[1] and Ahmet Furkan Tuntaş[2]
[1]*İnternal Medicine, Endocrinology and Metabolism, Fırat University, Elazıg, Turkey;* [2]*İnternal Medicine, Fırat University, Elazıg, Turkey*

Introduction: Pituitary apoplexy is an extremely rare condition, and estimated prevalence is approximately 6.2 cases per 100 000 people. Pituitary apoplexy, characterized by acute ischemia or hemorrhage of the pituitary gland, can be life-threatening, and it may be precipitated by various factors. Diabetes is one such major factor. In approximately 80% of cases, the presence of a pituitary adenoma is unknown before the occurrence of apoplexy. This report aimed to present a rare case of acute pituitary apoplexy that developed while the patient was being followed for diabetic foot at our clinic.

Case: A 79-year-old man with a 15-year history of type 2 diabetes mellitus, hypertension, ischemic heart disease, and hyperlipidemia was admitted to our endocrinology clinic for a discharging wound on the second toe of the left foot that had appeared approximately 15 days earlier. As his diabetes was poorly controlled owing to HbA1c of 10.7%, intensive insulin therapy was initiated. For the diabetic foot, daily wound care and broad-spectrum antibiotic therapy were conducted based on clinical, laboratory, and imaging assessments. During follow-up, cranial imaging was performed owing to sudden severe headache, deterioration in general condition, intermittent diplopia, hypotension, and nausea and vomiting, incidentally revealing a pituitary macroadenoma measuring approximately 3×2 cm compatible with subacute hemorrhage. This was deemed indicative of pituitary apoplexy. Based on visual field examination and multidisciplinary evaluation, surgery was not considered and conservative treatment was planned. His laboratory findings are shown in the table. Under close monitoring with physical examination and clinical and laboratory follow-up, the patient was started on stress-dose hydrocortisone and appropriate fluid replacement for hemodynamic stabilization; treatment for his other chronic comorbidities was continued. The patient's general condition stabilized, and the headache and diplopia subsided. As the patient developed permanent pituitary insufficiency, hydrocortisone and levothyroxine replacement therapy were instituted.

Conclusion: Given the high morbidity and mortality associated with pituitary apoplexy, it is crucial that treatment decisions are made through multidisciplinary evaluation.

Table 1 Laboratory findings of the patient.

IGF-1 (ng/mL)	64	71-290
GH (ng/mL)	<0.05	0.06-5
FSH (mIU	1.5	0.7-11
LH (mIU)	0.14	1.7-8.6
Total testosterone (ng/mL)	15.7	181-772
TSH (IU/mL)	0.03	0.55-4.78
st4 (ng/dL)	0.72	0.89.1.76
st3 (pg/mL)	1.44	1.57.4.71
ACTH (pg/mL)	<5	0-46
Cortisol (mcg/dL)	1.59	6.2-19.4
Prolactin (ng/mL)	0.86	4.1-18.4
Glucose (mg/dL)	91	74-106
Creatinine (mg/dL)	1	0.5-1.3
AST (U/L)	34	0-34
ALT (U/L)	45	10-49
HbA1c (%)	10.7	4.6-6
CRP (mg/L)	52	0-5

Abstract citation ID: lvag096.1524

EP1300 - ECE_2441 - Unusual presentations of AVP deficiency presenting as cognitive impairment and renal function impairment

Furhana Hussein, Gideon Mlawa, Edel Casey and Nemanja Stojanovic
Barking Havering and Redbridge Hospitals NHS Trust, London, United Kingdom

Introduction: Cranial diabetes insipidus (DI) known as AVP deficiency is a rare disorder caused by impaired secretion in arginine vasopressin (AVP) in central DI or response in nephrogenic DI. Affects 1 in 25 000 people and usually presents with polyuria and polydipsia. The most common acquired causes include autoimmune, infection, primary or secondary tumours, neurosurgery and head trauma.

Here we discuss two cases in which AVP deficiency presented with cognitive and renal function impairment.

Case 1: 31 year-old female admitted with reduce oral intake, dehydration, cognitive impairment, and acute kidney injury (AKI). Past medical history TB meningitis which led to stroke. Blood test showed hypernatraemia 174 mmol/L and MRI showed increase in size of lesion in left hypothalamus and midbrain with further new lesions. Plasma glucose 33.6 mmol/L suggesting new onset of Type 2 diabetes. Endocrine input was required as serum osmolality remained high despite treatment of hyperglycaemia. Serum osmolality was 314 mosmol/kg, urine osmolality 481 mosmol/kg. She was started on DDAVP which led to clinical improvement and normalised serum osmolality.

She was treated with quadruple anti-tuberculous medication for 14 months and required second-line anti-tuberculous medication.

Case 2: 54 year-old male initially presented to different hospital with cognitive impairment, memory issues alongside worsening headaches. CT showed Chordoid Glioma of third ventricle requiring VP shunt, debulking of tumour and radiotherapy.

He was reviewed in endocrine clinic for low testosterone on background of third ventricle pathology and found to have high osmolality and was admitted to hospital for water deprivation test. He was diagnosed with AVP deficiency and full pituitary profile revealed partial hypopituitarism secondary to his third ventricle tumour.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

He was treated with hydrocortisone, desmopressin, levothyroxine, testosterone.

Conclusion: Here we discuss two cases in which AVP deficiency initially presented as cognitive impairment due to severe dehydration and AKI thought to be secondary to hypothalamic or brain injury. It is important that a multidisciplinary team approach is used for individualised management of these patients to achieve the best outcome.

Question:

1. Have come across unusual presentation of AVP deficiency?
2. Have you seen cognitive or renal impairment as initial presentation of AVP deficiency in your patients?

Abstract citation ID: lvag096.1525

EP1301 - ECE_1817 - "Vanishing" macroprolactinoma—complete Tumour regression after a decade of cabergoline therapy

Zhenya Ruseva[1,2], Radina Dimitrova[1,2], Mira Siderova[1,2] and Kiril Hristozov[1,2]

[1]*Second department of Internal diseases, Medical University of Varna, Clinic of Endocrinology and Metabolic diseases, Varna, Bulgaria;* [2]*Second department of Internal diseases, UMHAT "Sveta Marina" Varna, Clinic of Endocrinology and Metabolic diseases, Varna, Bulgaria*

Introduction: Prolactinomas are the most common functioning pituitary adenomas. They are characterised by autonomous prolactin secretion and a wide spectrum of clinical manifestations. These range from hypogonadism and infertility to mass effects in larger tumours. They occur more frequently in women but tend to be larger and more aggressive in men. Treatment options include medical therapy with dopamine agonists, transsphenoidal surgery and, in selected cases, radiotherapy. Treatment is tailored to the characteristics of the tumour, the preferences of the patient and the patient's response to therapy.

Case Report: A 30-year-old male presented with decreased libido, erectile disorder, ejaculatory failure and gynaecomastia with increased breast sensitivity over the last two years. Laboratory hormonal analysis revealed hyperprolactinemia and secondary hypogonadism (prolactin 1821 mIU/L; LH 0.753 mIU/L; FSH 2.28 mIU/L; total testosterone 4.61 nmol/L). An MRI scan of the pituitary gland showed an oval lesion measuring 11/8/11 mm in the right pituitary lobe, which was displacing the infundibulum slightly to the left. There was no evidence of compression of the optic chiasm or the suprasellar cerebrospinal fluid spaces, nor invasion of the cavernous sinus or the depicted parts of the internal carotid artery and carotid siphon. Treatment with cabergoline at a dosage of 2×0.5 mg weekly was initiated, and the patient was monitored regularly. Normalisation in prolactin levels and gonadal function was observed, which led to reducing the cabergoline dosage to 0.25 mg weekly. The MRI follow-up of the adenoma revealed disappearance of the tumour formation within 10 years. During this period no changes in the heart valves was registered.

Conclusions: Despite emerging recommendations that increasingly favour early surgical intervention in patients with prolactinomas, this case underscores the enduring effectiveness of long-term pharmacological therapy. Sustained treatment with dopamine agonists can lead not only to biochemical control but also to profound tumour regression, even complete radiological disappearance, in carefully monitored patients. This outcome highlights the heterogeneity of prolactinoma behaviour and reinforces the importance of individualized management strategies. Pharmacological therapy remains a valid and potentially curative approach, particularly for patients who respond well, tolerate treatment and prefer to avoid surgical risks.

Keywords pituitary adenoma, prolactinoma, tumor regression, cabergoline

Abstract citation ID: lvag096.1526

EP1676 - ECE_1686 - Predictive molecular biomarkers in aggressive Pituitary Tumors

Angeliki Theodorou[1], Andrew Lin[2,3,4], Jamal Benhamida[5], Subhiksha Nandakumar[6], Tina Alano[7], Anthony Heaney[8], Julie M. Silverstein[9], Kelly Braun[10], Sharon L. Wardlaw[11], Nazanin K. Majd[12], Andjela T. Drincic[13], Jie Chen[13], Dawn Armstrong[14], Marc Rosenblum[5], Viviane Tabar[2,3] and Eliza Geer[1,2,3]

[1]*Endocrinology, Medicine, Memorial Sloan Kettering Cancer Center, New York, United States;* [2]*Neurosurgery, Memorial Sloan Kettering Cancer Center, New York, United States;* [3]*Multidisciplinary Pituitary and Skull Base Tumor Center, Memorial Sloan Kettering Cancer Center, New York, United States;* [4]*Neurology, Memorial Sloan Kettering Cancer Center, New York, United States;* [5]*Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, United States;* [6]*Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center, New York, United States;* [7]*Memorial Sloan Kettering Cancer Center, New York, United States;* [8]*University of California Los Angeles, Los Angeles, United States;* [9]*Barnes Jewish Hospital, Saint Louis, United States;* [10]*Barrows Neurological Inst, Phoenix, United States;* [11]*New York-Presbyterian/Columbia University Irving Medical Center, New York, United States;* [12]*Md Anderson Cancer Center, Houston, United States;* [13]*University of Nebraska Medical Center, Omaha, United States;* [14]*Memorial University of Newfoundland, Saint John's, Canada*

Aggressive behavior in pituitary tumors is characterized by rapid growth or progression despite standard treatments, including surgery, radiotherapy (RT), and medical therapies. Within this subset of tumors, there is heterogeneity in clinical behavior with limited predictive biomarkers. To identify prognostic biomarkers, we performed next-generation sequencing of tumor and a matched normal sample from 38 patients with aggressive pituitary tumors, comprised of 18 (47.4%) metastatic and 20 (52.6%) non-metastatic tumors, on a sequencing protocol. We then correlated genetic profile with clinical behavior, including progression-free survival (PFS), defined as the time from the first progression after RT until the time of next progression, which was available for 34 of 38 patients. A pathogenic or likely pathogenic mutation in *TP53, ATRX, DAXX,* or *SF3B1* was identified in 52.9% of metastatic and 60.0% of locally aggressive tumors ($P = .746$) and was associated with shorter PFS (median 10.3 ($n = 20$) vs 25 ($n = 13$) months; $P = .015$). In contrast, the presence of a USP8 mutation in corticotroph tumors (14.3%) was associated with a longer PFS (150.0 ($n = 3$) vs 14.0 ($n = 16$) months; $P = .026$). Among the corticotroph tumors ($n = 21$), recurrent chromosomal loss of heterozygosity (defined as loss of ≥10 of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

the following chromosomes: 1, 2, 3, 4, 6, 10, 11, 15, 17, 18, 21, and 22) was identified in 80% of cases and was associated with shorter PFS (11.8 ($n = 14$) vs 150 ($n = 5$) months; $P = .015$). Cell-cycle pathway alterations (CCND1/2/3 amplification, CDK4/6 amplification, CDKN2A/B/C loss, RB1 loss) were identified in at least one tumor sample in 24.3% of the cohort in both corticotroph tumors and those within the PIT1 lineage. These alterations were frequently subclonal and associated with metastatic dissemination (47.1% metastatic cohort vs 5.0% locally aggressive cohort; OR = 15.6; $P = .006$). Given that cell cycle alterations drive tumor progression, we interrogated our cohort for patients treated with a CDK4/6 inhibitor. Of the 4 patients treated with an inhibitor, tumor stabilization was achieved in 2 patients for 12 and 24 months. This study demonstrates the utility of genetic profiling pituitary tumors for clinical decision making; sequential tumor sampling may be valuable for detecting acquired mutations of prognostic importance.

Abstract citation ID: lvag096.1527

EP1684 - ECE_2135 - The Canadian acromegaly registry: a national registry for real-world evidence

Syed Imran[1], Deanna Badiuk[2], Constance Chik[3], Marie-Eve Domingue[4], Ezzat Shereen[5], Fabienne Langlois[6], Kirstie Lithgow[7], Heather Lochnan[8], Juan Andres Rivera Ramirez[9], Stan Van Uum[10] and Victoria Hodgkinson[11]

[1]Dalhousie University, Halifax, Canada; [2]Acromegaly Canada, Chilliwack, Canada; [3]University of Alberta, Edmonton, Canada; [4]Université Laval, Québec, Canada; [5]University Health Network, Etobicoke, Canada; [6]Université De Sherbrooke, Sherbrooke, Canada; [7]University of Calgary, Calgary, Canada; [8]The Ottawa Hospital, Ottawa, Canada; [9]McGill University, Montreal, Canada; [10]St Joseph's Health Care London, London, Canada; [11]Lumiio Inc., Calgary, Canada

Background: The Canadian Acromegaly Registry (CAR) is a nationwide disease registry that collects both clinic- and patient-reported data on individuals with acromegaly. Although recent advances in multimodal therapy have improved patient outcomes, there remains a critical need for real-world evidence to address knowledge gaps in rare disorders. The objective of CAR is to better assess the needs of the Canadian acromegaly population to enhance patient-focused care. Here, we present baseline data on the initial cohort of patients enrolled in CAR.

Methods: CAR is currently active at 8 academic centres across 4 provinces with planned nationwide expansion. Data are collected at each centre by trained coordinators and include both clinic-reported data on disease onset, progression, treatments, as well as patient-reported outcomes. Additional data include biomarkers, surgical history, radiotherapy, medication use, tumor data and comorbidities.

Results: As of December 15, 2025, 187 participants are registered with complete baseline data. Patients were 51% (96) females and mean age at diagnosis was 47 (+/−14) years. Overall, 35% patients reported having symptoms of acromegaly at diagnosis, 14% were found incidentally, and 51% were unknown/not answered. Of the 35% diagnosed based on symptoms, 82% had classical facial features at diagnosis, 80% reported hand and 82% reported foot enlargement. The baseline IGF-1 (% upper limit of normal) was reported in 64 individuals, with a mean of 217% (+/−122). Of the 93 patients with baseline tumor size reported, tumor size was >1 cm in 72% and <1 cm in 28%. Primary therapy was surgery in 115 (61%) patients, 31 (17%) also received radiotherapy and 40% were receiving medical therapy. The most commonly reported comorbidities were arthritis (30%), hypertension (28%), obstructive sleep apnea (25%), dyslipidemia (18%), and diabetes mellitus (13%).

Conclusions: CAR has been established to collect a prospective and retrospective, longitudinal dataset that will help evaluate acromegaly care and outcomes. Efforts to expand into other academic and community centres are ongoing to create a comprehensive national dataset.

Abstract citation ID: lvag096.1528

EP1909 - ECE_3955 - Developing PCOS cell therapy using human GnRH cell repopulation in a GnRH-Killswitch mouse model

Jacob Short[1,2], Robert Harris[1], Elisabet Stener-Victorin[1], Frida Holm[1] and Susan Wray[2]

[1]Karolinska Institutet, Solna, Sweden; [2]US National Institute of Neurological Disorders & Stroke, Bethesda, United States

GnRH cells are the final integrator of the LH surge generator in the hypothalamus and sole initiators of the LH pulse signal in the pituitary. The aetiology of Polycystic Ovarian Syndrome (PCOS) involves dysregulation of the feedback regulation facilitated by the GnRH pulse. As such, GnRH cells represent an opportunity to intervene in the neuroendocrine origin of hormone dysfunction through replacement of endogenous cells with engineered neurons to regulate the GnRH pulse. We made a GnRH cell knockout mouse model, *GnRH-Killswitch*, inducible with diphtheria toxin. This model is useful for robust depletion of GnRH neurons at postnatal timepoints and permanent central deactivation of the reproductive system while retaining the ovaries. Human embryonic stem cells differentiated to GnRH cells are transplanted into the third ventricle to repopulate the empty niche. We have engineered the human cells to express murine IL-10 to extend graft survival in immunocompetent mice. Immunocompetent mice are used for this human chimera strategy to more accurately model the reproductive system and reduce the overall number of animals required to develop this protocol. Subsequently, existing strategies will be used to integrate estrous cycle timing into the engineered replacement cells. Using this new model will provide insight into how one can 1) regulate dysfunctional pulse generators, 2) prevent feedback amplification in neuroendocrine systems and 3) treat hormone disorders such as PCOS.

Abstract citation ID: lvag096.1529

EP1304 - ECE_2731 - Characterization of detransition cases in a specialized gender identity clinic in the Canary Islands

Kevin David Díaz Gorrín, Selena Rodriguez Fernandez, Javier Panizo Fra, Paula Pérez, Ana Paola Leon Ocando, Óliver Quintero Rodríguez, Itziar Aznar Ondoño, Juan Ignacio Márquez De La Rosa, Laura Mesa Suárez and Patricia Cabrera García

Endocrinology and Nutrition, Hospital Universitario de Canarias, San Cristóbal de La Laguna, Spain

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Gender detransition, understood as the process of discontinuing or reversing a gender transition, is an emerging and poorly understood phenomenon. The aim of this study was to clinically and demographically characterize individuals who underwent some form of detransition after being evaluated at the specialized Gender Identity Clinic of the Endocrinology and Nutrition Department at the Complejo Hospitalario Universitario de Canarias since 2023.

Material and Methods: A retrospective descriptive study was conducted analyzing sociodemographic and clinical variables of patients who attended the Endocrinology and Nutrition clinics from 2023 until 2025.

Results: Twenty-one detransition cases were identified. Of these, 57.1% had identified as trans men, 28.6% as trans women, and 14.3% as non-binary individuals. The mean age was 23 years (range 16-45). Regarding geographic distribution, 42.9% lived in the southern area of Tenerife, 38.1% in the north, and 19.0% in La Palma. Hormonal treatment had been initiated in 85.7% of cases, with a mean duration of 26.2 months (median: 23), while 14.3% had not started treatment. Gender-affirming surgery had been performed in 38.1% of individuals. The most frequent reasons for detransition were identifying as non-binary (23.8%), treatment side effects (19%), and doubts regarding gender identity (14.3%). According to the Expósito-Campos classification, 71.4% were categorized as secondary detransitions.

Conclusions: Most observed detransitions were secondary, with many individuals maintaining a trans or non-binary identity. The predominant profile was a young person assigned female at birth who initiated hormonal treatment during adolescence and detransitioned in early adulthood. A significant proportion had undergone gender-affirming surgery.

Abstract citation ID: lvag096.1530

EP1305 - ECE_3741 - Clinical profile and implications of primary vs secondary medical detransitions: experience from a transgender care unit in spain

Mariana Jesús Gomes Porras[1,2,3,4], Mónica Tomé García[1] and Guadalupe Cano Oncala[5]

[1]*Endocrinology and Nutrition, Regional University Hospital of Málaga, Malaga, Spain;* [2]*Institute of Biomedical Research of Málaga (IIBIMA), BIONAND Platform, Málaga, Spain;* [3]*Biomedical Research Networking Center for Diabetes and Associated Metabolic Diseases (CIBERDEM), Group CB07/08/0019, Málaga, Spain;* [4]*Endocrinology and Nutrition, Regional University Hospital of Málaga, Málaga, Spain;* [5]*Psychology, Regional University Hospital of Málaga, Málaga, Spain*

Background: Detransition is the process of partially or completely stopping or reversing social, medical, and/or administrative changes during gender transition, which may be temporary or permanent.

Objective: To compare the clinical profile of transgender individuals who underwent primary vs secondary medical detransition and received follow-up at the Transgender Care Unit (TCU) of a Spanish hospital between 1999-2025.

Material and Methods: This cross-sectional descriptive study included 40 transgender individuals aged ≥14 years who reported deciding to discontinue cross-sex hormone therapy (CHT). Severe psychiatric comorbidity was defined as the presence of self-harm, suicidal ideation, and/or suicide attempts. Detransitions were classified as primary, with identity desistance, or secondary, without identity desistance.

Results: Of the 40 detransition cases, 36 (90%) began follow-up at the TCU in the last 8 years. 72.5% ($n = 29$) were secondary detransitions, all partial and 65.5% permanent. The remaining 27.5% ($n = 11$) were primary, all complete and permanent. Regret was reported exclusively in primary detransitions, in a markedly high proportion (72.7% vs 0%, $P < .001$). The median time from the start of medical gender transition to detransition was 22 months (range:1-300), with primary detransitions lasting longer than secondary ones [25 months (range:5-300) vs 22 months (range:1-108), $P = .3$, respectively].

Overall, 62.5% ($n = 25$) were transgender men. The median current age of the individuals was 24.5 years (range:18-61). The median age at the first consultation at the TCU was 19.5 years (range:14-61), while the median age at initiation of CHT was 18 years (range: 14-44), which was lower due to prior self-administered hormone therapy in 20% of cases. A total of 65% of participants ($n = 26$) lacked family support (primary 72.7% vs secondary 62%, $P = .5$). All participants had psychiatric comorbidities, which were severe in 52.5% of cases (primary 54.5% vs secondary 51.7%, $P = .8$). A total of 12 individuals (30%) underwent sex reassignment surgery (SRS), with a similar proportion in primary and secondary detransitions (primary 27.3% vs secondary 31%, $P = .81$). Four of these 12 individuals (33.3%) underwent SRS involving genital/gonadal procedures, a proportion that was clinically significant among primary detransitions (primary 2/3 individuals, 66.6% vs secondary 2/9 individuals, 22.2%; $P = .29$).

Conclusions: Distinguishing between primary and secondary detransitions has important psychological and therapeutic implications. In our cohort, primary detransitions were characterized by a longer duration of CHT, a higher proportion of genital/gonadal SRS, and elevated rates of negative affect, such as regret, combined with a high prevalence of severe psychiatric comorbidity.

Abstract citation ID: lvag096.1531

EP1306 - ECE_2077 - Testosterone formulations in gender-affirming hormone therapy: efficacy, safety, and subject satisfaction

Emilia Gomez Hoyos[1,2], Lucía Estévez Asensio[1], Esther Delgado Garcia[1], Marta Mesonero Alonso[3], Maria Jose Bartolome Albistegui[3], Ruth Gonzalez Collantes[3], Alicia Perez Bustillo[3], Ana Casas Marcos[3], Carmen Rodriguez Fernandez[3] and Daniel De Luis Román[1]

[1]*Endocrinology and Nutrition, Clínico University of Valladolid Hospital. IBioVall.IENVA.CIBEROBN, Valladolid, Spain;* [2]*Endocrinology, Hospital Clinic Universitario de Valladolid, Valladolid, Spain;* [3]*Clínico University of Valladolid Hospital, Valladolid, Spain*

Introduction: Gender affirming hormone therapy (GAHT) in transgender men favors their virilization.

Aims: To evaluate the effects, the development of adverse events, and the associated satisfaction-CRES-4 questionnaire- with different testosterone formulations one year after initiation of GAHT.

Material and Methods: Retrospective study in transgender men with GAHT (>1 year), attended at the Transgender Medicine Unit

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

of the Clinico of Valladolid Hospital from January 2014 to January 2025. Recording of clinical, analytical and CRES-4 questionnaire. Statistical analysis of the data by the SPSS-V17 program.

Results: A total of 69 trans men aged 24 [22-24] years were included, with initiation of GAHT at 18 [17-21] years. Fifty-one (75%) started intramuscular short-acting testosterone ester at 100 mg every 15 days, with an increase to 200 mg at 3 months, and 17 (25%) started testosterone gel at 50 mg/day. After one year, serum testosterone levels were 411 [251-680] vs 760 [483-1248] ng/dL ($P = .030$), and estradiol levels were 49 [34-79] vs 48 [35-62] pg/mL ($P = .824$) in the ester and gel groups, respectively. Within the testosterone range of 260-1000 ng/dL, 32/43 subjects r eceiving esters and 12/14 receiving gel achieved target levels ($P = .316$). Estradiol <50 pg/mL was observed in 23/45 subjects in the ester group and 8/13 in the gel group ($P = .366$). Adverse effects included erythrocytosis in 9 (80%) vs 2 (20%) subjects ($P = .521$). The change in total cholesterol was 5 [−15 to 20] vs −3 [−11.0 to 10.7] mg/dL ($P = .462$), and triglycerides changed by 3.5 [−8 to 26] vs −28 [−31 to −0.95] mg/dL ($P = .024$) in the ester and gel groups, respectively. The CRES-4 score was 255 [230-267] vs 262 [242-275] points ($P = .146$) in the ester vs gel groups, respectively.

Conclusion: Testosterone gel may offer a more favorable efficacy and safety profile than intramuscular short-acting testosterone esters. Importantly, treatment satisfaction, as assessed by CRES-4, was comparable between both formulations.

Abstract citation ID: lvag096.1532

EP1307 - ECE_2315 - The effect of inositol on fractalkine-mediated metabolic inflammation in women of reproductive age with prediabetes

Mariana Ivanishchak[1], Iryna Kostitska[1], Nadiia Zherdova[2] and Sofiia Shelever[1]
[1]*Endocrinology, Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine;* [2]*Endocrinology, Center for Innovative Medical Technologies of NAS of Ukraine, Kyiv, Ukraine*

Prediabetes in women of reproductive age is accompanied by chronic low-grade inflammation, which plays a key role in the progression of insulin resistance and the development of cardiometabolic complications. Fractalkine, a chemokine with both adhesive and chemotactic properties, is a key mediator of the interaction between adipose tissue, the immune system, and the endothelium. Standard therapeutic approaches for prediabetes have a limited impact on markers of dysadipocytokinemia, which substantiates the need for additional pathogenetically targeted interventions.

Objective: To evaluate the effect of inositol on serum fractalkine levels in women of reproductive age with prediabetes.

Materials and Methods: The study included 36 women aged 19-44 years diagnosed with prediabetes (mean duration 1.8 ± 0.2 years), with glycated hemoglobin (HbA1c) of 6.0 ± 0.4% and fasting plasma glucose of 6.1 ± 0.2 mmol/L. All participants had class II-III obesity (BMI-37.4 ± 1.65 kg/m^2) and insulin resistance (IR) (HOMA-IR- 8.2 ± 0.4). The patients were randomized into two groups (Gr): Gr A ($n = 18$) received basic basic medical therapy (BMT), including lifestyle modification, metformin 500-2000 mg/day, alpha-lipoic acid 600 mg/day, and cholecalciferol 800-10 000 IU/day; Gr B ($n = 18$) received BMT supplemented with inositol at a daily dose of 2000 mg. The duration of follow-up was 12 weeks. Serum levels of fractalkine, leptin, and insulin were measured at baseline and at the end of the study using enzyme-linked immunosorbent assay (ELISA).

Results: After 12 weeks of therapy, women in Gr A demonstrated a favorable trend toward a reduction in serum fractalkine levels from 2.48 ± 0.13 ng/mL to 2.02 ± 0.24 ng/mL; however, this change did not reach statistical significance ($P = .09$). In contrast, group B showed a significant decrease in fractalkine concentrations from 2.41 ± 0.31 ng/mL to 1.28 ± 0.36 ng/mL ($P < .001$), with significantly lower levels compared to the BMT-only group ($P = .002$). In Gr B, the reduction in fractalkine was accompanied by statistically significant improvements in key carbohydrate and hormonal parameters. Fasting plasma glucose decreased from 6.12 ± 0.48 to 5.41 ± 0.39 mmol/L ($P < .001$), HbA1c from 6.3 ± 0.4% to 5.7 ± 0.3% ($P < .001$), HOMA-IR from 8.21 ± 0.62 to 6.15 ± 0.51 ($P < .001$), and serum leptin levels from 28.6 ± 4.2 to 20.3 ± 3.6 ng/mL.

Conclusions: In women of reproductive age with prediabetes, the addition of inositol to standard therapy attenuates fractalkine-mediated metabolic inflammation, which is accompanied by significant improvements in metabolic parameters and may contribute to a reduction in cardiometabolic risk.

Abstract citation ID: lvag096.1533

EP1308 - ECE_2575 - How Lysophosphatidylcholine affects human Granulosa cell survival gene expression

Isabel Nogueira[1], Andre Lagoa[1], Thatiane Luca[1], Tania Maria Ortiga-Carvalho[1,2] and Flavia Bloise[1]
[1]*Universidade Federal do Rio de Janeiro, Instituto de Biofísica Carlos Chagas Filho, Rio de Janeiro, Brazil;* [2]*Instituto de Biofísica Carlos Chagas Filho—UFRJ, Rio de Janeiro, Brazil*

Hashimoto's thyroiditis is one of the most prevalent autoimmune diseases in women of reproductive age. Although it has been associated with impaired female fertility, the underlying mechanisms are still unclear. Follicular fluid is a key component of the oocyte microenvironment, with a distinct metabolic profile that is essential for adequate oocyte development. Previous work from our group demonstrated that the follicular fluid composition of Hashimoto's patients differs from that of euthyroid patients', with glycerophospholipid metabolism being the most significantly altered pathway, characterized by increased lysophosphatidylcholine 16:0 levels. This bioactive lipid acts as a second messenger, regulating inflammation and mitochondrial function. However, its role in the reproductive axis remains poorly understood. Therefore, this study aimed to investigate the lysophosphatidylcholines' impact on granulosa cell physiology, which is central cell to follicular development. Human granulosa cells line (COV434) were exposed to lysophosphatidylcholine 16:0 (0 µM—control, 50 µM and 100 µM—dose observed in euthyroid patients, 150 µM and 200 µM—dose observed in Hashimoto's thyroiditis patients) for 24 hours. Cell viability was assessed using the PrestoBlue assay and the expression of genes related to cell adhesion (CTNNB1), intercellular communication (GJA1), steroidogenesis (STAR) and the prostaglandin pathway (PTGS2) was analyzed by RT-qPCR. Data were analyzed by one-way ANOVA followed by Tukey's multiple comparisons test,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

with $P < .05$ considered statistically significant. At physiological concentrations (50 μM), lysophosphatidylcholine increased granulosa cell viability by 33% ($P = .0187$). Conversely, exposure to 150 μM decreased viability in almost 40% ($P = .0061$) and 200 μM in over 80% ($P < .0001$). Based on these viability results, subsequent gene expression analyses were performed using 50 and 150 μM lysophosphatidylcholine. The genes associated with cell adhesion (CTNNB1), intercellular communication (GJA1) and steroidogenic (STAR) pathway did not show alterations in expression. However, cells exposed to the 150 μM dose showed increased expression of PTGS2 (1.56 ± 0.13) compared to both control (1.00 ± 0.25; $P = .0013$) and 50 μM (0.75 ± 0.37; $P < .0001$) groups, suggesting an upregulation of the inflammatory prostaglandin pathway, consistent with known effects of lysophosphatidylcholine in other cell types. Our results suggest that, at concentrations comparable to those observed in Hashimoto's patients, lysophosphatidylcholine decreases granulosa cell viability and increases PTGS2 gene expression. Investigating additional genes associated with lysophosphatidylcholine metabolism and mitochondrial function will be essential to further clarify the molecular pathways underlying these effects.

Abstract citation ID: lvag096.1534

EP1309 - ECE_2687 - Empirical evaluation of Thyroid function and ovarian reserve using one-way ANOVA

Fotima Makhmudova and Khurshida Nasirova
Tashkent state medical university, Tashkent, Uzbekistan

Ovarian reserve (OR) reflects follicular quantity and quality and determines female reproductive potential. Diminished ovarian reserve (DOR) is associated with reduced fertility and lower effectiveness of assisted reproductive technologies.[1] Beyond aging, hypothyroidism significantly contributes to OR impairment. Thyroid hormone imbalance disrupts folliculogenesis, ovulation, and steroidogenesis via the hypothalamic–pituitary–gonadal axis, accelerating follicular depletion.[2] Immuno-inflammatory processes, including systemic inflammation, oxidative stress, may further promote follicular atresia and adverse reproductive outcomes.

Objective: To evaluate the association between thyroid function and ovarian reserve in women of reproductive age, with particular emphasis on hormonal, inflammatory markers.

Methods: A total of 100 women aged 18-38 years were enrolled and divided into 3 groups: healthy euthyroid women with normal OR(control, $n = 20$); women with DOR and hypothyroidism(DOR + hypothyroidism, $n = 40$); and women with DOR and euthyroid status (DOR+euthyroidism, $n = 40$). Serum levels of thyroid-stimulating hormone (TSH), anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), C-reactive protein (CRP), complement C3, ceruloplasmin were measured. Blood samples were collected in the early follicular phase (cycle days 2-4). One-way ANOVA with Dunnett's T3 post-hoc test was applied for statistical analysis.

Results: TSH levels were significantly higher in the DOR+hypothyroidism group (6.97 ± 0.61 mIU/L) compared with controls (1.57 ± 0.12 mIU/L) and the DOR+euthyroidism group (1.76 ± 0.08 mIU/L) ($P < .001$). AMH levels were significantly lower in women with DOR +hypothyroidism (0.57 ± 0.05 ng/mL) than in controls (3.98 ± 0.17 ng/mL) and women with DOR+euthyroidism (0.98 ± 0.08 ng/mL) ($P < .001$). No significant intergroup differences were observed for FSH ($P = .973$). CRP levels were highest in the DOR+hypothyroidism group (30.25 ± 1.58 mg/L), compared with controls(3.09 ± 0.48 mg/L) and the DOR+euthyroidism group (13.53 ± 0.94 mg/L) ($P < .001$). Complement C3 and ceruloplasmin followed a similar pattern, being maximal in the DOR+hypothyroidism group (6.76 ± 0.64 and 84.55 ± 4.59), intermediate in the DOR+euthyroidism group (2.57 ± 0.30 and 51.35 ± 2.14), and minimal in controls (1.18 ± 0.06 and 34.30 ± 2.08) ($P < .001$). Age did not differ significantly between groups ($P = .156$).

Conclusions: Hypothyroidism is associated with a more pronounced decline in OR, reflected by significantly reduced AMH levels compared with euthyroid women with DOR. Elevated inflammatory markers indicate that systemic inflammation and oxidative stress contribute to ovarian dysfunction in hypothyroid patients. Routine assessment and timely correction of thyroid dysfunction should be considered essential in the evaluation and management of women with DOR and infertility.

Abstract citation ID: lvag096.1535

EP1311 - ECE_3107 - Metabolic dysfunction–Associated Steatotic Liver Disease (MASLD) in lean women with PCOS: prevalence, phenotypic distribution, and predictive value of HOMA-IR

Valentina Elezovic Kovacevic[1,2], Sanja Ognjanovic[1,2], Bojana Popovic[1,2], Dusan Ilic[1], Milica Opalic Palibrk[1], Lena Radic[1], Katarina Krstic[1], Natalija Dragicevic[1] and Djuro MacUt[1,2]
[1]Department for Endocrine Tumors and Hereditary Cancer Syndromes, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Belgrade, Serbia; [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction: Polycystic ovary syndrome (PCOS) is a common endocrine disorder frequently associated with metabolic dysfunction, which overlaps with the pathophysiological mechanisms underlying metabolic dysfunction–associated steatotic liver disease (MASLD). We assessed the presence of hepatic steatosis in women with PCOS using the validated non-invasive Fatty Liver Index (FLI), calculated based on body mass index (BMI), waist circumference (WC), triglycerides, and gamma-glutamyl transferase.

Methods: FLI was analysed in 164 lean women with PCOS (median BMI 22.2 kg/m^2 [IQR 15.8], median WC 78 cm [IQR 15]) to determine the prevalence of MASLD overall and across PCOS phenotypes defined by the Rotterdam criteria. Participants were stratified into MASLD-positive and MASLD-negative groups based on FLI cut-off values (≥60), and metabolic and hormonal parameters were compared. Receiver operating characteristic (ROC) analysis was performed to identify the optimal HOMA-IR cut-off for determining the presence of MASLD.

Results: Phenotype A was the most prevalent (48.8%), followed by phenotypes D (19.5%), B (18.9%), and C (12.8%). Oligo/amenorrhea and anovulation were present in 43.9% and 81.7% of women, respectively, while hyperandrogenism was observed in 80.5%. Polycystic ovarian morphology was confirmed in 81.7%; insulin resistance (HOMA-IR) was present in 61% of patients. The overall prevalence of MASLD assessed by FLI was 13.4%, with phenotype-specific rates of 13% in phenotype A, 6% in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

phenotype B, 3% in phenotype C, and none in phenotype D. Statistically significant differences in FLI values were present between phenotypes A and D, B and C, and C and D (all $P < .001$). MASLD-positive women (13.4%) had significantly higher waist circumference ($P < .001$), triglycerides ($P < .001$), fasting insulin ($P < .001$), and HOMA-IR ($P < .001$). Regarding hormonal parameters, SHBG was significantly lower, while FAI and estradiol were significantly higher in MASLD-positive women (all $P < .001$), with no significant differences in total testosterone, DHEA-S, or androstenedione ($P > .05$). ROC analysis showed that HOMA-IR was a good predictor of MASLD (AUC = 0.884, 95% CI: 0.818-0.950; $P < .001$), with an optimal cut-off of 3.13 (91% sensitivity, 57% specificity). Alternative thresholds of 3.4-3.6 are giving similar sensitivity with improved specificity (~65%-67%).

Conclusions: MASLD is relatively common among women with PCOS, even in a lean population and shows phenotype-specific distribution. HOMA-IR appears to be a reliable predictor of MASLD, suggesting that MASLD screening should be considered even in normal-weight women with PCOS, particularly those with elevated HOMA-IR.

Abstract citation ID: lvag096.1536

EP1312 - ECE_1595 - Childhood adversity, poverty, and PCOS: results from a rural county cross-sectional survey

Akanksha Misra and Kylie King
State University of New York, Plattsburgh, United States

Objective: To explore the impact of rural childhood experiences and poverty on PCOS by determining the following: a). Associations of adverse childhood experiences (ACEs) with (potential) PCOS. b). Whether social determinants of health (SDoH) mediate this relationship. c). How challenges of growing up in rural areas- ACEs, SDoH and parental involvement- might impact the likelihood of PCOS.

Background: PCOS has for some time now been demonstrated as a bio-eco-social syndrome significantly impacted by social, emotional, and environmental factors. ACEs specifically might be dysregulating maturation of the hypothalamic-pituitary ovarian axis and/or the development of metabolic dysfunction, serving as precursors for PCOS. As interdisciplinary scholars in rural New York where poverty, foster care, and addiction issues are rampant, we build on our previous and other studies demonstrating correlations between SDoH, ACEs, and development of features of PCOS. We hope to highlight social and emotional factors impacting PCOS development, which could inform preventative and healing therapies for underserved populations.

Methods: Cross-sectional survey of adult respondents ($N = 145$) living in the North Country region of New York State, gathering data on SDoH, PCOS diagnosis and potential PCOS indicators (irregularity, male pattern hair growth, and weight gain), parental involvement, and ACEs. All analyses were conducted in R.

Results and Discussion: In an OLS model predicting confirmed and potential PCOS, ACEs score emerged as the only statistically significant predictor. Item-level correlations identified verbal abuse and emotional neglect and abuse as most strongly associated with PCOS indicators. Mediation analyses provided no evidence that SDoH mediated the relationship between ACEs and PCOS. Parental background and involvement composites were associated with ACEs but not with SDoH or PCOS indicators. While larger, unbiased population studies across different rural demographics are needed to make generalizations, our small study highlights a few things: a). Emotional neglect and abuse and verbal abuse in childhood might serve as precursors for PCOS, as consistently demonstrated in other high quality studies. b). ACEs could occur irrespective of adverse SDoH and/or more expansive frameworks for SDoH and their interactions with ACEs need to be explored, and c). The role of parent(s) in childhood might be an overlooked factor to be more deliberately explored in future research. Either way, routine attention to childhood love and care, especially for rural populations experiencing high levels of childhood adversity, should be part of any therapeutic plan of treatment.

Abstract citation ID: lvag096.1537

EP1313 - ECE_3497 - When hydration harms: two cases of peripartum hyponatraemia

Lia Anguelova, Mike Matheou, Bahram Jafar-Mohammadi, Christine May and Aparna Pal
Endocrinology, OCDEM, Oxford, United Kingdom

Encouraging hydration during labour is a common practice intended to prevent dehydration, maintain uterine activity, avoid ketosis, and support fetal wellbeing. However, excessive fluid intake, particularly in the presence of oxytocin, may lead to dilutional hyponatraemia with potentially serious maternal and neonatal consequences. We report two cases of peripartum hyponatraemia occurring in otherwise low-risk pregnancies.

Case 1: A 40-year-old primigravida with no significant past medical history and an uncomplicated pregnancy presented in spontaneous labour. Labour progress was slow, and oxytocin augmentation was commenced. During the second stage, she became increasingly confused, with poor ability to follow instructions for guided pushing, and was transferred to a high-dependency unit. Oxytocin doses were further escalated, and operative vaginal delivery with forceps was required. She sustained a postpartum haemorrhage of approximately 900 mL, treated with two doses of ergometrine and a further oxytocin infusion (40 units diluted in 5% dextrose). She consumed approximately 2 litres of oral fluids during labour.

Venous blood gas analysis revealed severe hyponatraemia (serum sodium 110 mmol/L). Neurological examination showed a Glasgow Coma Scale (GCS) score of 12, nystagmus, and a sixth cranial nerve palsy. She was admitted to intensive care for close monitoring. Significant polyuria occurred, necessitating cautious fluid replacement (dextrose 5%) to avoid rapid sodium correction. Serum sodium normalised over 48 hours, with complete neurological recovery within 24 hours. The neonate was healthy.

Case 2: A 34-year-old woman (G2P0) presented in spontaneous labour at a local hospital. A dark urine sample prompted encouragement of oral fluid intake, and she consumed approximately 2-2.5 litres of water during labour. She required transfer for emergency caesarean section due to obstructed labour. Pre-operative serum sodium was 120 mmol/L, falling to 115 mmol/L following oxytocin administration. Plasma osmolality was 242 mOsm/kg and urine osmolality 117 mOsm/kg. She remained asymptomatic with a GCS of 15/15. Postoperatively, she

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

was managed with fluid restriction and careful monitoring, with gradual normalisation of sodium over 48 hours. The neonate was healthy.

Conclusions: Peripartum dilutional hyponatraemia is a potentially serious but preventable complication of labour. Excessive oral intake, hypotonic intravenous fluids, and oxytocin use are key risk factors. Neurological symptoms during labour or postpartum should prompt urgent electrolyte assessment. Careful fluid management and avoidance of rapid sodium correction are essential to prevent harm. Greater awareness is needed, as this condition is likely under-recognised.

Abstract citation ID: lvag096.1538

EP1314 - ECE_2251 - Trafficking of Follicle-Stimulating Hormone Receptor (FSHR) is modulated by the interaction with G Protein-Coupled Estrogen Receptor (GPER)

Clara Lazzaretti[1], Carmela Perri[1,2], Samantha Sperduti[1,3], Giada Mercanile[1,4], Manuela Simoni[1,3,5] and Livio Casarini[1,3]
[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [2]International PhD School in Clinical and Experimental Medicine (CEM), University of Modena and Reggio Emilia, Modena, Italy; [3]Center for Genomic Research, University of Modena and Reggio Emilia, Modena, Italy; [4]Department of Dermatology, Surgical, Medical and Dental Department of Morphological Sciences Related to Transplant, Oncology and Regenerative Medicine, University of Modena and Reggio Emilia, Modena, Italy; [5]Department of Medical Specialties, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy

Follicle-stimulating hormone receptor (FSHR) and G protein-coupled estrogen receptor (GPER) are expressed in the ovary, where they regulate folliculogenesis by forming membrane heterocomplexes in granulosa cells. FSHR/GPER heteromers sustain oocyte survival by reprogramming FSH-dependent pro-apoptotic signals into anti-apoptotic/proliferative events. We evaluated whether FSHR/GPER heterocomplex-specific trafficking impacts FSH-mediated signalling.

HEK293 cells were transiently transfected with tagged FSHR-, GPER-, and biosensor-coding plasmids. FSHR- and FSHR-GPER-expressing cells were treated with 10 nM FSH, in the presence and in the absence of the dynamin inhibitor Dynasore. We evaluated FSHR interactions with GPER, Gs protein, endosomal marker RAB-GTPase (Rab) 5, β-arrestin 2, membrane marker CAAX, cytoplasm marker FYVE, as well as intracellular cAMP accumulation and extracellularly-regulated kinases 1 and 2 (ERK1/2) phosphorylation by bioluminescence resonance energy transfer (BRET), while cAMP-response element (*CRE*) activity by reporter gene system. Data from 3 to 5 experiments were analyzed using Kruskal-Wallis test and Dunn's post-test ($P < .05$).

In GPER/FSHR co-expressing cells, FSHR-CAAX interaction was reduced compared to what found in FSHR-expressing cells, whereas FSHR-FYVE increased, indicating that GPER favoured the FSHR maintenance at the membrane and endocytic compartments. In fact, GPER reduced the recruitment of β-arrestin 2 to FSHR, as well as FSHR internalization via Rab5-positive early endosomes. GPER/FSHR co-expression prevents FSHR coupling to Gs protein, leading to inhibition of FSH-dependent cAMP accumulation, *CRE* activation, and ERK1/2 phosphorylation. Cell treatment by the internalization blocker Dynasore did not change the FSH-dependent signalling pattern, suggesting that GPER/FSHR complexes exert their effects in the cell surface.

We found that GPER inhibits FSH-dependent signalling via a molecular interaction with FSHR occurring in the cell membrane, confirming it could be a regulatory mechanism for ovarian physiology.

Abstract citation ID: lvag096.1539

EP1315 - ECE_2111 - Thyroid-related polyautoimmunity: effects on anticipated menopause

Marco Centanni, Ilaria Stramazzo, Maria Flavia Bagaglini, Matteo Nocito and Camilla Virili
Sapienza Università di Roma, Endocrine Unit, SM Goretti Hospital, Medical-Surgical Science and Technology, Roma, Italy

Background: An association between autoimmune disorders and an anticipated menopause has been reported. Autoimmune thyroid disease (ATD) is the most prevalent autoaggressive disorder worldwide and plays a pivotal role in polyautoimmunity. However, data about the presence of premature ovarian insufficiency (POI) and early menopause (EM) framed in thyroid-related poly autoimmunity, are rather scanty. In this view, we described the association between anticipated menopause and ATD isolated or framed in poly-autoimmune syndromes in a large cohort of women.

Study Design: We retrospectively evaluated 7690 postmenopausal women from 2018 and 2024 in a tertiary center for thyroid diseases. Three subgroups were examined: women with nonautoimmune endocrinopathies ($n = 5697$; group A) or with isolated Hashimoto's thyroiditis ($n = 1689$; group B) and/or with thyroid-related poly autoimmunity ($n = 304$ group C). All diagnosis of associated autoimmune disorders were based on histology and concordant immunology or on Consensus statements.

Results: In the whole sample 213 out of 7690 (2,77%) women experienced unexplained anticipated menopause, 115 of them (1.50%) showed spontaneous premature ovarian insufficiency (POI) and 98 (1.27%) an early menopause (EM). The kinship familial heritage for autoimmune disorders in women with anticipated menopause was significantly different ($P = .0296$) in the three groups being higher in women with poly-autoimmunity. The prevalence of POI was higher in women with poly autoimmunity (5.92%) (Group C) than in group B (1.84%) and in group A (1.16%; $P < .0001$). Similarly, EM has been observed in 1.07% in the group A and 0.89% in group B ($P =$ ns) while in women with poly-autoimmunity was much higher (7.23%; Chi-square test: $P < .0001$). A spontaneous miscarriage was observed in 52/213 women (24.4%) with anticipated menopause (EM+POI), being significantly higher in women with poly autoimmunity (3.61% vs 0.53%, 0.71%, respectively) than in the group A and B, respectively ($P < .0001$). The percentage of miscarriage was higher in women with POI than the one observed in EM group (30.2%vs 17.7%; $P = .038$). Among the autoimmune disorders, atrophic gastritis was the most frequently observed autoimmune comorbidity, followed by rheumatic disorders and cutaneous autoimmunity. Indeed, Fisher's exact test revealed a significant different distribution of anticipated menopause (POI+EM) ($P = .019$), being psoriatic arthritis the more and celiac disease the lesser associated. Univariate analysis

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

revealed that familiarity was the more relevant independent variable associated with POI in poly-autoimmunity.

Conclusions: Our data suggest that young women with thyroid-related poly autoimmunity, born to a family with thyroid autoimmunity and/or poly-autoimmunity, should be checked prospectively to guide fertility preservation and family planning.

Abstract citation ID: lvag096.1540

EP1316 - ECE_2060 - Adherence to gender affirming hormonal treatment in 6326 Danish transgender persons. A nationwide register-based study

Louise Lehmann Christensen[1,2], Jens-Jakob Møller[3], Katrine Rubin[2,3], Guy T' Sjoen[4], Marianne Skovsager Andersen[1,2] and Dorte Glintborg[1,2]
[1]Department of Endocrinology, Odense, Denmark; [2]Syddansk Universitet, Odense M, Denmark; [3]OPEN, Odense, Denmark; [4]Endocrinology, Gent, Belgium

Background: Gender affirming hormonal treatment (GAHT) is a cornerstone in transgender care. Population-based data are sparse regarding adherence to GAHT in transgender persons.

Aim: To assess use and adherence to GAHT.

Design: A national register-based Danish cohort study in individuals diagnosed with gender dysphoria (TG persons) year 2000-2024. The main study outcome was use of GAHT and GAHT adherence. Masculinizing GAHT was defined by use of testosterone and feminizing GAHT by use of estradiol. GAHT adherence was defined as purchase of GAHT within 600 days intervals.

Results: The cohort included 6326 TG persons divided according to birth sex: $N = 3277$ transgender men (TransM) and $N = 3049$ transgender women (TransF). The median (interquartile range) age at study inclusion was 21 (9) years for TransM and 26 (12) years for TransF. The median follow up duration was 3.8 years and use of GAHT occurred in $N = 1559$ (47.6%) TransM and $N = 1527$ (50.1%) TransF. In GAHT users, GAHT adherence was observed in $N = 1421$ (91.1%) TransM and in $N = 1355$ (88.7%) TransF during follow up. The rate of GAHT non-adherence during follow up was 2.1 (1.8; 2.5) per 100 person years in transM and 2.9 (2.5; 3.4) in TransF. Higher GAHT adherence was predicted by baseline age <25 years, more recent study inclusion, Danish ethnicity, higher personal income, no psychiatric diagnosis (in TransF), and no gender affirming surgery (in TransM). In TG persons with GAHT non-adherence, 29.7% (41/138) TransM and 19.8% (34/172) TransF later resumed GAHT during follow up.

Conclusions: TG persons showed high adherence to GAHT, but further studies regarding reasons for GAHT non-adherence are needed.

Abstract citation ID: lvag096.1541

EP1317 - ECE_3653 - The effects of complex III deficiency on the Hypothalamic-Pituitary-Gonadal (HPG) axis

Irit Hochberg[1,2,3], Michal Toren[1], Osnat Admoni[4], Dov Tiosano[1,5], Hanna Mandel[1,6], Galit Tal[5], Shoji Yano[7], Marc Weigensberg[7] and Jan Idkowiak[8]
[1]Bruce Rappaport Faculty of Medicine, Technion—Israel Institute of Technology, Haifa, Israel; [2]Hadera, Israel; [3]Rambam Medical Center, Institute of Endocrinology, Diabetes and Metabolism, Haifa, Israel; [4]Clalit Health Services, Pediatric Endocrinology Center, North District, Israel; [5]Rambam Medical Center, Pediatric Metabolic Disorders and Pediatrics Ward B, Haifa, Israel; [6]Galil Medical Center, Clinical Genetics Institute, Nahariya, Israel; [7]Pediatric Endocrinology, Los Angeles General Medical Center, Los Angeles, United States; [8]Department of Metabolism and Systems Science, University of Birmingham, College of Medicine and Health, Birmingam, United Kingdom

Mitochondrial Complex III deficiency, a disorder affecting the electron transport chain, is associated with recurrent metabolic decompensation, including hypoglycemia, impaired hepatic synthetic function, lactic acidosis, and multisystem involvement. We report the first characterization of puberty in two pairs of siblings with this condition, both demonstrating a sexual dimorphism in occurrence of puberty, gonadal hormone biosynthesis and gonadal-pituitary feedback.

Two siblings of from a consanguineous Arab Muslim family with genetically confirmed Complex III deficiency caused by a biallelic UQCRC2 Arg183Trp mutation were followed from early childhood because of repeated metabolic crises. The female sibling, now 36 years old, did not develop spontaneous adrenarche or puberty. Evaluation beginning at 12 years of age demonstrated consistently elevated gonadotropins (LH 35 IU/L, FSH 60 IU/L), undetectable estradiol levels, and ovaries of normal size without follicular development. She has since been treated with hormone replacement therapy. The male sibling, currently 35 years old, entered puberty spontaneously at 13 years, achieving normal virilization and external genital development; however, he has markedly reduced testicular volume and azoospermia. Laboratory testing showed persistently increased LH (70 IU/L) and FSH (100 IU/L) since age 13, supraphysiologic testosterone concentrations (14 ng/mL), and high–normal estradiol levels (50 pg/mL). Pituitary hormone profiles were otherwise unremarkable in both individuals.

Assessment of serum steroids by LC-MSMS confirmed elevated levels of testosterone and dehydrotestosterone in the male.

Two additional unrelated siblings from a Mexican family, homozygous for the same UQCRC2 variant, demonstrated a comparable phenotype. The female, who is currently 18 years old, failed to initiate adrenarche or puberty, and the male, who is currently 17 years old, had spontaneous pubertal development. Both siblings had elevated gonadotropins, the female had low estradiol levels, while the male had normal testosterone concentrations and small testes.

These results may confirm previous observations reported by other groups that in animal models and in-vitro models complex III disruption enhances androgen production in Leydig cells.

The surprising absence of expected gonadotropin suppression by testosterone in the two males, and especially in the older male who has testosterone which is significantly higher than normal raises the possibility that there is mitochondrial involvement in the gonadal–pituitary feedback mechanisms.

These novel observations, characterized by the coexistence of elevated gonadotropins with high or normal testosterone may provide new insights into the role of mitochondrial Complex III in human gonadal steroidogenesis and endocrine feedback regulation.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1542

EP1318 - ECE_1139 - Two siblings with normosmic hypogonadotrophic hypogonadism caused by an FGFR-1 gene variant

Beenish Zaki and Stephen Hyer
Diabetes and Endocrinology, Epsom and St. Helier Hospital NHS trust, London, United Kingdom

Background: Mutations in the fibroblast growth factor receptor 1 (FGFR1) gene disrupt gonadotropin-releasing hormone (GnRH) neuron development and are a known cause of congenital hypogonadotropic hypogonadism (CHH), including Kallmann syndrome. FGFR1 plays a crucial role in embryonic cell proliferation, differentiation, and migration, particularly within the forebrain and olfactory system. While FGFR1 mutations classically present with anosmia and midline defects, some individuals exhibit normosmic CHH without syndromic features. Increasing genetic heterogeneity within disorders of sexual development highlights the importance of genetic testing.

Objective: To describe two adolescent brothers with normosmic hypogonadotropic hypogonadism and delayed puberty, emphasizing the diagnostic value of identifying an FGFR1 variant in the absence of olfactory or structural abnormalities.

Case Summary: Both brothers presented with absent pubertal progression. Examination showed Tanner stage I-II genitalia, small testicular volumes, and sub- physiological testosterone levels. Gonadotropins (LH/FSH) were inappropriately low at baseline and after stimulation, while prolactin, thyroid, and adrenal function were normal.

MRI of the hypothalamic–pituitary region was unremarkable, and olfactory testing confirmed normal smell. Given the familial presentation, targeted NGS using a CHH gene panel identified a shared pathogenic FGFR1 variant, confirming FGFR1-related normosmic hypogonadotropic hypogonadism. Testosterone replacement therapy (Nebido® 1 g every 12 weeks) successfully induced and maintained pubertal development. Growth hormone therapy was not required.

Results:

Table 1 Summary of clinical and endocrine findings.

Parameter	Sibling 1	Sibling 2
Age at presentation (years)	17.0	15.8
Tanner stage (genitalia)	I-II	I
Bone age delay	3 years	3.5 years
Testosterone (nmol/L)	2.1	0.6
LH (IU/L)	1.0	0.2
FSH (IU/L)	1.4	1.2
IGF-1 (nmol/L)	16.1	12.3
Pituitary MRI	Normal	Normal
Genetic result	Pathogenic *FGFR1* variant	Same variant

Discussion: Fibroblast Growth Factor Receptor 1 (FGFR1) is a receptor tyrosine kinase essential for embryonic development, hypothalamic–pituitary axis formation, and metabolic regulation. Pathogenic FGFR1 variants include loss-of-function missense, nonsense, frameshift, splice-site mutations, and rare deletions. These mutations are a recognized cause of congenital hypogonadotropic hypogonadism (CHH) and Kallmann syndrome, and may also be associated with growth hormone abnormalities.

FGFR1-related disorders demonstrate marked phenotypic heterogeneity. In addition to endocrine manifestations, affected individuals may exhibit craniofacial anomalies, skeletal abnormalities, hearing loss, and neurodevelopmental features.

Identification of FGFR1 mutations supports early and accurate diagnosis, guides pubertal induction and fertility treatment strategies using gonadotropins or pulsatile GnRH, and enabling genetic counselling for autosomal dominant inheritance with incomplete penetrance.

Abstract citation ID: lvag096.1543

EP1320 - ECE_1672 - Comparative effects of Inositol-based therapy, berberine and their combination on androgen levels and insulin resistance in women with Polycystic Ovary Syndrome

Vesselina Yanachkova[1], Svetoslav Stoev[2] and Hristina Lebanova[3]
[1]*Research Institute, Medical University of Pleven, Pleven, Bulgaria;* [2]*Pleven, Bulgaria;* [3]*Faculty of Pharmacy, Medical University-Pleven, Pleven, Bulgaria*

Background: Polycystic ovarian syndrome (PCOS) is among the most prevalent disorders affecting women of reproductive age. The primary pathophysiological features of this condition are hyperandrogenemia and insulin resistance. Reducing circulating androgen levels is crucial for improving metabolic and reproductive markers in women with PCOS. Enhancing insulin sensitivity with different insulin-modulating treatments can have significant effects on the androgen levels.

Objective: To assess the impact of inositol-based therapy, berberine, and the combination of inositol and berberine on androgen levels and insulin resistance in women diagnosed with PCOS.

Methods: A cohort of 115 women diagnosed with PCOS was observed over a period of 6 months. Patients were divided in three groups: women receiving inositol monotherapy ($n = 40$), those undergoing berberine monotherapy ($n = 40$), and participants in a combined regimen of inositol and berberine ($n = 35$). In all patients, baseline and six-month post-therapy assessments were conducted for serum levels of total testosterone, DHEAS, androstenedione, 17-hydroxyprogesterone, fasting plasma glucose, and immunoreactive insulin, with the latter evaluated using the HOMA index.

Results: An improvement in testosterone levels was observed in 26 (70%) of the women administered inositol, in 18 (45.4%) treated with berberine, and in 28 (80%) receiving combination therapy. The proportion of patients exhibiting improvement in testosterone levels was markedly greater in the group receiving the inositol/berberine combination than in those treated with berberine alone ($P < .05$). No statistically significant difference was observed between the combined therapy group and inositol monotherapy group ($P = .54$). All three patient groups showed reductions in serum levels of total testosterone, DHEAS, androstenedione, and 17-hydroxyprogesterone, alongside improvements in fasting glucose and immunoreactive insulin levels, as well as a reduced HOMA index over the six-month duration.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusions: The observational data indicate that the administration of combined insulin-modulating therapy with inositol and berberine can lead to a substantial improvement in hyperandrogenemia and insulin resistance in women diagnosed with PCOS. Inositol monotherapy demonstrated superior therapeutic efficacy compared to berberine monotherapy. While our findings endorse a synergistic, non-hormonal therapy approach for regulating insulin and addressing hyperandrogenism in PCOS, additional studies with larger patient populations are necessary for confirmation and validation.

Keywords PCOS, androgen, insulin resistance, inositol, berberine

Abstract citation ID: lvag096.1544

EP1322 - ECE_3584 - Effect of vitamin D_3 on oxidative stress and apoptosis in the liver of female rats with induced Polycystic Ovary Syndrome

Jakub Wizner[1], Kinga Kamińska[2], Ewa Drąg-Kozak[3], Patryk Sambak[4], Anna Błasiak[4], Agnieszka Rak[5] and Małgorzata Grzesiak[1]

[1]*Department of Endocrinology, Jagiellonian University, Faculty of Biology, Institute of Zoology and Biomedical Research, Kraków, Poland;* [2]*Department of Animal Biotechnology, University of Agriculture, Kraków, Poland;* [3]*Department of Animal Nutrition and Fisheries, University of Agriculture, Kraków, Poland;* [4]*Department of Neurophysiology and Chronobiology, Jagiellonian University, Faculty of Biology, Institute of Zoology and Biomedical Research, Kraków, Poland;* [5]*Laboratory of Physiology and Toxicology of Reproduction, Jagiellonian University, Faculty of Biology, Institute of Zoology and Biomedical Research, Kraków, Poland*

Introduction: Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder of the female reproductive system affecting women of reproductive age. The diagnosis of PCOS requires the presence of at least two of the following features: hyperandrogenism, oligo- or anovulation, and cystic ovarian morphology on ultrasound. Elevated androgen level contributes to clinical manifestations such as acne, androgenic alopecia, and hirsutism, while increased luteinizing hormone (LH), observed in up to 60% of PCOS patients, further enhances androgen synthesis and disrupts follicular maturation, leading to menstrual irregularities and infertility. PCOS is also strongly associated with metabolic disturbances, including insulin resistance and hyperinsulinemia, which are considered central mechanisms linking PCOS with metabolic associated fatty liver disease. Vitamin D_3 (VD) deficiency is reported in approximately 85% of women with PCOS, and its active form, calcitriol, exhibits steroid hormone-like properties with pleiotropic effects on metabolic homeostasis, immune modulation, and cellular differentiation. Recent studies suggest that VD supplementation may alleviate insulin resistance and hyperinsulinemia in PCOS, indicating its potential role in improving liver-related metabolic dysfunctions. However, the impact of VD on oxidative stress and apoptosis in hepatic tissue under PCOS conditions remains insufficiently explored. The present study aimed to investigate the effect of VD supplementation on reactive oxygen species (ROS)/reactive nitrogen species (RNS) level, zinc and copper concentration, antioxidant *Sod1* gene expression and apoptosis in the liver of rats with letrozole-induced PCOS.

Materials and Methods: The experiment was conducted using female Wistar rats divided into four groups: control (C), VD-supplemented (VD), letrozole-treated (L) to induce PCOS, and letrozole and VD-treated (VD+L). Oxidative stress was assessed by measuring ROS/RNS level, while *Sod1* mRNA expression was analysed using quantitative real-time PCR. Hepatic zinc and copper concentrations were determined by atomic absorption spectrometry, while apoptosis was evaluated by the abundance of caspase-3 using Western blot.

Results: The results demonstrated that VD supplementation significantly reduced ROS/RNS level ($P < .05$) in PCOS rats and partially restored *Sod1* expression ($P < .05$) in the VD+L group. In the L and VD+L groups, the hepatic zinc concentration was reduced in comparison to the control and VD groups ($P < .001$ and $P < .01$). A decrease in caspase-3 abundance was observed in the VD+L group in comparison to the PCOS rats, however it was not significant.

Conclusions: These findings suggest that vitamin D_3 supplementation may mitigate oxidative stress and apoptosis in the liver with PCOS conditions, supporting its potential as an additional therapeutic strategy.

Abstract citation ID: lvag096.1545

EP1323 - ECE_3761 - Regulatory T cells, T helper 17 cells, and hypoxia-inducible factor 1α expression in polish women with PCOS phenotype D

Justyna Kuliczkowska-Płaksej[1], Aleksandra Jawiarczyk-Przybyłowska[1], Aleksandra Zdrojowy-Wełna[1], Anna Brona[1], Barbara Stachowska[1], Łukasz Gojny[1], Agnieszka Zembska[1], Jowita Halupczok-Żyła[2], Martyna Strzelec[1] and Marek Bolanowski[1]

[1]*Department of Endocrinology and Internal Diseases, Wroclaw Medical University, Wroclaw, Poland;* [2]*Department of Clinical and Experimental Pathology, Wroclaw Medical University, Wroclaw, Poland*

Background: Polycystic ovary syndrome (PCOS) is a common disorder associated with reproductive, metabolic, and inflammatory abnormalities. Several studies have reported alterations in T-cell subpopulations in PCOS, including an increased number of proinflammatory T helper 17 (Th17) cells and a decreased number of regulatory T (Treg) cells compared with healthy, fertile women. However, data regarding the abundance of different T-lymphocyte subpopulations in the normoandrogenic phenotype D remain limited. Hypoxia-inducible factor-1α (HIF-1α) is a transcription factor that regulates cellular responses to hypoxia and is expressed in nearly all cell types, including lymphocytes. Beyond its primary role in immune regulation, HIF-1α is involved in metabolic processes, and its dysregulation has been associated with obesity, insulin resistance, and local inflammation. Evidence suggests that HIF-1α may be a key regulator influencing the balance between Treg and proinflammatory Th17 cells.

Objective: This study aimed to assess the abundance of Treg and Th17 lymphocytes, HIF-1α expression within these populations, and their ratios in women with PCOS phenotype D compared with healthy controls.

Methods: The study included 49 women with PCOS phenotype D and 40 age-, BMI-, and body-mass-matched healthy women with regular menstrual cycles selected from cases visiting Department of Endocrinology and Internal Diseases, University Hospital in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Wroclaw. Anthropometric, hormonal, metabolic, and inflammatory parameters were evaluated. Peripheral blood T-cell subpopulations and intracellular HIF-1α expression were analyzed using multiparameter flow cytometry.

Results: No significant differences were observed between the groups in total leukocyte counts, lymphocyte subsets, or absolute numbers of Treg and Th17 cells. However, women with PCOS exhibited significantly higher Treg/Th17 and HIF-1α-positive Treg/HIF-1α-positive Th17 ratios. HIF-1α-positive Treg cells correlated positively with markers of adiposity and insulin resistance in both groups, suggesting an association between metabolic status and immune regulation. Despite normoandrogenemia, women with PCOS had higher hs-CRP levels, indicating persistent low-grade inflammation.

Conclusions: In women with PCOS phenotype D, the absolute numbers of Treg and Th17 cells did not differ from those in the control group; however, the Treg/Th17 ratio and the ratio of HIF-1α-expressing cells were significantly higher. These findings may reflect persistent low-grade inflammation in PCOS, although the precise significance of increased HIF-1α expression within Treg cells remains unclear. Our results also suggest that PCOS phenotype D differs substantially from the classic form of the syndrome not only in the severity of metabolic disturbances but also in immunological characteristics, despite the presence of low-grade inflammation.

Abstract citation ID: lvag096.1546

EP1324 - ECE_3855 - Role of adropin on human placenta cells proliferaton and endocrine pathways. In vitro studies on JEG-3 cells

Urszula Nowak[1], Monika Dawid[1,2], Sylwia Kula[1] and Agnieszka Rak[1]

[1]Laboratory of Physiology and Toxicology of Reproduction, Institute of Zoology and Biomedical Research, Faculty of Biology, Jagiellonian University, Cracow, Poland; [2]Doctoral School of Exact and Natural Sciences, Jagiellonian University, Kraków, Poland

Background: Adropin is a peptide hormone encoded by the *ENHO* (energy homeostasis-associated) gene and belongs to the adipokine family. It is well known for its role in the regulation of glucose and lipid metabolism and its beneficial effects on insulin sensitivity. Recent studies suggest that adropin may also regulate endocrine pathways in the female and male reproductive systems in murine models. Importantly, circulating adropin levels in women change during pregnancy and may correlate with pregnancy-related complications. However, the role of adropin in the human placenta, a key organ of pregnancy, remains poorly understood.

Objective: This study aimed to investigate the effects of adropin on proliferation and endocrine function of human placental cells.

Methods: Human choriocarcinoma JEG-3 cells were treated with adropin at concentrations of 1, 10, and 100 nM for 24, 48, and 72 hours ($n = 3$). Human chorionic gonadotropin (hCG) and progesterone (P_4) secretion were assessed using ELISA, while cell proliferation was measured using a BrdU assay. Based on these results, 10 nM adropin was selected for subsequent experiments. Cell cycle distribution was analyzed by flow cytometry. Gene and protein expression analyses were performed using RT-qPCR and Western blotting to assess markers related to endocrine function (*CGB*, *3βHSD*; hCG, 3βHSD) and proliferation (*PCNA*; PCNA, Cyclin E) following treatment with 10 nM adropin for 24, 48, and 72 hours. Statistical analyses were conducted using one-way ANOVA and Student's *t*-test.

Results: Adropin exerted time-dependent effects on JEG-3 cell proliferation, increasing proliferative activity after 24 and 48 hours while reducing it after 72 hours of incubation. Cell cycle analysis suggested a potential role of adropin in regulating the transition between the G0/G1 and S phases. Additionally, adropin modulated the endocrine activity of placental cells, as evidenced by reduced hCG and P_4 secretion after 72 hours, accompanied by altered expression of endocrine- and proliferation-related genes and proteins. Western blot analysis revealed time-dependent changes in the expression of PCNA, Cyclin E, hCG, and 3βHSD following adropin treatment.

Conclusions: These findings suggest that adropin plays a modulatory role in human placental cell proliferation and endocrine function, potentially contributing to placental development and metabolic adaptation during pregnancy. The dynamic effects of adropin on placental cells may indicate its involvement in early pregnancy processes, including implantation and placental formation. Further studies are required to elucidate the underlying molecular mechanisms.

Funding: Ministry of Science and Higher Education, Poland, Diamond Grant no. DI2019 0110 49.

Abstract citation ID: lvag096.1547

EP1325 - ECE_1292 - Body image concern in women with Polycystic Ovary Syndrome (PCOS): a comparative analysis of two assessment tools

Aspasia Manta[1], Sophie Broughton[2], Shams Ali Baig[3], Eleni Armeni[4] and Punith Kempegowda[1]

[1]Department of Applied Health Sciences, University of Birmingham, Birmingham, United Kingdom; [2]Midland Metropolitan University Hospital, Sandwell and West Birmingham NHS Trust, Birmingham, United Kingdom; [3]Medical School, University of Birmingham, Birmingham, United Kingdom; [4]Royal Free London NHS Foundation Trust, University of Birmingham, Birmingham, United Kingdom

Background: Body image dissatisfaction is a prevalent concern among women with polycystic ovary syndrome (PCOS), yet there is no consensus on the optimal assessment tool for this population. The Body Image Concern Inventory (BICI) and the Multidimensional Body-Self Relations Questionnaire—Appearance Scales (MBSRQ-AS) are commonly used, but their comparative performance in PCOS remains unexplored. This study aimed to compare the BICI and MBSRQ-AS in women with PCOS, evaluating agreement, reliability, and associations with clinical and demographic characteristics.

Methods: A cross-sectional sample of 163 women with confirmed PCOS completed an online questionnaire including the BICI, MBSRQ-AS, clinical measures (body mass index [BMI], modified Ferriman-Gallwey [mFG] score), and sociodemographic data. Internal consistency of the questionnaires was assessed using Cronbach's alpha. Pearson correlations and regression analyses examined relationships between body image scores and clinical variables.

Results: The BICI demonstrated excellent internal consistency ($\alpha = .93$) and was significantly associated with BMI and mFG scores. The MBSRQ-AS showed acceptable reliability ($\alpha = .73$), while

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

higher BMI consistently predicted poorer outcomes on its subscales. Subscale analysis of the MBSRQ-AS further revealed significant associations between higher BICI scores and lower Appearance Evaluation ($r = -0.559$, $P < .001$) and Body Areas Satisfaction ($r = -0.652$, $P < .001$), alongside increased Overweight Preoccupation ($r = 0.557$, $P < .001$) and Appearance Orientation ($r = 0.335$, $P < .001$). Hierarchical regression analysis showed that MBSRQ-AS scores explained additional variance in BICI scores beyond clinical features, indicating distinct contributions to body image assessment.

Conclusions: Both the BICI and MBSRQ-AS identify elevated body image concerns in women with PCOS, but capture distinct constructs. The BICI is more sensitive to appearance-related distress, whereas the MBSRQ-AS reflects broader attitudinal aspects. The selection of assessment tools should be context-driven to optimally address body image concerns in this population.

Abstract citation ID: lvag096.1548

EP1326 - ECE_2593 - Phenotypic and genetic heterogeneity of 46,XY gonadal dysgenesis: a pediatric case series

Beatriz Tavares Da Silva, Miguel Saraiva, Catarina Figueiredo, Catarina Mendes, Joana Freitas, Lia Ferreira, Maria João Oliveira, Isabel Palma and Teresa Borges
Unidade Local de Saúde de Santo António, Porto, Portugal

Background: The 46,XY differences of sex development (DSD) represent a rare group of conditions arising from discordance between chromosomal and phenotypic sex. In cases of complete 46,XY gonadal dysgenesis (GD), the absence of testicular differentiation results in hypergonadotropic hypogonadism and preserved Müllerian structures. These patients face a substantial risk of developing gonadal malignancies, necessitating early identification and management. We describe the clinical, biochemical, and molecular profiles of four pediatric patients with 46,XY DSD of distinct etiologies, aiming to highlight the diagnostic challenges and the necessity of multifaceted long-term management strategies.

Results: Four patients with complete 46,XY GD were included. Molecular analysis identified pathogenic variants in three cases: one WT1 splice-site variant (c.1432+4C>T) and two SRY variants (p.Arg30Ile and p.Glu89Argfs*15). The fourth patient was diagnosed based on clinical and biochemical criteria without an identified genetic variant. Gonadal malignancy was confirmed in 75% of cases ($n = 3$), including bilateral gonadoblastoma and mixed germ cell tumor. All patients underwent bilateral gonadectomy and subsequent pubertal induction (ages 12-16). At the latest follow-up (ages 16-21), full pubertal development and menarche were achieved in 100% of cases, with bone mineral density maintained within age-matched norms (Z-score: −0.3 to −1.7). Late diagnosis in the SRY group was associated with final heights significantly exceeding target height (up to +1.89 SD).

Conclusions: This case series underscores the marked phenotypic and genetic heterogeneity of 46,XY gonadal dysgenesis and the high prevalence of early-onset malignancy (75%). Precise molecular diagnosis is important for timely tumor risk stratification, guiding the timing of prophylactic gonadectomy and optimizing pubertal induction to prevent excessive final height. A proactive, multidisciplinary approach is essential to safeguard bone health and ensure long-term psychosocial well-being in these complex DSD patients.

Table 1 Clinical, genetic, and endocrine characteristics of four patients with 46,XY differences of sex development (DSD).

Features	Case 1	Case 2	Case 3	Case 4
Age at diagnosis/ presentation	11 y (SRNS since 4 y)	Neonatal period (Turner work-up)	6 y (precocious pubertal signs)	16 y (post-tumor resection)
Genetic finding	WT1 (NM_000378.6): c.1432+4C>T (splice-site)	None identified	*SRY* (NM_003140.3) c.89G>T, p.Arg30Ile (exon 1)	*SRY (NM_003140.3)* c.264dup, p.Glu89Argfs*15
Main diagnosis	*WT1* (heterozygous splice-site variant, not Frasier-associated)	Frasier syndrome (46,XY DSD + CKD)	Complete 46,XY gonadal dysgenesis (Swyer)	Complete 46,XY gonadal dysgenesis (Swyer)
Age at gonadectomy	13 y (bilateral)	1 y (bilateral)	6 y (bilateral)	16-17 y (right tumor, left streak gonad)

Abstract citation ID: lvag096.1549

EP1327 - ECE_1211 - Ovarian steroid cell tumour: a rare cause of severe hyperandrogenism in a postmenopausal woman

Ana Majic Tengg and Jelena Andric
Department of Endocrinology, Diabetes, Metabolic disorders and Clinical Pharmacology, Clinical Hospital Dubrava, Internal Medicine Clinic, Zagreb, Croatia

Steroid cell tumours of the ovary represent an exceptionally rare subgroup of androgen-producing ovarian neoplasms, accounting for less than 0.1% of all ovarian tumours. These lesions may secrete marked amounts of testosterone, androstenedione, and dehydroepiandrosterone sulphate (DHEAS), resulting in rapidly progressive hyperandrogenism. In postmenopausal women, new-onset androgen excess should prompt immediate investigation for an androgen-secreting tumour, given the low likelihood of benign or

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

functional causes. We present a rare case of severe hyperandrogenism in a postmenopausal woman secondary to an ovarian steroid cell tumour.

A postmenopausal woman presented with progressively worsening androgenic symptoms, including marked alopecia and hirsutism, without overt signs of virilization. Her medical history included multinodular goiter with subclinical hyperthyroidism, osteopenia, hypertension, and hyperlipidaemia. Initial laboratory evaluation revealed markedly elevated total and free testosterone, DHEAS, and androstenedione. A goserelin (GnRH agonist) suppression test was conducted, resulting in a significant reduction of serum testosterone levels, supporting an ovarian source of androgen excess. Pelvic ultrasonography demonstrated solid-appearing ovaries of normal size, along with a 12-mm ill-defined echogenic lesion within the endometrial cavity.

Given the severity of hyperandrogenism and imaging findings, the patient underwent laparoscopic bilateral adnexectomy. Histopathological analysis identified a steroid cell tumour, not otherwise specified (SCT-NOS) of the right ovary, composed of uniform cells with eosinophilic cytoplasm. Immunohistochemical staining was positive for SF1, inhibin, and calretinin, and negative for EMA and synaptophysin, confirming the diagnosis. No malignant features were noted. The left ovary showed no histopathological abnormalities.

Postoperatively, the patient exhibited rapid biochemical improvement, with normalization of testosterone and androstenedione. DHEAS levels decreased substantially, although occasional mild elevations persisted and were monitored. Clinically, hyperandrogenic symptoms gradually regressed. Although SCT-NOS is generally considered benign, rare recurrences have been reported; therefore, a structured follow-up plan was implemented, including annual pelvic MRI for five years with periodic androgen profiling.

This case highlights that ovarian steroid cell tumours, although rare, should be considered in postmenopausal women presenting with abrupt or severe hyperandrogenism. While timely surgical intervention is typically curative, long-term endocrine and radiologic follow-up remains essential given the unpredictable clinical course of these uncommon tumours.

Abstract citation ID: lvag096.1550

EP1328 - ECE_1737 - Persistent elevation of gonadotropin levels following gonadectomy despite continued gender-affirming hormone therapy in transgender individuals

Ye Liu[1,2], Jia Yang[3], Xinzhu Wang[3], Bailin Pan[3] and Tianpei Hong[1]

[1]Beijing, China; [2]Department of Endocrinology and Metabolism, Peking University Third Hospital, Beijing, China; [3]Peking University Third Hospital, Beijing, China

Background: Following gonadectomy, the dynamic changes of gonadotropins and the reconstitution of hypothalamic-pituitary-gonadal (HPG) axis feedback under gender-affirming hormone therapy (GAHT) remain unclear.

Methods: This retrospective study analyzed 88 transgender individuals (63 transgender women [TW] and 25 transgender men [TM]) after gonadectomy on stable GAHT with 212 clinical observations. Hormone levels were measured across postoperative intervals and stratified by serum estradiol (E2) or total testosterone (T) levels. Linear mixed-effects models and generalized linear models (GLM) were used to analyze trends and associations.

Results: Both TW and TM exhibited persistently elevated FSH and LH levels across all postoperative time points, remaining significantly above cisgender reference ranges (all $P < .05$) (Tables 1 and 2). Gonadotropin levels showed an inverse dose-response relationship with sex hormones (E2 for TW, T for TM) (Table 3), but GLM indicated that suppressing LH to cisgender reference ranges would require significantly supraphysiological concentrations (E2≥1525.9 pmol/L for TW, T≥47.9 nmol/L for TM).

Conclusions: Gonadotropin levels remain sustained elevated post-gonadectomy despite GAHT. This indicates an incomplete re-establishment of HPG axis feedback, highlighting unique endocrine profiles in post-operative transgender individuals and the need to investigate the potential long-term implications of sustained high gonadotropins.

Data are presented with median (IQR).

Table 1 Characteristics of participants.

	Transgender women ($n = 63$, observations = 142)	Transgender men ($n = 25$, observations = 70)
Age at gonadectomy (years)	25.0 (22.2–28.3)	28.4 (25.6–33.0)
FSH (mIU/mL)	41.0 (20.0–66.7)	68.1 (26.1–104.5)
LH (mIU/mL)	25.7 (14.2–43.1)	31.7 (14.8–48.4)

Table 2 Gonadotropin levels over time after gonadectomy in transgender individuals.

Postoperative time (months)	[1.5, 6)	[6, 12)	[12, 18)	[18, 24)	≥24
Transgender women					
FSH (mIU/mL)	40.8 (11.9-83.5)	41.7 (19.9-70.0)	51.4 (27.1-71.4)	29.9 (18.8-46.1)	42.4 (25.2-63.6)
LH (mIU/mL)	30.4 (11.4-53.8)	26.1 (10.6-42.5)	25.4 (15.6-35.9)	22.1 (12.2-27.6)	26.2 (15.4-37.9)

(*continued*)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Table 2 Continued

Postoperative time (months)	[1.5, 6)	[6, 12)	[12, 18)	[18, 24)	≥24
Transgender men					
FSH (mIU/mL)	63.3 (13.8-97.4)	66.7 (33.6-103.0)	48.0 (0.6-104.0)	52.0 (3.3-84.9)	85.9 (35.4-114.0)
LH (mIU/mL)	29.2 (5.6-68.8)	28.3 (16.3-48.0)	22.6 (0.1-45.6)	24.1 (4.8-37.8)	34.5 (18.0-49.3)

Table 3 Gonadotropin levels after gonadectomy stratified by sex hormone concentration.

Estradiol or testosterone level relative to target range	Below	Within	Above
Transgender women			
FSH (mIU/mL)	35.6 (23.7–71.5)	26.0 (5.2–45.2)	18.6 (11.0–50.2)
LH (mIU/mL)	27.9 (17.2–43.6)	11.6 (6.3–30.7)	18.8 (9.8–28.7)
Transgender men			
FSH (mIU/mL)	73.5 (43.1-113.0)	62.6 (12.8-94.9)	25.2 (3.6-38.3)
LH (mIU/mL)	38.9 (22.6-59.0)	26.5 (4.9-43.7)	16.5 (3.6-19.6)

Abstract citation ID: lvag096.1551

EP1329 - ECE_3108 - Longitudinal changes in bone mineral density (BMD) in patients with Klinefelter Syndrome (KS): a prospective observational study in a real-world setting

Francesco Costantino[1,2], Daniele Renda Livraghi[1], Veronica Maria Denichelis[1], Sara De Vincentis[1] and Vincenzo Rochira[1,2]

[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [2]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero- Universitaria of Modena, Modena, Italy

Introduction: Patients with Klinefelter syndrome (KS) are at risk of low bone mineral density (BMD) and fragility fractures. Therefore, guidelines recommend regular DXA assessments at the lumbar spine and femur, along with fracture risk evaluations. While BMD loss is largely attributed to hypogonadism, additional mechanisms independent of serum testosterone may also play a role. This study aimed to evaluate the longitudinal changes in BMD in KS.

Methods: This prospective, observational, longitudinal, real-world study included KS who underwent at least two evaluations of bone status and pituitary–gonadal axis. Osteoporosis, osteopenia, and age-adjusted low BMD were defined by DXA (Hologic) according to WHO and ISCD criteria.

Results: 56 patients with KS were included. At baseline, the mean age was 36.25 ± 14.86 years with mean total testosterone levels of 4.09 ± 2.90 ng/mL. The initial DXA revealed an average BMD of 0.98 ± 0.14 g/cm^2 at the total femur (TF), 0.88 ± 0.14 g/cm^2 at the femoral neck (FN) and 0.98 ± 0.12 g/cm^2 at the lumbar spine (L1-L4). The prevalence of osteoporosis, osteopenia, and low BMD for age were 3.6%, 10.7%, and 14.3%, respectively. Only two fragility fractures were observed and no patient had ever received osteoactive therapies.

Follow-up DXA scans were available after a remarkable interval of 7.68 ± 6.24 years. No significant differences in BMD were detected at FN, TF, or L1-L4 when comparing baseline and follow-up measurements. Regarding testosterone replacement therapy (TRT), 23 KS initiated TRT during follow-up, 16 were already on TRT at baseline and 14 never received TRT. Longitudinal BMD changes were not significantly different among TRT initiators, those already treated at baseline and TRT-naïve. Respectively, the average BMD percentage changes were −3.69%, −2.24% and +3.07% at TF; +1.82%, +5.42% and +3.07% at FN and −5.42%, −3.73% and −1.30% at L1-L4.

Conclusions: Despite the widespread belief that bone involvement is highly prevalent in Klinefelter syndrome, our longitudinal data indicate a low prevalence of reduced BMD and osteoporosis, along with preserved skeletal stability over time. Importantly, BMD trajectories appear largely independent of testosterone replacement therapy, with neither significant bone loss nor relevant gains at sites typically associated with fragility fractures. These findings challenge the current perception of skeletal fragility in KS and suggest that bone risk may be overestimated. Prospective studies incorporating fracture outcomes are needed to refine bone health assessment and management strategies in this population.

Abstract citation ID: lvag096.1552

EP1331 - ECE_3501 - Early cardiovascular risk and metabolic dysfunction in women with Polycystic Ovary Syndrome

Shakhzoda Uchkunkhonova[1] and Zulaykho Shamansurova[2]

[1]Medical school, Central Asian University in Tashkent—CAU, Tashkent; [2]Medical school, Central Asian University in Tashkent—CAU, Akfa Medline University Hospital, Tashkent, Uzbekistan

Introduction: Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age. Although traditionally considered a gynecological condition, growing evidence indicates that PCOS is a systemic endocrine–metabolic disorder characterized by insulin resistance, hyperinsulinemia, and an increased risk of cardiometabolic complications. Early identification of metabolic abnormalities in women with PCOS is

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

therefore essential for preventing long-term outcomes such as type 2 diabetes mellitus and cardiovascular disease.

Objective: To assess cardiometabolic risk in women with PCOS based on published metabolic and endocrine data.

Methods: Data from recent open-access, peer-reviewed clinical studies published between 2018 and 2025 were systematically reviewed and analyzed. Extracted variables included age, body mass index (BMI), fasting glucose, lipid profile parameters, insulin resistance indices (HOMA-IR), and surrogate markers of cardiometabolic risk such as the triglyceride–glucose (TyG) index. Cardiometabolic risk was interpreted in accordance with established cardiovascular risk assessment frameworks.

Results: Data from a total of 842 women with PCOS aged 18-36 years were analyzed. Mean BMI ranged from 24.1 to 28.1 kg/m^2. HOMA-IR values ranged from 2.05 to 5.08, indicating a high prevalence of insulin resistance. Insulin resistance was observed in 57.5% of women, including those with both normal and elevated BMI. While total cholesterol and triglyceride levels were generally within reference ranges, elevated TyG index values were identified in 61% of participants, suggesting early metabolic syndrome–related alterations. Hyperinsulinemia was associated with enhanced ovarian androgen production and disruption of the hypothalamic–pituitary–ovarian axis, contributing to reproductive dysfunction. Despite young age, women with PCOS demonstrated an increased estimated cardiovascular risk compared with the general population.

Conclusions: Women with PCOS exhibit early metabolic disturbances and an increased cardiovascular risk, even at a young age. These findings highlight the importance of regular cardiometabolic risk assessment and early preventive strategies in women diagnosed with PCOS.

Keywords polycystic ovary syndrome, insulin resistance, cardiometabolic risk, cardiovascular disease, metabolic syndrome

Abstract citation ID: lvag096.1553

EP1334 - ECE_3839 - Erectile dysfunction years after cessation in men with previous anabolic androgenic steroid use

Yeliz Bulut, Jon Rasmussen and Caroline Kistorp
Department of Nephrology and Endocrinology, Rigshospitalet, København Ø, Denmark

Background and Aims: Impaired erectile function have been associated with previous anabolic androgenic steroid (AAS) use. However, overall sexual function and the prevalence of erective dysfunction remain still to be elucidated among men with previous AAS use. The primary aim of the current study was to assess sexual function in current and previous AAS users compared with controls who had never used AAS.

Methods: In this cross-sectional study, men involved in recreational training were grouped according to their history of AAS use, as current AAS, former AAS (discontinued AAS use >3 months), and never users. We assessed self-evaluated sexual function using the 15-item International Index of Erectile Function (IIEF-15), which consists of five domains: erectile function (ranging from 1 to 30, accordingly, erective dysfunction is present with a score ≤24 and severe dysfunction < 6), orgasmic function (ranging from 0 to 10), sexual desire (ranging from 2 to 10), intercourse satisfaction (ranging from 0 to 15), and overall sexual satisfaction (ranging from 2 to 10). A higher score indicates better sexual function.

Results: We included 118 previous and 278 current AAS users, and 54 never users. The mean (SD) age of all participants was 35.2 (8.8) years. The accumulated duration of AAS use, geometric mean (95% CI), among current users was 188 (166;213), and among former users, 100 (82;122) weeks, $P < .001$. Among former users, the elapsed duration since AAS cessation, geometric mean (95% CI), was 2.1 (1.6;2.7) years. The prevalence of erectile dysfunction was increased in former AAS users ($n = 37$ (34%)) compared with current users (50 (19%)) and never users (5 (10%)), $P < .01$. Furthermore, severe erectile dysfunction was only present in former AAS users (12%) and current users (3%) with none reporting in the group of never AAS users, $P < .01$. Analyzed as a continuous variable, erectile function, sexual desire, intercourse satisfaction, orgasmic function and overall satisfaction were reduced among former users compared with never AAS users, $P < .001$. In a multivariable linear regression model among men with previous AAS use, using erectile function as the dependent variable, adjusted for age, every doubling of accumulated duration of AAS use (log2) was independently associated with impaired erectile function, ($P < .05$), whereas time since cessation was not.

Conclusions: Men with previous AAS use displayed a higher prevalence of erectile dysfunction alongside impairments across all five sexual function domains 2.1 years following cessation, suggesting that sexual function does not fully recover after AAS cessation.

Abstract citation ID: lvag096.1554

EP1335 - ECE_1956 - Meningioma in a patient with Turner syndrome

Eleni Palioura[1], Nikolaos Kalogeris[1], Konstantinos Barkas[2] and Andromahi Vryonidou[1]
[1]*Department of Endocrinology and Diabetes Center, Hellenic Red Cross Hospital, Athens, Greece;* [2]*Department of Neurosurgery, General Hospital of Nikaia, Athens, Greece*

Introduction: Turner syndrome is the most common sex chromosome abnormality in females, characterized by complete or partial loss of one X chromosome. There is limited evidence in the literature pointing to increased incidence of neoplasms, including meningiomas, in patients with Turner syndrome; however, no causal interference has yet been established.

Case Report: We present the case of a 40–year-old woman with Turner syndrome (45,X karyotype) who was regularly followed at our department since the age of 23, after transition from pediatric to adult care. Patient presented some typical physical features of Turner syndrome including short stature, low posterior hairline, short neck, large and low set ears, down-slanting eyes and small chin. She had no congenital cardiac anomalies, but was found to have a horseshoe kidney with normal renal function. During childhood, she received growth hormone therapy starting from age $7^{9/12}$ and continuing for seven consecutive years (until age $14^{3/12}$) with final height 147 cm. Hormone replacement therapy (HRT) was initiated with conjugated estrogen, and cyclic medroxyprogesterone acetate was introduced after menarche at age 12 years and 8 months; this therapeutic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

approach was continued until age 22. Subsequently, patient received combined oral contraceptive pills containing ethinyl estradiol and gestodene for one year that was afterwards switched to oral regimen of estradiol valerate and dienogest until the age of 38. Since then, she is under hormone substitutive therapy consisted of transdermal 17β-estradiol and cyclic micronized progesterone. At age 39, the patient complained for dizziness and bilateral tinnitus. Magnetic resonance imaging (MRI) of the brain revealed a large extraparenchymal lesion (47 × 28 × 25 mm) located in the right parietal region, adjacent to the midline. The lesion had lobulated margins and was heterogeneously enhanced. It was in contact with the interhemispheric fissure and the superior sagittal sinus and caused displacement of the cortical gyri of the parietal cortex. Based on neuroimaging findings, the mass was presumed to represent a meningioma. Repeated brain MRIs at 6 and 12 months showed no differentiation and a follow-up examination by neurosurgeon was scheduled for the next year.

Discussion: To the best of our knowledge, this represents the 16th reported case in the literature of meningioma occurrence in a patient with Turner syndrome. It remains to be elucidating whether this coexistence is incidental or is related to genetic (loss of X chromosome) and/or hormonal (GH and HRT) factors implicated in Turner syndrome's pathogenesis and management.

Abstract citation ID: lvag096.1555

EP1336 - ECE_1771 - Unmasking XXYY syndrome: a case report highlighting endocrine and neurological manifestations

Ana Gheorghe Milea[1,2] and Carmen Emanuela Georgescu[1,2]
[1]*Department of Endocrinology, Clinical County Emergency Hospital Cluj-Napoca, Cluj-Napoca, Romania;* [2]*Department of Endocrinology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania*

Background: XXYY syndrome is a rare sex chromosome aneuploidy, most commonly resulting from meiotic nondisjunction during spermatogenesis and, less frequently, from post-zygotic mitotic errors occurring in early embryogenesis.[1] The condition is classically associated with increased height, gonadal dysfunction, and a wide spectrum of neurodevelopmental and behavioral abnormalities.[2]

Case: Presentation: We report the case of a male patient, the first child of a non-consanguineous couple, born at term with documented perinatal distress. Initial developmental assessment revealed delayed gross motor milestone acquisition; however, significant improvement in motor function was observed following early intervention and structured rehabilitation.

At 8 years of age, the patient underwent a comprehensive neurological evaluation after three epileptic seizure episodes. Brain magnetic resonance imaging identified a pineal region tumor, radiologically consistent with a pinealocytoma, measuring 11 × 11 × 12.7 mm. Serum α-fetoprotein and β-human chorionic gonadotropin were negative. Serial imaging demonstrated stability in lesion size over time. Therapy with valproate was initiated and maintained for two years, after which treatment was discontinued at the family's request, with no subsequent seizure recurrence. The patient was also diagnosed with mild intellectual disability, mixed-type attention-deficit/hyperactivity disorder and socio-pragmatic communication disorder.

At the age of 16, he was referred for endocrine evaluation due to incomplete pubertal development, six years after pubertal onset. Presenting complaints included progressive weight gain, psychomotor agitation, and aggressive behavior. Physical examination revealed extreme tall stature (+3.91 SD), obesity, eunuchoid body proportions, and Tanner stage III pubertal development. Laboratory investigations demonstrated hypergonadotropic hypogonadism, primary hypothyroidism and dyslipidemia. Based on the clinical and hormonal findings, Klinefelter syndrome was initially suspected, prompting cytogenetic analysis, which ultimately revealed a diagnosis of 48,XXYY syndrome. Hormone replacement therapy with levothyroxine and transdermal testosterone was initiated, leading to a favorable clinical evolution.

Conclusions: This case illustrates the marked phenotypic diversity of XXYY syndrome. The coexistence of hypergonadotropic hypogonadism with tall stature, primary hypothyroidism, obesity, epilepsy, cognitive impairment, and a pineal region tumor highlights the diagnostic complexity of this condition. Early recognition and cytogenetic confirmation are essential to enable tailored hormonal therapy and coordinated multidisciplinary follow-up.

References

1. Hanley AP, Blumenthal JD, Lee NR, Baker EH, Clasen LS, Giedd JN. Brain and behavior in 48, XXYY syndrome. *Neuroimage Clin*. 2015;8:133-139. https://doi.org/10.1016/j.nicl.2015.04.009
2. Tartaglia N, Ayari N, Howell S, D'Epagnier C, Zeitler P. 48,XXYY, 48,XXXY and 49,XXXXY syndromes: not just variants of Klinefelter syndrome. *Acta Paediatr*. 2011;100(6):851-860. https://doi.org/10.1111/j.1651-2227.2011.02235.x

Abstract citation ID: lvag096.1556

EP1337 - ECE_3006 - Finding zebras: identifying a novel mutation causing testotoxicosis

Viviana Adam[1], Alexandru Florescu[1,2], Andra Berigoi[2], Irina Puscasu[2], Teodora Vintilă[2], Stefana Bilha[1,2], Anca Matei[1,2] and Cristina Preda[1,2]
[1]*Universitatea de Medicină şi Farmacie 'Grigore T. Popa' Iaşi, Iaşi, Romania;* [2]*Endocrinology, Spitalul Sf. Spiridon Iaşi, Iaşi, Romania*

Introduction: Testotoxicosis, also known as familial male limited precocious puberty, is a rare cause of peripheral precious puberty (PPP) caused by an activating mutation of the gene encoding for the LH receptor on Leydig cells (LHCGR gene, cr2p21). Left untreated, this can cause psychosocial complications; advanced bone age and low adult height; as well as central precocious puberty.

Case Report: We examined a 5 year, 8 month old boy that was directed to the Endocrinology Clinic because of increased testicular volume, penile enlargement, and scrotal, pubic and upper lip hair. Family history was negative for precocious puberty. On clinical examination, height was 119 cm (−0.42 SD), weight was 20kg, BMI 14.2 kg/m^2 (normal), Tanner stage 2. Wrist X-ray showed a bone age of 5 years and 6 months. Hormonal evaluation demonstrated a markedly increased testosterone level, more than 10 times the upper limit of normal (7.22 nmol/L), with low FSH and LH levels (0.411 mIU/mL and 0.146 mIU/mL, respectively). Low 17OH-progesterone ruled out congenital

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

adrenal hyperplasia; imaging studies and tumor markers excluded testicular/adrenal tumors; while McCune Albright syndrome and iatrogenic PPP were excluded based on history and physical examination. Testotoxicosis was diagnosed by exclusion, and treatment with aromatase inhibitors (anastrozole, 1 mg/day) and bicalutamide (25 mg/day) was initiated. Genetic testing was later performed, identifying a previously unreported mutation in the LHCGR gene: (c.1193T>C, p.(Met398Thr). At 6 and 12 month reevaluation, no side effects were reported except for mild headache occasionally, pubertal signs regressed; gonadotropin levels remained low, while elevated testosterone persisted; and bone X-ray didn't demonstrate advancement of bone age. After 18 months, Diphereline stimulation test confirmed central precocious puberty (FSH = 3.55 mIU/mL, LH = 3.71 mIU/mL), and GnRH analogue treatment was added to the treatment plan.

Conclusions: The limited studies available suggest optimal treatment of testotoxicosis is with a combination of aromatase inhibitors and antiandrogen medications. Testosterone levels shouldn't be used as a marker for treatment efficacy; but rather focus should be on gonadotropin levels and decreasing the bone age to chronological age ratio, if advanced at diagnosis. In our case, despite early diagnosis and appropriate treatment, PPP progressed to central precocious puberty, underlying the importance of close monitoring during treatment, even if pubertal signs regress. Finally, genetic studies of the child and both parents should be carried out whenever possible; in our case, a previously unreported mutation in the LHCGR gene was identified, and the correlation between genotype and phenotype will be further explored during follow-up.

Abstract citation ID: lvag096.1557

EP1338 - ECE_1482 - Anti-Müllerian hormone as a marker of ovarian reserve to preserve female fertility in radioiodine treatment of Thyroid Carcinoma

Barbora Havlinova[1,2], Katerina Koprivova[1,3] and Jiri Dolezal[1,4]

[1]Charles University Faculty of Medicine in Hradec Králové, Hradec Králové, Czech Republic; [2]3rd Department of Internal Medicine—Metabolic Care and Gerontology, University Hospital Hradec Králové, Hradec Králové, Czech Republic; [3]Department of Clinical Immunology and Allergology, University Hospital Hradec Králové, Hradec Králové, Czech Republic; [4]Department of Nuclear Medicine, University Hospital Hradec Králové, Hradec Králové, Czech Republic

Context: Differentiated thyroid carcinoma is the most common endocrinological malignancy with women being more frequently affected. There are discussions about adverse effects of radioiodine (^{131}I) on ovarian function and female fertility. Anti-Müllerian hormone (AMH) is regarded as the best endocrine marker for evaluating the physiological loss of oocytes in healthy women with regard to age.

Objective: The aims of the project are to determine ovarian reserve assessed by AMH, to determine the absorbed dose of ^{131}I in the ovary of women undergoing radioiodine treatment based on the magnitude of ^{131}I activity administered, and to evaluate the relationship between absorbed dose of ^{131}I and change in AMH level.

Materials and Methods: Over a three-year period, 74 serum samples were collected from women with thyroid carcinoma and 4 serum samples from healthy premenopausal women. AMH levels were measured using the ELISA method. In total, 5 measurements were obtained, with the first performed before radioiodine therapy and subsequent measurements at regular intervals 4-6 months. AMH levels before and after treatment were compared. At the same instant, hypothalamic-pituitary axis function was examined.

Results: We found a significant effect on reducing AMH levels and thus ovarian reserve after ^{131}I (median 3.56 vs median 1.25, $P <$ .0001). There was a strong correlation with age ($r = -0.616$ and -0.752, respectively)—AMH decreases with increasing age. The relationship between changes in AMH and menstrual cycle disturbance has not been demonstrated.

Conclusions: The question of possible long-term side effects of radioiodine remains open and therefore the need to inform patients. Consequently, predicting the end of ovarian function by assessing a simple serum biomarker could help to select an appropriate treatment strategy for young women planning pregnancy.

Abstract citation ID: lvag096.1558

EP1340 - ECE_2650 - Impact of dyslipidemia on the probability of pregnancy in women undergoing IVF: a systematic review and meta-analysis

Panagiotis Anagnostis[1,2], Julia Bosdou[3], Christos Venetis[3], Evangelia Katsika[3], Kokkoni Kiose[3], Marisia Stavrinidou[3], Leonidas Zepiridis[3], Grigorios Grimbizis[3] and Efstratios Kolibianakis[3]

[1]3rd Department of Internal Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]Unit for Human Reproduction, 1st Department of Obstetrics and Gynecology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece

Background/Aims: Dyslipidemia, including high concentrations of total cholesterol (TC) or low-density lipoprotein cholesterol (LDL-C) or triglycerides (TG), as well as low levels of high-density lipoprotein cholesterol (HDL-C), adversely affect cardiovascular health. However, its specific impact on in vitro fertilization (IVF) is unknown. The purpose of this study was to systematically review and meta-analyze the best available evidence regarding the impact of dyslipidaemia on IVF outcomes. The primary outcome was live birth rates, while secondary outcomes included clinical pregnancy rates, cumulative live birth and miscarriage rates.

Methods: A comprehensive literature search in PubMed, Scopus and Google Scholar was conducted until 10 January 2026. Data from eligible studies were independently extracted by two reviewers, including demographic, methodological and clinical information. Study quality was assessed using the Newcastle-Ottawa Scale. Statistical heterogeneity was evaluated using the I^2 statistic, and meta-analyses were conducted using random- or fixed-effects models, depending on the presence of significant heterogeneity. Results were expressed as relative risks (RR) or weighted mean differences (WMD) with 95% confidence intervals (CIs) and were analysed using an intention-to-treat principle.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: Six retrospective studies ($n = 11\,685$) published between 2018 and 2024 with moderate-to-low risk of bias were analysed. Sample size ranged from 127 to 3372 patients. Clinical pregnancy rates were lower in patients with dyslipidemia compared to those without (RR 0.85, 95% CI 0.74-0.99; random effects model; I^2 73.4%; five studies, 5477 patients). Dyslipidemia was associated with higher miscarriage rate (RR 1.24, 95% CI 1.01-1.53; I^2: 0%; four studies, 5019 patients) compared with normal lipid profile. Furthermore, patients with dyslipidemia had lower live birth rates compared to those without (RR 0.82, 95% CI 0.68-0.99; I^2 89.4%; three studies, 4972 patients).

Conclusions: This systematic review and meta-analysis is the first performed so far on this topic, showing decreased pregnancy outcomes in women with dyslipidaemia compared to those without. This underscores the importance of lipid profile screening before infertility treatment and necessitates prompt lifestyle intervention to reduce this effect.

Abstract citation ID: lvag096.1559

EP1342 - ECE_2956 - Endocrine, metabolic, and skeletal characteristics of Klinefelter syndrome in a long-term real-world cohort

Ema Cindro Kostelec[1], Primož Kotnik[1,2], Tadej Battelino[1,2], Mojca Jensterle[1,3], Tomaz Kocjan[1,3], Andrej Janez[1,3] and Kristina Groti Antonic[1,3]
[1]*Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia;* [2]*Department of Endocrinology, Diabetes and Metabolism, University Children's Hospital, University Medical Center Ljubljana, Ljubljana, Slovenia;* [3]*Department of Endocrinology, Diabetes and Metabolism, University Medical Center Ljubljana, University Children's Hospital, Ljubljana, Slovenia*

Background: Klinefelter syndrome is frequently underdiagnosed and characterized by progressive hypogonadism and a high burden of multisystem comorbidities. Although testosterone replacement therapy is central to management, real-world data on timing of initiation, transition from pediatric to adult care and long-term follow-up remain limited.

Aim: To characterize age at diagnosis, describe the endocrine phenotype, and assess long-term clinical characteristics and management of patients with KS in a real-world clinical cohort.

Materials and Methods: We conducted a retrospective analysis of medical records for 62 patients treated at University Medical Centre Ljubljana by pediatric and adult endocrinology teams from 1976 to 2025. Analyzed parameters included demographics, hormonal profiles, anthropometrics, metabolic markers, bone mineral density, and comorbidities.

Results: Mean age at initial evaluation was 31.7 ± 12.1 years; only 9 of 62 patients (14.5%) were diagnosed in childhood. At testosterone initiation, mean testosterone levels were low (4.38 ± 2.70 nmol/L), with elevated luteinizing hormone (17.1 ± 11.6 IU/L) and follicle-stimulating hormone (33.5 ± 16.6 IU/L). Metabolic syndrome affected 32.7% of patients, insulin resistance 58.3%, and altered body composition was common (mean BMI 28.3 ± 6.4 kg/m^2 at diagnosis, rising to 34.6 ± 5.8 kg/m^2 with metabolic syndrome). Reduced bone mineral density occurred in 20.8% of patients under 50 years and 66.7% of those 50 years or older; testosterone therapy yielded positive effects. Additional comorbidities encompassed autoimmune (3%), oncologic (1%), neuropsyhiciatric (19%), cardiovascular and thromboembolic disorders (40%). All nine childhood-diagnosed patients transitioned successfully to adult care via a dedicated transition clinic, though 30.7% of the cohort overall discontinued regular follow-up.

Conclusions: Klinefelter syndrome in this real-world cohort was most often diagnosed in adulthood. Patients had high burden of metabolic and skeletal abnormalities. These findings highlight the importance of earlier diagnosis, timely testosterone therapy, and structured long-term endocrine management to reduce cumulative morbidity.

Abstract citation ID: lvag096.1560

EP1343 - ECE_3558 - Rare 5′-UTR variants creating new upstream open reading frames provide a potential novel genetic mechanism in congenital hypogonadotropic hypogonadism

Georgios Markantes[1,2], Jack Fu[3], Harrison Brand[3], Michael Talkowski[3], Lacey Plummer[1], Stephanie Seminara[1], Ravikumar Balasubramanian[1] and Maria Stamou[1]
[1]*Reproductive Endocrine Unit, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States;* [2]*Division of Endocrinology, Department of Internal Medicine, University of Patras School of Health Sciences, Patras, Greece;* [3]*Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, United States*

Background: Congenital hypogonadotropic hypogonadism (CHH) is a genetically heterogeneous disorder with numerous genes implicated in its pathogenesis. To date, most studies have focused on the coding regions of the genome, leaving ~50% of the CHH genetically unsolved. While the impact of non-coding regions in disease pathogenesis has recently emerged, the role of non-coding variants affecting upstream open reading frames (uORFs) within the 5′ untranslated regions (5′-UTRs), which are known to suppress downstream translation, has not been thoroughly studied.

Objective: In this study, we aimed: (i) to assess whether patients with CHH are enriched for rare 5′-UTR variants creating new uORFs, and thus having the potential to suppress downstream translation of known CHH genes compared to reproductively normal controls, (ii) to phenotypically characterize CHH individuals harboring such 5′-UTR variants.

Methods: Whole exome sequencing data of 1403 CHH subjects and 7999 reproductively normal controls from the Mass General Brigham Biobank (MGBB) was analyzed using the GATK pipeline to identify rare 5′UTR variants [minor allele frequency (MAF) <0.1% in autosomal dominant genes and <1% in autosomal and X-linked recessive genes] in 82 known CHH genes. The variants' functional effect was assessed using the UTRannotator, a VEP plugin that identifies variants disrupting existing or creating new uORFs.

Results: We detected 50 5′-UTR variants (MAF<1%) with a predicted effect in 30 genes. Such variants were more common in CHH vs controls (1.3% vs 0.7%, $P = .034$). Variants creating new uORFs were also more common in CHH probands (CHH 0.8%—Controls 0.3%, $P = .0159$), and this pertained to autosomal dominant genes ($P = .06$) but not to autosomal and X-linked recessive ($P = .114$). Variants disrupting existing uORFs were equally prevalent in CHH and Controls (0.5% vs 0.4%, $P =$ ns). Of the 11 CHH

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

probands harboring variants creating new uORFs 6 were males and 5 females; 7 had anosmia (Kallmann syndrome) and 4 normosmic CHH; and 4 had additional non-reproductive characteristics (eg, clinodactyly, short metacarpal, learning disability/speech impairment, amblyopia, ptosis, strabismus).

Conclusions: CHH cases are enriched for rare 5′UTR variants that create new uORFs in autosomal dominant genes compared to controls, underscoring the emerging role of non-coding variants in the genetic background of CHH.

Keywords congenital hypogonadotropic hypogonadism (CHH), Kallmann syndrome, 5′ untranslated regions (5′-UTR), upstream open reading frames (uORFs)

Abstract citation ID: lvag096.1561

EP1344 - ECE_1600 - Cytokine dynamics following initiation of gender-affirming hormone therapy in transgender subjects

Yaël Sertons[1], Sarah Collet[1], Jeroen Vervalcke[1], Justine Defreyne[1], Sven C. Mueller[2], Mattias Hofmans[3], Carolien Bonroy[3], Valentino D'onofrio[4], Guy Snaterse[1], Guy T'sjoen[1] and Lapauw Bruno[1]

[1]Endocrinology, Ghent University Hospital, Ghent University Hospital, Gent, Belgium; [2]Psychology, Ghent University, Gent, Belgium; [3]Laboratory Medicine, Ghent University Hospital, Ghent University Hospital, Gent, Belgium; [4]Diagnostic Sciences, Ghent University, Gent, Belgium

Background: Sex is a major source of biological variation in humans, including immune responses. Evidence suggests that sex steroids have immunomodulatory properties, as they can potentially influence cytokine profiles and subsequently (auto)inflammatory responses. As a result, differences in sex steroid exposure could contribute to the known sex-related disparities in infectious and autoimmune diseases.

Objective: To study the effects of gender-affirming hormone therapy (GAHT) on the levels of multiple inflammatory cytokines and other related serum analytes in transgender individuals.

Material and Methods: Serum samples were collected from hormone-naïve trans women (TW) ($n = 30$) and trans men (TM) ($n = 30$) who initiated GAHT at the Ghent University Hospital, Belgium. Cisgender men (CM) ($n = 10$) and cisgender women (CW) ($n = 10$) were included as controls. Serum samples were collected at baseline and after ±6 months of treatment. High-sensitivity C-reactive protein (hs-CRP) was measured using immunoassay. Serum immune-related biomarkers (irBMs), including cytokines and chemokines, were determined using a commercial multiplex assay (Olink®), consisting of 45 markers. Serum estradiol and testosterone were determined using liquid-chromatography tandem mass spectrometry (LC-MS/MS).

Results: In total, 37 biomarkers could be detected, whereas 8 parameters were partially or completely below limits of quantification. After ±6 months of GAHT in TW, serum levels of ten cytokines (CCL2, CCL7, CCL11, CCL13, CCL19, CXCL9, CXCL10, CXCL11, IL15 and TNFSF10) significantly decreased, whereas IL7 increased. In TM, eight factors significantly increased (CCL2, CCL7, CCL11, CCL13, CCL19, IL17C, MMP1 and TNFSF10). In marked contrast, six of the cytokines that decreased in TW, increased in TM, showing an inverse relationship. Other immune-related biomarkers were not significantly affected, and levels of hs-CRP did not show a clinically relevant change over time. Within the cisgender reference cohort, three irBMs (CXCL10, CSF1 and OSM) were significantly higher in CW as compared to CM.

Conclusions: Six months of estrogen with antiandrogen treatment decreased serum levels of several cytokines and chemokines in TW. In contrast, cytokine and chemokine levels increased in TM upon treatment with testosterone. These distinct and generally opposite changes suggest a sex steroid-dependent impact, which could contribute to the sex-related disparities in (auto)inflammatory diseases. However additional research should explore potential clinical consequences, as well as the mechanisms involved.

Abstract citation ID: lvag096.1562

EP1346 - ECE_2904 - Hyperprolactinemia in Polycystic Ovary Syndrome: clinical and biochemical differences from normoprolactinemic PCOS

Ersen Karakilic[1], Ceren Tufan[1], Emre Sedar Saygılı[1], Büşra Tunç Topuz[1] and Hayri Bostan[2]

[1]Endocrinology and Metabolism, Canakkale Onsekiz Mart University Faculty of Medicine, Canakkale, Türkiye; [2]Canakkale, Türkiye

Background: Polycystic ovary syndrome(PCOS) is a prevalent endocrine disorder characterized by hyperandrogenism and ovulatory dysfunction. Although mild hyperprolactinemia is frequently reported in PCOS, its clinical relevance and contribution to hyperandrogenism remain uncertain.

Objective: To compare the clinical, hormonal, and metabolic characteristics of hyperprolactinemic and normoprolactinemic women with PCOS and to evaluate the independent association between prolactin levels and hyperandrogenemia.

Methods: This retrospective observational study included 372 women aged 18-40 years diagnosed with PCOS according to the Rotterdam criteria between 2018 and 2025. Patients were classified as hyperprolactinemic ($n = 133$) or normoprolactinemic ($n = 239$) based on baseline serum prolactin levels, after exclusion of secondary causes of hyperprolactinemia. Clinical features, hormonal profiles, and metabolic parameters were compared between groups. Correlations between prolactin and hormonal variables were assessed using Spearman's analysis. Multivariable linear regression was performed to identify independent predictors of total testosterone levels.

Results: Hyperprolactinemic PCOS patients exhibited significantly higher LH/FSH ratios, total testosterone, DHEAS, and TSH levels compared with normoprolactinemic patients (all $P <$ .05), while age, estradiol, metabolic parameters, lipid profiles, and the prevalence of hirsutism, acne, and menstrual irregularities were similar between groups. Prolactin levels showed positive correlations with total testosterone ($r = 0.246$), DHEAS ($r = 0.182$), and TSH ($r = 0.196$) (all $P \leq .001$). In multivariable regression analysis, prolactin ($B = 0.003$, $P = .001$), LH/FSH ratio ($B = 0.045$, $P < .001$), and HOMA-IR ($B = 0.008$, $P = .029$) were independently associated with higher total testosterone levels, whereas TSH and age were not(Table 1).

Conclusions: Mild hyperprolactinemia in PCOS is associated with a more pronounced hyperandrogenic hormonal profile, independent of insulin resistance and age. These findings support a potential contributory role of prolactin in PCOS-related hyperandrogenism and suggest that hyperprolactinemic PCOS may

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

represent a distinct endocrine phenotype warranting further prospective investigation.

Table 1 Multivariable linear regression analysis for total testosterone.

Variable	B	Standardized β	95% CI (Lower)	95% CI (Upper)	*P* value
Prolactin (ng/mL)	0.003	0.183	0.001	0.005	.001
LH/FSH ratio	0.045	0.254	0.027	0.064	<.001
HOMA-IR	0.008	0.117	0.001	0.015	.029
TSH (mIU/L)	0.013	0.047	−0.016	0.043	.378
Age (years)	−0.004	−0.086	−0.009	0.001	.108

B indicates unstandardized regression coefficients; β indicates standardized coefficients; CI, confidence interval. The coefficient of determination was $R^2 = 0.144$ and adjusted $R^2 = 0.131$. No multicollinearity was detected.

Abstract citation ID: lvag096.1563

EP1347 - ECE_3043 - Phenotype of Polycystic Ovary Syndrome in women with and without obesity: comparison of clinical, hormonal, metabolic and sexual features

Chiara Manzini[1], Elisa Delle Donne[1], Emma Dorato[1], Luca Persani[1,2], Linda Vignozzi[3], Marco Bonomi[1,2], Silvia Federici[1,2], Elisa Maseroli[4] and Biagio Cangiano[1,5]
[1]*Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy;* [2]*Endocrinology Department & Lab of Endocrine and Metabolic Research, IRCCS Istituto Auxologico Italiano, Milan, Italy;* [3]*Department of Experimental Clinical and Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy;* [4]*Andrology, Women's Endocrinology and Gender Incongruence Unit, Careggi Hospital University, Florence, Italy;* [5]*Milan, Italy*

Background: Obesity and Polycystic Ovary Syndrome (PCOS) share key pathophysiological mechanisms, including insulin resistance, hyperandrogenism and hypothalamic-pituitary-ovarian axis dysfunction. In literature, it is debated whether gonadal alterations in PCOS with and without obesity arise from distinct pathophysiological mechanisms. Some manifestations of PCOS are influenced by body mass index (BMI), but the specific ways in which obesity affects the gonadal axis remain unclear.

Aim: To compare clinical, hormonal, and sexual parameters between women with PCOS and severe obesity and women with PCOS without obesity, focusing on extreme BMI categories to minimize phenotypic overlap.

Materials and Methods: In this retrospective cross-sectional study we collected clinical data (age, BMI, Ferriman–Gallwey [F&G] score), hormonal parameters (LH, FSH, total testosterone, sex hormone binding globulin [SHBG], Δ4-androstenedione [D4A], dehydroepiandrosterone sulfate [DHEAS], anti-Müllerian hormone [AMH]), metabolic parameters (fasting glucose, lipid profile), and sexual function data (Female Sexual Function Index [FSFI]) from ninety-six women with PCOS and BMI ≥35 kg/m^2 (G1) or ≤29.9 kg/m^2 (G2). Patients were recruited from three centers (Auxologico San Luca, Careggi Hospital and Auxologico Piancavallo Hospital).

Results: Twenty-seven patients belonged to G1 and sixty-nine to G2. We found no significant difference between the two groups in terms of age, FSFI scores, LH and FSH levels, and the LH/FSH ratio. G1 showed higher F&G scores ($P = .0410$). Total testosterone and DHEAS levels were similar between groups, whereas SHBG was significantly lower and the free androgen index was higher in G1. D4A levels were lower in G2 ($P = .0444$). AMH levels were lower in G1 ($P = .0106$) and positively correlated with LH, D4A and the ovarian theca cell stimulation index (D4A × LH), independently of age, BMI, and HOMA index.

Discussion: We found that PCOS in patients with severe obesity is characterized by an increased clinical hyperandrogenism, exacerbated by reduced SHBG levels and increased free androgen fractions as compared with patients without obesity. In patients with severe obesity, we observed lower AMH levels correlating with reduced thecal stimulation, as suggested by the D4A × LH index. These findings support the hypothesis of blunted central stimulation in women with PCOS and severe obesity, consistent with the effects of obesity observed in male functional hypogonadotropic hypogonadism.

Conclusions: These findings seem to delineate a distinct endocrine, metabolic and reproductive clinical profile of PCOS due to severe obesity, characterized by reduced hypothalamic–pituitary stimulation, likely mediated by multiple interrelated factors.

Abstract citation ID: lvag096.1564

EP1348 - ECE_3975 - Serum sex hormone binding globulin is inversely associated with 11-oxygenated androgens and insulin resistance in women with PCOS

Eka Melson[1,2], James M. Hawley[1,3], Angela Taylor[4], Tara McDonnell[5], Veronika Tandl[6], Thais P. Rocha[7], Fozia Shaheen[4], Cornelia Missbrenner[6], Fannie Lajeunesse-Trempe[8], Aled Rees[9], Channa Jayasena[2], Larissa Gomes[7], Harpal S. Randeva[10], Georgios K. Dimitriadis[8], Alice J. Sitch[4], Karl Storbeck[11], Michael W. O'reilly[5], Barbara Obermayer-Pietsch[6] and Wiebke Arlt[1,2]
[1]*MRC Laboratory of Medical Sciences, London, United Kingdom;* [2]*Imperial College London, London, United Kingdom;* [3]*Department of Biochemistry, Wythenshawe Hospital, Manchester, United Kingdom;* [4]*University of Birmingham, Birmingham, United Kingdom;* [5]*Beaumont Hospital, Dublin, Ireland;* [6]*Medical University of Graz, Graz, Austria;* [7]*Universidade de São Paulo, São Paulo, Brazil;* [8]*King's College Hospital NHS Foundation Trust, London, United Kingdom;* [9]*University Hospital of Wales, Cardiff & Vale University Health Board, Cardiff, United Kingdom;* [10]*University Hospitals Coventry & Warwickshire NHS Trust, Coventry, United Kingdom;* [11]*Department of Biochemistry, Stellenbosch University, Stellenbosch, South Africa*

Background: Women with PCOS are at increased risk of insulin resistance and associated metabolic complications, with androgen excess identified as a major driver. Sex hormone binding globulin (SHBG) is a major determinant of androgen bioavailability; both increased levels of insulin and androgens suppress hepatic SHBG biosynthesis. Testosterone and the adrenal-derived active 11-oxygenated androgen 11-ketotestosterone are major contributors to PCOS-related androgen excess and activate the androgen receptor equipotently. However, it is not known

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

whether they differ in their impact on SHBG. Here, we examined the relationship between serum SHBG, insulin resistance and circulating classic and 11-oxygenated androgens in a large cohort of women with PCOS.

Methods: We prospectively recruited treatment-naïve women with PCOS diagnosed according to Rotterdam Criteria. We collected baseline fasting blood samples and measured classic and 11-oxygenated androgens using a validated liquid chromatography-mass spectrometry multi-steroid profiling assay. Serum SHBG, plasma insulin and glucose were measured using electrochemiluminescence immunoassays. Fasting plasma glucose and insulin were used to calculate the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) as a surrogate marker of systemic insulin resistance. Multivariate linear regression models adjusted for body mass index (BMI) were used to assess the association of SHBG with circulating concentrations of classic androgens, 11-oxygenated androgens, and the HOMA-IR.

Results: A total of 488 women with PCOS were included in the analysis [Median BMI 27.5 IQR (22.4-34.6) kg/m^2; median age 28 IQR (25-32) years]. After adjustment for BMI, SHBG was negatively associated with serum androstenedione, the central precursor of both classic and 11-oxygenated androgens ($\beta = -1.6$, $P = .02$). Similarly, SHBG was negatively associated with the potent 11-oxygenated androgen 11-ketotestosterone ($\beta = -3.8$, $P = .05$) and the slightly weaker 11-oxygenated androgen 11β-hydroxytestosterone ($\beta = -7.3$, $P = .001$). SHBG was also inversely associated with HOMA-IR ($\beta = -.03$, $P = .001$) and this relationship persisted even after adjustment for BMI ($\beta = -.02$, $P = .01$). By contrast, testosterone positively correlated with SHBG ($\beta = 3.5$, $P = .03$).

Conclusions: Serum SHBG is negatively associated with androgen excess and insulin resistance in women with PCOS. Active 11-oxygenated androgens, but not testosterone, exhibited a strong negative correlation with serum SHBG. Underlying mechanisms remain to be explored but may include that 11-oxygenated androgens exert a stronger direct suppression of hepatic biosynthesis or indirectly impact more on SHBG by driving hyperinsulinaemia.

Abstract citation ID: lvag096.1565

EP1349 - ECE_2763 - Beyond infertility: themes in quality of life and lived experiences in adults with Klinefelter syndrome

Brien Mehmet[1,2], Sofia Llahana[1], Channa Jayasena[3], Steve Gillard[1] and Andrew Dwyer[4,5]

[1]School of Health & Medical Sciences, City St George's, University of London, London, United Kingdom; [2]Department of Endocrinology and Diabetes, Royal Free Hospital NHS Foundation Trust, London, United Kingdom; [3]Department of Investigative Medicine, Imperial College London, Hammersmith, London W12 ONN, United Kingdom; [4]Endocrinology, Diabetes, and Metabolism Service, Massachusetts General Hospital, Boston, Massachusetts 02114, United Kingdom; [5]Harvard Reproductive Endocrine Sciences Centre and Reproductive Endocrine Unit, Boston, United States

Background: Klinefelter syndrome (KS) is a sex chromosome aneuploidy (47, XXY) and the most common genetic cause of hypogonadism in men, affecting 1 in 450-600 male births. Alongside hypogonadism, KS is associated with a variety of complex comorbidities influencing patients' cardiometabolic health, fertility, and mental health. This contributes to increased care needs, whilst population-based studies report a 40% increased mortality risk. An earlier systematic review conducted by the authors, suggested significantly lower Quality of Life in adults with KS across all domains "physical health," "psychological health," "level of independence," and "environment." However, qualitative research providing in-depth understanding of how KS influences QoL domains in this population remains limited. This research explored the lived experiences of adults with KS and generated themes describing factors that influence QoL.

Methods: A qualitative study utilising one-hour semi-structured interviews was conducted with fourteen adults with KS. Participants were recruited via the memberships lists of a national patient support group (The Klinefelter's Association) and a closed Facebook group affiliated with a local KS clinic. Interviews were thematically analysed using a hybrid inductive and deductive coding framework based on pre-existing literature, and the World Health Organisation's quality of life guidelines.

Results: Thematic analysis identified several themes describing how adults with KS experience and interpret quality of life. Suggesting multidimensional influences where physical challenges, psychological health and future expectations are often described. Physical health was influenced by fatigue, sleep disturbances, body composition, and body image concerns, as well as the different responses to testosterone replacement therapy. Hospital and medical management experiences were integral to quality of life. Participants described a variety of challenges and benefits to accessing specialist care, treatment optimisation, clinician knowledge and effective communication, and continuity of care. Psychological health was more complex theme, with anxiety/depression, concentration issues, and difficulties regulating emotions being clearly described. However, infertility often had strong emotional significance, further influencing psychological health, shaping self-perceived identity, relationships, and future life plans. Social connections were challenging and often difficult due to communication issues and misunderstandings, leading to loneliness. Participants described making attempts to gain independence but were limited by health and social barriers.

Conclusions: Quality of life in adults with KS is influenced by an interconnected framework encompassing physical, psychological, and social factors. Optimal patient care requires a holistic, multidisciplinary approach that promotes improvement in mental health, social functioning, and self-efficacy to reduce adverse outcomes associated with this condition.

Abstract citation ID: lvag096.1566

EP1350 - ECE_2081 - Assessment of metabolic aging in females with Polycystic Ovary Syndrome: a cross-sectional Biobank study

Kawthar Sultan, Khawla Ali, Nitya Kumar, Sawsan Saeed, Meshal Abdulla, Stephen Atkin, Pearl Wasif and John Flood

Royal College of Surgeons in Ireland-Bahrain, Busaiteen, Bahrain

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder amongst females of reproductive age. PCOS is characterized by several metabolic abnormalities including obesity and increased risk of insulin resistance (IR), both of which may contribute to accelerated metabolic aging. Metabolic age is major indicator of health and physical fitness.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

It is estimated by comparing the individual's Basal metabolic rate (BMR) to populations of the same chronological age. However, Current assessment of metabolic aging remains insufficient in females with PCOS.

Objective: To assess metabolic aging in females with PCOS.

Methods: This was a retrospective cross-sectional study utilizing data from the Polycystic Ovary Syndrome Biobank in Bahrain. Subjects' metabolic age was calculated via bioelectrical impedance. The difference between metabolic age and chronological age (age gap) was obtained for each subject. Positive values indicate a higher metabolic age than chronological age, while negative values indicate a metabolic age lower than the chronological age. HOMA-IR was utilized to estimate insulin resistance.

Results: Forty-seven PCOS subjects vs 63 control subjects were enrolled in the study. Within the PCOS cohort, metabolic age was positively correlated with age gap ($r = 0.883$, $P < .001$), HOMA-IR ($r = 0.498$, $P = .008$), c-peptide ($r = 0.371$, $P = .019$), overall body fat percentage ($r = 0$ .808, $P < .001$), body mass index (BMI) ($r = 0.649$, $P < .001$), prevalence of infertility ($r = 0$ .306, $P = .036$), and prevalence of weight gain ($r = 0$ .448, $P = .002$). Conversely, negative correlations were observed between metabolic age and free testosterone ($r = -0.484$, $P = .003$), clinical/biochemical hyperandrogenism ($r = -0.347$, $P = .018$), the total Ferriman-Gallway score ($r = -0.349$, $P = .018$), and prevalence of acne ($r = -0.356$, $P = .014$). No significant correlation was found between SHBG and metabolic age ($r = -0.0770$, $P = .687$). Higher HOMA IR values significantly predict higher metabolic age independent of chronological age ($\beta = .349$, $P = .029$). Compared to subjects without PCOS, the PCOS group showed a trend towards higher metabolic age ($r = 2.53$), though this didn't reach statistical significance ($P = .103$).

Conclusions: In PCOS, a higher metabolic age was associated with features of cardiovascular risk such as IR and obesity, and with enhanced infertility. Conversely, in PCOS the negative metabolic age suggested that free testosterone and hirsutism may relate more to actual chronological age.

Abstract citation ID: lvag096.1567

EP1351 - ECE_3492 - Menstrual distress, premenstrual symptoms, personality vulnerability traits and mental health

Mina Hagen[1], Ljiljana Marina[2,3], Natalija Antic[2], Kristina Saravinovska[2], Ana Andjelkovic[1], Anja Bosnjak[1] and Dunja Vujosevic[1]

[1]Psychology Department, Faculty of Media and Communications, Singidunum University, Belgrade, Serbia; [2]National Center for Infertility and Endocrinology of Gender, Clinic of Endocrinology Diabetes and Metabolic Diseases, University Clinical Center of Serbia, Belgrade, Serbia; [3]Faculty of Medicine, University of Belgrade, Belgrade

Menstrual distress (MD) and premenstrual symptoms (PMS) are an important indicator of how a woman's neuroendocrine system reacts to cyclical ovarian hormonal changes and are recognized as chronic stressors. Personality vulnerability (PV) traits such as Negative Affectivity, Detachment, Antagonism, Disinhibition and Psychoticism refer to stable patterns of emotional reactivity, stress coping, and interpersonal functioning that influence symptom burden and healthcare behavior. The aim was to examine whether menstrual stressors are selectively associated with specific PV traits. A total of 180 female students aged 20-35 years ($M = 22.56$; $SD = 2.88$) participated in the study. Exclusion criteria were known uterine disorders, known mental disorders, pregnancy or lactation. Forward stepwise regression analyses were performed using PV dimensions (Negative Affectivity, Detachment, Antagonism, Disinhibition, Psychoticism; assessed via PID-5-BF) as outcomes. Predictors included MD (MEDI-Q: Total Score, Menstrual Symptoms [MS], Menstrual Symptoms Distress [MSD]), PMS (SPAF), age, and hormonal contraceptive use (dummy variable). Reliability was high for SPAF and MEDI-Q ($\alpha = .85$), PID-5 trait alphas ranged from .63 (Detachment) to .71 (Antagonism). Menarche and cycle characteristics were also collected. Analysis of the PV traits revealed that scores exceeding 2—indicating moderate or higher symptom levels were found in 55 students for Negative Affectivity, 6 for Detachment, 4 for Antagonism, 4 for Disinhibition and 10 for Psychoticism. Results from SPAF indicated that 156 students met the cutoff for Moderate/Severe PMS (score >26), while 106 students reported clinically relevant menstrual distress (MEDI-Q Total Score >19). For Negative Affectivity, the final model ($F(2177) = 12.890$; $P < .001$) included SPAF ($\beta = .28$; $P < .001$) and MSD ($\beta = .18$; $P < .05$), explaining 12.7% of variance. For Antagonism, hormonal contraceptive use was the only significant predictor ($F(1178) = 4.544$; $P < .05$; $\beta = .16$; $P < .05$), explaining 2.5% of variance. No significant predictors emerged for Disinhibition, Detachment or Psychoticism ($P > .05$). Although MD and PMS were associated with higher Negative Affectivity, the cross-sectional design does not allow conclusions about causality or directionality. It is possible that stable emotional vulnerability amplifies cyclical symptom perception and distress, while recurrent severe symptoms may also reinforce anxiety-like responses over time through sleep disruption, anticipatory stress, and reduced coping capacity, which may contribute to a vicious cycle of symptom amplification and distress. These findings support the need for a multidisciplinary approach combining endocrine evaluation with targeted symptom management and stress-focused psychological interventions.

Abstract citation ID: lvag096.1568

EP1352 - ECE_3353 - Performance of an automated LC-MS/MS platform for steroid hormones and vitamin D determination in routine clinical practice

Federico Ponzetto[1], Veronica Pirana[1], Alessia Cosentino[2], Alessia Melis[1], Fabio Settanni[3], Manuela Lucchiari[3], Antonello Nonnato[3], Simona Montefiori[2] and Giulio Mengozzi[1]

[1]Clinical Biochemistry Laboratory, Department of Medical Sciences, University of Turin, Turin, Italy; [2]Roche Diagnostics S.p.A. Italy, Monza, Italy; [3]Clinical Biochemistry Laboratory, City of Health and Science University Hospital, Turin, Italy

Background-Aim: Liquid chromatography-tandem mass spectrometry (LC-MS/MS) is considered the reference method for the measurement of steroid hormones and vitamin D; however, its routine implementation in clinical laboratories is often limited by complex workflows, long turnaround times, and high operator dependency. A fully automated LC-MS/MS solution has recently become available, with the aim of simplifying analytical processes and facilitating broader clinical adoption. The aim of this

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

study was to evaluate the real-world analytical performance and workflow impact of a fully automated LC-MS/MS system for routine steroid hormone and vitamin D testing in a clinical laboratory setting.

Methods: A fully automated LC-MS/MS platform (cobas® i 601, Roche Diagnostics), integrating sample preparation, chromatographic separation, mass spectrometric detection, calibration, and quality control into a single continuous workflow, was implemented at the Clinical Biochemistry Laboratory of the City of Health and Science University Hospital of Turin in May 2025, representing the first installation of this system in Italy. Method comparison studies were performed on routine patient samples for multiple endocrine analytes, including testosterone, androstenedione, aldosterone, estradiol, 17-hydroxyprogesterone, DHEA, cortisol, and 25-hydroxyvitamin D. Results obtained with the automated LC-MS/MS system were compared with existing routine methods (automated chemiluminescent immunoassays or conventional LC-MS/MS using commercial kits) by Passing-Bablok regression and Bland-Altman analysis. Workflow efficiency and turnaround times were also evaluated.

Results: A total of 977 patient samples were included in the comparison studies. Strong correlations were observed between the automated LC-MS/MS platform and routine methods for all analytes, with coefficients of determination (R^2) ranging from 0.92 to 0.99. As expected, method-dependent biases were more evident in comparisons with immunoassays, whereas agreement with routine LC-MS/MS methods was generally excellent, with slopes close to unity and limited bias. Full automation resulted in a substantial reduction in hands-on time and overall turnaround time. For example, the analysis of an 84-sample batch of aldosterone and estradiol was completed in approximately 2 hours and 40 minutes, compared with approximately 23 hours using a conventional LC-MS/MS workflow.

Conclusions: In a real-world clinical setting, the fully automated LC-MS/MS platform demonstrated robust analytical performance for a broad panel of steroid hormones and vitamin D. The integration of all analytical steps into a continuous automated workflow significantly improved laboratory efficiency, supporting the routine use of LC-MS/MS for endocrine testing in high-throughput clinical laboratories.

Abstract citation ID: lvag096.1569

EP1354 - ECE_1640 - Exposure to PFAS impedes the meiotic maturation of mouse oocytes, affecting antioxidant responses and mitochondrial activity while causing DNA damage

Aleksandra Tatarczuch[1], Katarzyna Kotarska[2], Zbigniew Polański[3] and Anna Ptak[1]
[1]*Laboratory of Physiology and Toxicology of Reproduction, Jagiellonian University, Institute of Zoology and Biomedical Research, Cracow, Poland;* [2]*Laboratory of Genetics and Evolution, Jagiellonian University, Institute of Zoology and Biomedical Research, Cracow, Poland;* [3]*Cracow, Poland*

Background: Per- and polyfluoroalkyl substances (PFAS) are synthetic chemical compounds that remain in the environment for a long time due to their exceptional durability. Their widespread presence—including in drinking water, personal care products, furniture and packaging materials—makes human exposure to PFAS almost inevitable. A growing number of epidemiological studies indicate that women exposed to these compounds have elevated levels of PFAS in body fluids, including follicular fluid (FF). The data collected suggest that exposure to PFAS may adversely affect oocyte maturation and meiosis, leading to a deterioration in oocyte quality. As a result, this may reduce reproductive potential and decrease the chances of successful fertilization and embryo development.

Aim of study: The aim of study was to investigate the effect of a mixture of PFAS on the resting pool mice oocytes at germinal vesicle stage with particular emphasis on the induction of DNA damage and the assessment of their ability to continue meiotic maturation.

Methods: Oocytes were isolated from mature ovaries of female outbred OF1 mice and treated for 24 hours and then additionally 18 hours with PFAS mixture called Mix (PFOS, 224 ng/mL; PFOA, 145 ng/mL; PFHxS, 213 ng/mL; PFDA, 9 ng/mL; PFHpA, 6 ng/mL; PFUnDA, 4 ng/mL; PFNA, 2 ng/mL). The efficiency of meiotic maturation of oocytes was assessed based on morphological criteria, DNA damage were measured by RT-qPCR, mitochondrial activity, reactive oxygen species (ROS) levels and reduced glutathione (GSH) content were assessed using fluorescent dyes: MitoTracker Deep Red, H_2DCFDA and monochlorobimane (mBCl), respectively.

Results: Exposure of oocytes in the GV stage to a PFAS mixture led to a significant increase in GSH levels with a simultaneous decrease in ROS levels. In addition, increased mitochondrial activity was also observed compared to the control group, as well as significantly increased nuclear DNA damage. Furthermore in vitro oocyte maturation in the PFAS treatment group was significantly delayed, manifested by the accumulation of oocytes at the GVBD stage and a reduced percentage of oocytes reaching the MII stage.

Conclusions: PFAS mixture disrupts the normal functioning of oocytes in the GV stage, causing simultaneous changes in redox homeostasis and mitochondrial activity and exacerbating nuclear DNA damage. Despite seemingly beneficial metabolic effects, exposure to PFAS leads to delayed meiotic maturation and reduced ability of oocytes to reach the MII stage, which may indicate a potentially adverse effect of these compounds on oocyte quality and developmental competence.

Abstract citation ID: lvag096.1570

EP1357 - ECE_2671 - Global trends in testosterone prescribing, 2012-2024

Joshua Gialouris[1,2], Wanxin Hou[1,2] and David Handelsman[1,2]
[1]*Andrology, ANZAC Research Institute, Sydney, Australia;* [2]*Andrology, Concord Repatriation General Hospital, Concord West, Australia*

Despite no new approved indications, global testosterone sales over the last four decades have increased by 100-fold, representing a pervasive form of prescription drug misuse. More recent reports suggest a reduction in testosterone prescribing in some countries following cardiovascular safety warnings and regulatory actions. The present study aimed to appraise contemporary multinational temporal trends in testosterone prescribing. In this observational, multinational survey, wholesale sales data to pharmacies for all testosterone products were obtained for 76 countries for each quarter from April 2012 to June 2024 inclusive.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

For each testosterone product type (short or long-acting injectable, transdermal, oral, implantable, miscellaneous [intranasal or sublingual] and low-dose transdermal for female menopausal symptoms), units sold were converted to defined monthly doses per quarter, reflecting total testosterone prescribing for each product. Total testosterone usage for each product was adjusted to annual male or female population estimates for each country. National testosterone prescribing was analysed per quarter overall and per product type on a per capita basis (defined monthly dose per 1000 men or women). Over 12 years, global per capita testosterone sales increased by 1.3-fold, with progressive increases observed in 52 out of 76 countries. The increase was driven predominantly by injectable products (increases of 2-fold and 1.5-fold for long and short-acting injectables, respectively). Per capita testosterone sales increased by 1.4-fold in USA. There was a 6-fold reduction in testosterone sales in Canada, driven by a precipitate, 13-fold reduction in transdermal product sales in Canada in 2015. Prescribing of low-dose transdermal testosterone for female use increased by 8-fold globally. Without any new indications, and amidst safety warnings, a progressive increase in testosterone use continued in most countries from 2012-2024. The pattern of increase may reflect growing testosterone misuse in younger men.

Abstract citation ID: lvag096.1571

EP1358 - ECE_2008 - Primary ovarian insufficiency with bilateral hypoacusis and craniofacial dysmorphism: a case requiring advanced genetic testing

Irina Bojoga[1,2,3] and Bogdan Pascu[2,3,4]
[1]*Elias University Emergency Hospital, Bucharest, Bucharest, Romania;* [2]*University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania;* [3]*National Institute for Mother and Child Health "Alessandrescu-Rusescu", Bucharest, Romania;* [4]*EASO COM Obesity Center, Yuno Clinic, Bucharest, Romania*

Introduction: Primary ovarian insufficiency (POI) can have an autoimmune etiology and may occur as part of a genetic syndrome. Early diagnosis is essential for timely initiation of hormone replacement therapy and normal pubertal development.

Case Presentation: We present the case of a 17-year-old female with a history of secondary amenorrhea, bilateral hypoacusis, and autoimmune thyroiditis with euthyroidism who was evaluated in our department for suspected POI. Menarche occurred at 13.5 years of age, followed by irregular menstrual cycles (2-3 cycles/year). Family history was significant for autoimmune thyroiditis in the mother and maternal grandmother, irregular menses in the mother, and hypoacusis in a 19-year-old brother.

Physical examination revealed normal height and weight, with characteristic facial dysmorphism including epicanthus, micrognathia (also present in both parents), long neck, small ears, and downslanting palpebral fissures. Dental anomalies were noted, including the absence of lateral incisors, one canine, and premolars. Dermatological findings included two café-au-lait spots on the lower limbs and one hyperchromic patch on the neck. Sexual development showed Tanner stage IV for breast development, but absent axillary and pubic hair, with normal external genitalia.

Laboratory investigations confirmed POI with markedly elevated FSH (99 mUI/mL) and LH (42.5 mUI/mL), suppressed estradiol (<9 pg/mL), undetectable AMH (<0.01 ng/mL), and low progesterone and testosterone levels. Anti-ovarian antibodies were slightly elevated, suggesting autoimmune oophoritis, while anti-adrenal antibodies were negative. Thyroid function tests showed euthyroidism (TSH = 4.07 mIU/mL, FT4 = 1.06 ng/dl) with positive anti-thyroid antibodies. Pelvic ultrasound demonstrated a small tubular uterus, thin endometrium and poorly visualized ovaries. Abdomino-pelvic MRI confirmed ovaries difficult to evaluate without focal lesions. Standard karyotype analysis revealed a normal 46,XX pattern, excluding chromosomal aneuploidies.

Given the complex phenotype, comprehensive genetic testing was recommended, including whole exome/genome sequencing (WES/WGS), focusing on genes associated with POI, craniofacial dysmorphism, and hypoacusis (CLPP, ERAL1, HARS2, HSD17B4, LARS2, TWNK, SLC26A4). Hormone replacement therapy (estrogen and progesterone) was initiated to prevent long-term complications of hypoestrogenism and support normal adolescent development. Cardiac evaluation was also recommended.

Conclusions: Although less common than other autoimmune endocrine pathologies such as thyroiditis or type 1 diabetes, autoimmune oophoritis should be considered in adolescent girls presenting with amenorrhea. Early diagnosis of POI is crucial for enabling treatment initiation and normal development. The association with bilateral hypoacusis and distinctive facial features suggests an underlying genetic syndrome requiring advanced genetic testing for etiological diagnosis and optimal management.

Abstract citation ID: lvag096.1572

EP1359 - ECE_1615 - Serum multi-steroid profiling analysis in Polycystic Ovary Syndrome (PCOS) and healthy individuals

Vera Dosedelova[1], James M. Hawley[1,2], Karl Storbeck[1,3] and Wiebke Arlt[1,4]
[1]*Medical Research Council Laboratory of Medical Sciences, London, United Kingdom;* [2]*Clinical Biochemistry, Manchester University NHS Foundation Trust, Manchester, United Kingdom;* [3]*Stellenbosch University, Stellenbosch, South Africa;* [4]*Imperial College London, London, United Kingdom*

Background: Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder in women. The defining feature of PCOS is androgen excess, which contributes to several symptoms such as hirsutism, acne and irregular periods. The adrenal-derived 11-oxygenated androgens were shown to significantly contribute to androgen excess in PCOS, however the clinical relevance and biological variation of 11-oxygenated androgens in PCOS and healthy population remain insufficiently understood. Here we developed a high-throughput serum multi-steroid profiling assay with low sample volume requirements for the investigation of steroid metabolome patterns and related clinical phenotypes and characterisation of the roles of classic vs 11-oxygenated androgens in women with PCOS.

Methods: We developed a multi-steroid profiling assay for ultra-high performance liquid chromatography—tandem mass spectrometry (UHPLC-MS/MS) that included 18 steroids encompassing central precursors as well as mineralocorticoids, glucocorticoids, and androgens, including both classic and 11-oxygenated androgens, eg, testosterone, androstenedione, DHEA, 11-ketotestosterone, 11-ketoandrostenedione, 11β-hydroxyandrostenedione, and 11β-hydroxytestosterone. Steroid extraction was carried out by supported liquid extraction (SLE) and full validation of the assay was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

undertaken. We recruited 5 healthy individuals who donated blood samples weekly for 10 consecutive weeks to study intraindividual variation of steroid secretion in healthy individuals.

Results: Steroids were purified from 100 µL of serum using SLE with ethyl acetate elution. Steroids were separated on the C18 column in the gradient elution of water and methanol both containing 0.01% formic acid. Post-column infusion of 2 mmol/L ammonium fluoride was employed to enhance signal sensitivity. Lower limits of quantification were between 0.04 and 2.1 nmol/L, matrix effects were between 95% and 101%, and absolute recoveries were between 100% and 125%. Accuracy ranged from 90% to 111% and imprecision was below 7.2% and 12% for within-run and between-run analyses, respectively. Data on healthy individuals and a large PCOS cohort will be presented.

Conclusions: We successfully developed and validated a UHPLC-MS/MS assay for multi-steroid profiling including comprehensive androgen analysis in serum of women with PCOS and healthy individuals. This assay will be applied to the UK & Ireland DAISy-PCOS Phenome cohort ($n = 892$).

Acknowledgement: This research was supported by the Medical Research Council (MC_UP_1605/15) and the Wellcome Trust (209492/Z/17/Z).

Abstract citation ID: lvag096.1573

EP1360 - ECE_2053 - Changes in lung function and cardiorespiratory fitness following gender affirming hormone treatment. A prospective clinical study

Louise Skøttrup Christiansen[1], Dorte Glintborg[1], Emilie Bukh Madsen[1], Sara Ravn Bach[1], Mathilde Kamp Nørlund[1], Marianne Andersen[1], Jan Frystyk[1], Rikke Hjortebjerg[2], Tine Taulbjerg Kristensen[1], Camilla Viola Palm[2], Pernille Hermann[1], Kurt Højlund[3], Guy T'sjoen[4], Jesper Rømhild Davidsen[5] and Louise Lehmann Christensen[1]

[1]Department of Endocrinology, Odense University Hospital, Odense, Denmark; [2]Odense, Denmark; [3]Steno Diabetes Center Odense, Odense University Hospital, Odense, Denmark; [4]Department of Endocrinology, Center for Sexology and Gender, Ghent University Hospital, Gent, Belgium; [5]South Danish Center of Interstitial Lung Diseases, Department of Respiratory Medicine, Odense University Hospital, Odense Respiratory Research Unit (ODIN), Department of Clinical Research, University of Southern Denmark, Odense, Denmark

Background: Lung function and cardiorespiratory fitness are key health determinants and closely linked to biological sex. Changes in lung function and cardiorespiratory fitness during gender affirming hormone therapy (GAHT) remain understudied.

Aim: To assess lung function and cardiorespiratory fitness following GAHT in adult transgender individuals.

Design and Methods: Prospective clinical study including 54 GAHT-naïve transgender individuals (21 transmasculine and 33 transfeminine), who were examined at baseline and 1 year after GAHT initiation. In addition, cross-sectional data were collected from 36 transmasculine individuals with a median GAHT duration of 77 months, and 26 transfeminine individuals with a median GAHT duration of 45 months. A sub-cohort participated in assessment of cardiorespiratory fitness. The primary outcomes were forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), peak expiratory flow (Vyaire Vyntus® CPX system) and maximal oxygen consumption (VO_2 max, bike ergometer).

Results: In GAHT-naïve transmasculine individuals, the median (interquartile range) age at study inclusion was 25 (22; 29) years. FEV1 increased by 110 mL, FVC increased by 130 mL and peak expiratory flow increased by 890 mL/s (all $P = .01$) after 1 year of GAHT. VO_2 max was unchanged.

In GAHT-naïve transfeminine individuals, the median (interquartile range) age at study inclusion was 26 (22; 32) years. Absolute VO_2 max decreased by 163 mL/min ($P = .04$), weight-adjusted VO_2 max decreased by 5.6 (mL/min)/kg ($P < .01$) and respiratory exchange rate decreased by 0.07 ($P < .01$) after 1 year of GAHT. FEV1, FVC and peak expiratory flow were unchanged. There was no significant difference in endpoints between the GAHT-naïve group at 1 year and GAHT-ongoing group.

Conclusions: FEV1, FVC and peak expiratory flow increased after 1 year of masculinizing GAHT, whereas VO_2 max decreased and lung function was unchanged within the first year of feminizing GAHT.

Abstract citation ID: lvag096.1574

EP1361 - ECE_1677 - "Effect of insulin sensitizers on Anti-Müllerian hormone in Polycystic Ovary Syndrome"

Aleksandra Stevchevska[1,2]

[1]Clinic for endocrinology, diabetes and metabolic disorders, Skopje, North Macedonia; [2]Ss. Cyril and Methodius University in Skopje (UKIM), Skopje, North Macedonia

Introduction: Elevated AMH level is considered an indicator of anovulation in PCOS. It is postulated that the use of insulin sensitizers will lead to a reduction in insulin resistance, hyperandrogenism and consequently AMH levels, as a result of ovulation induction in these patients.

Objective: The study aimed to determine the impact of therapy with the insulin sensitizers, Metformin and Myoinositol, on Anti-Mullerian hormone and to determine its association with insulin resistance in women with polycystic ovary syndrome.

Material and Methods: a prospective, randomized, clinical study was conducted at the PHI UC for Endocrinology, Diabetes and Metabolic Diseases in Skopje, in the period 2022/2023. The study included 64 women aged 18 to 40 years, diagnosed with polycystic ovarian syndrome, according to the 2003 Rotterdam criteria. The patients were divided into two groups: group A was placed on Metformin 1500 mg XR, group B on Myo-inositol 2gr TID, during 6 months. The parameters BMI, AMH, HOMA-IR (homeostasis model assessment index) and FAI (free androgen index) were monitored.

Results: After completion of treatment, a significant decrease in AMH levels was observed in both, group A ($P = .0012$) and group B ($P = .0014$). This was accompanied with decline in HOMA IR and FAI values after the end of treatment in both groups.

Conclusions: Given the results obtained, AMH could be considered as marker of the efficacy of treatment with insulin sensitizers in PCOS.

Keywords PCOS, insulin sensitizers, metformin, myoinositol, anti-Mullerian hormone

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1575

EP1362 - ECE_1278 - Neurofibromatosis type 1 presenting as disorder of sex development

Chan Jong Kim
Gwangju, South Korea

Indtroduction: Genitourinary neurofibromas with clitoral involvement in neurofibromatosis type 1 (NF-1) are rare, and even more infrequent are the neurofibromas involving genitalia in males. The most frequent presenting sign of neurofibroma in females is clitoromegaly with pseudopenis.

Case Report: Here, we report an unusual case of ambiguous genitalia owing to neurofibroma of the clitoris resulting in an enlarged pseudophallus. A six-year-old child reared as female visited to hospital for evaluation of genital ambiguity. There was no past history of salt wasting crisis or maternal exposure to androgenic drugs during pregnancy. The patient showed multiple cafe au lait spots on both buttocks, chest and abdomen. No gonads were palpable in the labioscrotal fold or inguinal region. Hormonal evaluation revealed normal prepubertal serum gonadotropins, 17 hydroxyprogesterone, dehydroepiandrosterone sulfate, and testosterone levels. The karyotype analysis revealed normal female 46, XX pattern. Genetic analysis revealed a c.3974 +1G>A in the *NF1* genes. This intronic pathogenic mutation results from a G to A substitution one nucleotide after coding exon 29 of the NF1 gene. This alteration has been observed in multiple individuals with NF-1.

Conclusions: Clitoral involvement in NF-1 appears to be more common than previously reported and the differential diagnosis of ambiguous genitalia should include clitoromegaly due to NF. Pathogenesis of clitoral lesions appears similar to other lesions of NF. Biopsy of such lesions appears to be justified only when malignancy is suspected.

Abstract citation ID: lvag096.1576

EP1363 - ECE_3272 - Central adiposity drives persistent MASLD risk in postmenopausal women with a phenotype of Polycystic Ovary Syndrome

Eleni Armeni, Nektaria Papanikola, Areti Augoulea, Michalis Apostolakis, Panagiota Chatzivasileiou, Alexandros Nakis, Iliana Karagkouni, Dimitra Owens, George Kaparos and Irene Lambrinoudaki
2nd Department of Obstetrics and Gynaecology, National and Kapodistrian University of Athens, Menopause Clinic, Aretaieio Hospital, Athens, Greece

Background: Polycystic ovary syndrome (PCOS) is increasingly recognised as a lifelong endocrine–metabolic condition, yet its contribution to metabolic dysfunction–associated steatotic liver disease (MASLD) beyond the reproductive years remains uncertain. Menopause is accompanied by adverse changes in fat distribution and metabolic risk, raising the question of whether PCOS-related susceptibility to MASLD persists after menopause and whether this risk is driven by overall obesity or by central adiposity. Addressing this gap has direct implications for long-term endocrine follow-up and prevention strategies in women with a history of PCOS.

Methods: We performed a cross-sectional analysis of 776 postmenopausal women (mean age 63.4 ± 7.0 years; mean menopausal duration 11.2 ± 8.3 years), including 101 (17.2%) with a PCOS phenotype defined by a documented history of oligo-/amenorrhoea and/or clinical hyperandrogenism. MASLD was defined using hepatic steatosis index (HSI≥36) in combination with metabolic dysfunction, defined as the presence of at least one cardiometabolic abnormality, including overweight or obesity, impaired glucose metabolism or type 2 diabetes, hypertension, dyslipidaemia, or insulin resistance. Multivariable logistic regression models examined associations between PCOS and MASLD, adjusting for smoking and menopausal duration. To dissect the role of adiposity, separate models incorporated body mass index (BMI), waist circumference, mid-upper arm circumference, and triceps skinfold thickness. Effect-modification analyses tested interactions between PCOS and adiposity measures, with robustness assessed using bootstrap resampling (1000 iterations). Model performance was evaluated using Nagelkerke R^2.

Results: MASLD prevalence was significantly higher in women with PCOS than in those without PCOS (59.3% vs 45.3%, $P = .048$). PCOS remained independently associated with MASLD after adjustment (adjusted OR = 1.82, 95%CI 1.02-3.24). While all adiposity measures were strong predictors of MASLD, only central adiposity demonstrated robust effect modification. A significant PCOS × waist circumference interaction persisted after bootstrap validation (bootstrap $P = .028$), whereas interactions with BMI and peripheral adiposity measures were not robust. Although BMI-based models showed higher overall explanatory power (Nagelkerke R^2 0.592), only waist-based models identified a stable interaction with PCOS (Nagelkerke R^2 0.392).

Conclusions: PCOS confers persistent susceptibility to MASLD well beyond menopause, with risk preferentially mediated through central fat accumulation rather than overall obesity. These findings identify central adiposity as a key mechanistic link between PCOS and MASLD and support prioritising waist circumference over BMI for long-term hepatic and metabolic risk stratification in postmenopausal women with a history of PCOS.

Abstract citation ID: lvag096.1577

EP1364 - ECE_3301 - Cardio-metabolic signaling pathways before and after gender affirming hormone therapy

Emma Linnea Jørgensen[1,2], Oliver Knudsen[2,3], Dorte Glintborg[1], Tine Taulbjerg Kristensen[1], Anja Frederiksen[3], Marianne Andersen[1], Jan Frystyk[1], Mads Thomassen[3], Louise Lehmann Christensen[1] and Mark Burton[3]
[1]Department of Endocrinology, Odense University Hospital, Odense C, Denmark; [2]Faculty of Health Sciences, University of Southern Denmark, Odense M, Denmark; [3]Department of Clinical Genetics, Odense University Hospital, Odense C, Denmark

Background and Aim: Transgender individuals have higher risk of cardiovascular disease compared to cisgender populations. Gender-affirming hormone treatment induces changes in sex hormone levels and cardiovascular risk factors in transgender individuals. This study aims to assess changes in RNA expression of cardio-metabolic pathways before and after initiation of feminizing or masculinizing gender affirming hormone therapy.

Material and Methods: This prospective, single-center cohort study included 30 transgender persons (15 transmasculine and 15 transfeminine). Whole blood was collected before and after

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

one year of gender-affirming hormone treatment, for RNA extraction and analysis using microarray. Body composition was determined by whole body DXA scan, and fasting lipid profile, and sex hormone were measured before and after gender-affirming hormone treatment. Paired analyses of RNA expression and cardiovascular risk markers were performed.

Results: In transfeminine persons, the median age (quartiles) was 25 (23;32) years at baseline. Feminising gender-affirming hormone treatment was followed by a 1.1 kg/m^2 (−0.0;2.2) increase in BMI ($P \leq .02$) and a 5.9% (4.2;7.3) increase in fat percentage ($P \leq .01$). In transmasculine persons, the median age was 27 (22;31) years at baseline. Masculinizing gender-affirming hormone treatment was followed by a 0.3 kg/m^2 (−1.3;1.1) increase in BMI ($P \leq .86$) and a −4.9% (−7.2; −3.8) decrease in fat percentage ($P \leq .01$). Feminizing and masculinizing gender-affirming hormone treatment changed biological pathways related to lipid metabolism, insulin signalling and plaque development. Transfeminine and transmasculine individuals differed regarding which pathways were most prominently altered after gender-affirming hormone treatment initiation.

Conclusions: RNA expression of pathways related to **lipid metabolism, insulin signalling and plaque development** were changed after one year of gender affirming hormone therapy. **Expression of** several genetic pathways relevant for cardiovascular disease changed during gender-affirming hormone treatment.

Abstract citation ID: lvag096.1578

EP1365 - ECE_2455 - Oligogenic hypogonadotropic hypogonadism: divergent clinical trajectories associated with heterozygous variants in WDR11, AIRE and FGFR1

Maria Mateniadou[1], Polyzois Makras[2], Maria Evangelia Koloutsou[1], Anna Papadopoulou[3], Chrysanthi Anamaterou[4], Polyxeni Delaporta[5], Eva Kassi[1], Antonis Kattamis[5], George Mastorakos[6] and Maria Yavropoulou[1]

[1]*Endocrinology Unit, First Department of Propaedeutic and Internal Medicine, National and Kapodistrian University of Athens, Medical School, Laikon University Hospital, Athens 11527, Greece;* [2]*Department of Endocrinology and Diabetes and Department of Medical Research, 251 Hellenic Air Force & VA General Hospital Athens, LCH Adult Clinic, Athens 11525, Greece;* [3]*National and Kapodistrian University of Athens, Medical School, Attikon University Hospital and Aghia Sophia Children's Hospital, Athens 12462, Greece;* [4]*Department of Nuclear Medicine, University Hospital Heidelberg, Heidelberg, Germany;* [5]*Thalassemia Unit, First Department of Pediatrics, National and Kapodistrian University of Athens, Medical School, Aghia Sophia Children's Hospital, ERN-EuroBloodNet Center, Athens 11527, Greece;* [6]*Endocrinology Unit, Diabetes Mellitus and Metabolism, National and Kapodistrian University of Athens, Medical School, Aretaieion University Hospital, Athens 11528, Greece*

Background: Hypogonadotropic hypogonadism (HH) is increasingly recognized as a genetically complex disorder characterized by incomplete penetrance and variable expressivity. Beyond classical monogenic inheritance, growing evidence supports an oligogenic model, whereby heterozygous variants in multiple genes regulating the hypothalamic–pituitary–gonadal (HPG) axis interact with developmental and systemic modifiers to determine clinical outcome.

Objective: To explore the role of heterozygous variants in HH-associated genes in shaping divergent phenotypes, including early-onset, reversible or persistent HH.

Methods: We describe three male patients with idiopathic HH who underwent detailed endocrine phenotyping, longitudinal clinical follow-up, neuroimaging, and whole-exome-sequencing. Genetic variants were interpreted according to ACMG-criteria and correlated with pubertal development, comorbidities, treatment response, and long-term gonadal axis function.

Case-1: A 16-year-old male presented with delayed puberty and biochemically-confirmed HH, with normosmia and no structural abnormalities of the pituitary gland on magnetic-resonance-imaging. Whole-exome-sequencing identified heterozygous variants in **WDR11** (NM_018117.12:c.371A>T, p.Asn124Ile; variant-of-uncertain-significance) and **AIRE** (NM_000383.4:c.769C>T, p.Arg257*; pathogenic). Following short-term testosterone priming, spontaneous recovery of gonadotropin and endogenous testosterone secretion was observed, consistent with reversible HH.

Case-2: A 30-year-old male was diagnosed with HH in early adulthood (age 20). Whole-exome-sequencing revealed a heterozygous **WDR11** variant (NM_018117.12:c.2246G>A,p.Arg749Gln; variant-of-uncertain-significance). Neuroimaging performed during childhood demonstrated generalized cortical atrophy, widened Sylvian fissures, and an atrophic brainstem, suggesting early neurodevelopmental involvement. Despite normosmia and the absence of structural pituitary abnormalities, pubertal development remained incomplete. The patient is currently maintained on long-term hormone- replacement-therapy.

Case-3: A 48-year-old male presented with long-standing HH and eunuchoid body proportions. His medical history was notable for intermediate-β-thalassemia, diagnosed at the age of 3 years, requiring monthly blood transfusions until the age of 7, when transfusions were discontinued following splenectomy. At the age of 39, he was diagnosed with familial Mediterranean fever, treated with colchicine, and regular monthly transfusions were reinitiated. Whole-exome-sequencing identified a heterozygous **FGFR1** variant (NM_001174063.3:c.266A>G,p.Gln89Arg; variant-of-uncertain significance). The patient exhibited persistent gonadotropin deficiency without spontaneous recovery and remains on lifelong hormone-replacement-therapy. Across cases, heterozygous variants were associated with markedly different clinical trajectories, suggesting that genetic background, systemic disease burden, and developmental modifiers collectively influence HPG axis integrity.

Conclusions: These observations support an oligogenic and modulatory model of HH, in which heterozygous variants in *WDR11*, *AIRE*, and *FGFR1* may interact with clinical and developmental factors to determine disease severity and reversibility. This framework has important implications for prognosis, genetic counseling, and individualized therapeutic strategies, emphasizing the need for periodic reassessment of endogenous gonadal function in selected patients.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1579

EP1366 - ECE_3905 - Impact of ADGRG2 gene mutations on spermatogenesis

Mélanie-Clothilde Lacharme[1], Lucie Renault[2], Delphine Mallet[3], Célia Renard[4], Anne-Valérie Decouvelaere[5], Roucher Florence[3], Frédérique Dijoud[6], Ingrid Plotton[1] and Jordan Teoli[3]

[1]*Service de Médecine de la Reproduction et Préservation de la Fertilité, CHU Lyon, HCL GH Est, Hôpital Femme Mère Enfant, Bron, France;* [2]*Centre Médical Ambroise Paré, Lyon, France;* [3]*Service de biochimie et biologie moléculaire, CHU Lyon, HCL GH Est, Bron, France;* [4]*CHU Lyon, HCL GH Est, Bron, France;* [5]*CYPATH, Villeurbanne, France;* [6]*CHU de Lyon, HCL GH Est, Anatomie et cytologie pathologiques, Bron, France*

Introduction: Infertility affects 15% of couples and a male factor is identified in 50% of the cases. Azoospermia is defined as the absence of spermatozoon in the ejaculate, and can be caused by an obstruction of the reproductive tract, known as obstructive azoospermia (OA). *CFTR* is the most frequent gene implicated in genetic OA, related to congenital bilateral aplasia of vas deferens (CBAVD). More recently it has been shown that *ADGRG2*, an X-linked gene, could be also less frequently involved

Case-Report: A 25-year-old patient presented with a 9-month history of primary infertility. He had no medical condition, no history of consanguinity nor hereditary disease. Semen analysis showed an acidic pH <6.5, a decreased volume of 0.4 mL, no visualized spermatozoon. Hormones levels were within normal range. Therefore, an OA was suspected. The initial investigation of *CFTR* (139 variants screened) was negative. After testicular ultrasonography, left varicocele was embolized. Pelvic magnetic resonance imaging revealed two homogenous testis with normal size (>15 mL for left or right side), dilated epididymis, and absent seminal vesicles and vas deferens. Extensive genetic analysis (sequencing of exons of *CFTR* and *ADGRG2* genes) was performed. It identified a novel hemizygous frameshift variant NM_001079858 (*ADGRG2*):c.332dup p.(Asn111Lys*fs**8), which introduces a premature stop codon. This variant was not found in databases of genetic variants of the general population (GnomAD v4); it was classified as pathogen, and held accountable for the CBAVD. The patient underwent testicular sperm extraction (TESE): pathological examination of testicular parenchyma showed normal architecture, regular seminiferous tubules with complete spermatogenesis, and Sertoli cells with normal appearance. Spermatozoa were successfully extracted and frozen. Because of the X-chromosome inheritance, there would be no risk to transmit the mutated allele to male descendance, but all female descendance will be carrier.

Discussion: Nonsense or frameshift variants of the *ADGRG2* gene are the second most frequent genetic variations leading to CBAVD, and are probably responsible for approximately 12% to 20% of isolated CAVD that are *CFTR* mutation-free. The loss of function of *ADGRG2* gene probably leads to fluid accumulation in the testis, leading to the occurrence of CBAVD. To our knowledge, this is the first time pathological examination was reported in an *ADGRG2*-mutated patient.

Conclusions: Genetic testing for variants in *ADGRG2* gene can be considered when a patient with CBAVD is *CFTR* mutation-free. If negative, a whole genome sequencing could be performed.

Abstract citation ID: lvag096.1580

P1368 - ECE_1642 - Estradiol burden predominantly affects downstream conjugation and transport of estrogen

Anushka Subrahmanian[1,2], Liisa Veerus[1], Anjali Patel[1,2], Dareen Shah[1,3], Adrija Kundu[1,4], Xingnan Li[5], Adrian Franke[5] and Martin Blaser[1]

[1]*Center for Advanced Biotechnology & Medicine, Rutgers University, Piscataway, United States;* [2]*Rutgers-Robert Wood Johnson Medical School, Piscataway, United States;* [3]*Vanderbilt University School of Medicine, Nashville, United States;* [4]*Department of Molecular Biology, Princeton University, Princeton, United States;* [5]*University of Hawai'i, University of Hawai'i Cancer Center, Honolulu, United States*

In mammals, estrogen processing is a complex multi-step process that spans nearly all organ systems. After production in the ovaries, estrogens circulate and interact with the intracellular estrogen receptors (ER) α and β to activate downstream effectors. Estrogen molecules may be glucuronidated in the liver and kidney by UDP-glucuronosyltransferases (UGTs) followed by transport of the resulting metabolites through ATP-binding cassette (ABC) transporters toward excretory pathways. Since it is unknown how excess estrogen load affects the homeostasis of these processes, we investigated by treating 43 eight-week-old conventional C57BL/6J female mice with either a subcutaneous estradiol (E2) pellet (0.25 mg/day for 21 days) or not (controls), with sacrifices over several weeks. From both treated and untreated mice, we analyzed serum samples for circulating estrogen levels and ovary, uterus, mammary gland, liver, and kidney samples for the expression of signaling genes *Esr1* and *Esr2* (ERα and β, respectively), conjugation genes *Ugt1a1* and *Ugt1a9* (UGT1a1 and 1a9, respectively), and ABC transporter genes *Abcc2* and *Abcg2* (multidrug resistance-associated protein 2 [MRP] and breast cancer resistance protein [BCRP], respectively). Serum E2 levels increased following E2 pellet implantation, with peak levels 19-fold higher in treated females compared to controls two weeks after implantation, along with a corresponding rise in a secondary serum estrogen, estrone (E1). Expression of *Esr1* was unaffected by the excess estrogen in all tissues, and ovarian *Esr2* was upregulated in treated females at treatment peak. The estrogen exposure suppressed the hepatic conjugation genes *Ugt1a1* and *Ugt1a9*, along with renal *Ugt1a9*, with all changes developing a few weeks to a month after the peak serum estradiol levels. In contrast, the E2 exposure caused renal *Abcc2* expression to rise over the month following treatment peak, with minimal changes to hepatic *Abcc2* and *Abcg2* in both tissues. Renal *Ugt1a9* expression was negatively correlated with serum E2, and there were no other associations with serum E1 or E2. Thus, following an estrogen implantation that acutely increased serum E2 levels, there initially was a corresponding increase in estrogen receptor activity, followed by a delayed decrease in estrogen conjugation and increase in renal estrogen transport; these changes highlight dynamic mechanisms for host adaptation to variation in circulating estrogen levels, with enhanced excretion to facilitate a return to baseline. With the increasing exposures to estrogens in contemporary life and their effects on disease development, improved characterization of host estrogen metabolism may aid in understanding estrogen-driven diseases and addressing appropriate interventions.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1581

EP1370 - ECE_1223 - Retrospective study comparing vaginal and semen microbial cultures before in vitro fertilization in infertile couples reveals lack of microbial similarity

Bernadett Nádasdi[1], Petra Lilla Zádori[1,2], Rita Sinka[3], Katalin Burián[4], Viktor Vedelek[3], János Zádori[2] and Anna Vágvölgyi[1]

[1]Department of Medicine, Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary; [2]Center of Reproductive Medicine, Department of Obstetrics and Gynecology, Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary; [3]Department of Genetics, Faculty of Science and Informatics, University of Szeged, Szeged, Hungary; [4]Department of Medical Microbiology, Albert Szent-Györgyi Health Center and Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary

Introduction: Infertility affects 15%-20% of couples worldwide, including approx. 3.5% of Hungarian children born via *in vitro* fertilization (IVF). Forecasting IVF success prior to starting treatment poses significant difficulties. Recent research indicates that vaginal and seminal microbiomes affect reproductive success through effects on local immune responses, embryo implantation, and gamete performance. This research sought to investigate links between initial clinical, biochemical, and microbial factors and IVF results.

Material and Methods: A retrospective single-center study analyzed 475 infertile couples receiving IVF, with or without intracytoplasmic sperm injection, at the University of Szeged from January 2022 to December 2023. Collected data included maternal age and demographics, reproductive background, pretreatment hormone profiles, ovarian stimulation details, and endometrial measurements. Microbiological assessments of vaginal discharge and semen samples covered *Lactobacillus* presence, pathogen types, and antibiotic sensitivities. The main endpoint was clinical pregnancy, with support vector machine (SVM), random forest (RF), and extreme gradient boosting (XGBoost) models used to test combined clinical-microbial predictors.

Results: Vaginal cultures tested positive in 121 women (25.5%), primarily showing *Candida albicans* (26%), *Streptococcus agalactiae* (17%), and *Escherichia coli* (17%). Semen cultures were positive in 134 men (29%), dominated by *Enterococcus faecalis* (46%) and *Escherichia coli* (23%). Monomicrobial growth was common, and shared pathogens between partners occurred infrequently (13 couples, under 3%). Vaginal *Lactobacillus* was inversely associated with pathogens such as *Candida albicans*, *Streptococcus agalactiae*, *Gardnerella vaginalis*, and *Enterococcus faecalis*. Clinical pregnancy rates showed no difference between positive and negative vaginal culture groups (36% vs 39%, non-significant). Machine learning identified maternal age as the top predictor, with microbial factors adding limited value and *Lactobacillus* as the key microbial element.

Conclusions: Microbial changes in vaginal and seminal samples frequently occur in IVF couples, but partner pathogen matching remains exceptional. *Lactobacillus* dominance shows protective effects, positioning it as a possible marker for fertility outcomes. While microbes alone are inadequate for forecasting IVF success, combining them with standard clinical data may enable tailored reproductive strategies.

Abstract citation ID: lvag096.1582

EP1371 - ECE_1351 - Menstrual management in females with intellectual and physical disabilities: a review of 25 years of evidence and practice

Shayma Ahmed[1,2], Ashraf Soliman[1], Fawziya Alyafei[1], Nada Alaaraj[1], Noor Hamed[1], Nada Soliman[3] and Ahmed Khalil[1]

[1]Pediatric's Endocrinology, Hamad Medical Center, Doha, Qatar; [2]Pediatric's Endocrinology, Hamad Medical Corporation- Qatar, Pediatric's, Doha, Qatar; [3]Public Health, Alexandria Health Directorate, MOH, Alexandria, Egypt

Background: Menstrual health management in females with intellectual disabilities (ID) and those who are bedridden due to physical disabilities presents complex medical, ethical, and caregiving challenges. Many affected individuals experience distress, pain, or hygiene difficulties related to menstruation and may lack the cognitive or physical capacity for independent menstrual care. As a result, caregivers assume substantial responsibility for daily management, while healthcare professionals must balance symptom control, safety, quality of life, and respect for patient autonomy. Over the past 25 years, increasing attention has been given to menstrual suppression and supportive strategies in this vulnerable population, alongside growing emphasis on rights-based and ethical frameworks.

Objective: To systematically review and synthesize evidence on menstrual management strategies, clinical outcomes, caregiver impact, and ethical considerations in females with intellectual and physical disabilities.

Methods: A structured literature review was conducted covering publications from 2000 to 2025 using PubMed, Scopus, and Google Scholar. Eligible studies included females with intellectual disabilities and/or severe physical immobility and addressed menstrual hygiene, menstrual suppression, caregiver roles, or ethical aspects of care. Both quantitative and qualitative studies were considered. After screening and appraisal, ten key studies with relevant clinical and ethical data were included in the final synthesis.

Results: Across studies, hormonal interventions were the most commonly reported and effective strategies for menstrual management. Combined oral contraceptives, depot medroxyprogesterone acetate (DMPA), and levonorgestrel-releasing intrauterine devices (LNG-IUDs) were associated with reduced menstrual bleeding, partial or complete amenorrhea, and improved hygiene. These outcomes translated into a meaningful reduction in caregiver burden and improved daily care when appropriate consent and monitoring were ensured. Qualitative evidence highlighted significant gaps in menstrual health support, particularly in low-resource settings, where caregivers often lacked training, guidance, and psychosocial support. Ethical concerns were prominent, especially reports of irreversible interventions such as sterilization in certain contexts without adequate informed consent. More recent literature emphasizes autonomy, proportionality, and shared decision-making, advocating individualized care plans that consider patient comfort, caregiver capacity, and long-term risks such as bone density loss and metabolic effects.

Conclusions: Effective menstrual management in females with intellectual and physical disabilities requires a multidisciplinary,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

individualized approach that integrates medical effectiveness with ethical safeguards and caregiver support. Hormonal menstrual suppression can substantially improve quality of life but must be carefully selected, monitored, and guided by informed consent. Strengthening policies, education, and research—particularly in under-resourced settings—is essential to optimize care and protect patient rights.

Abstract citation ID: lvag096.1583

EP1372 - ECE_2554 - Clinical and laboratory parameters in women with PCOS

Catherine Shepelkevich[1], Yuliya Dydyshka[2], Alla Shepelkevich[2] and Alena Yurenia[3]
[1]Belarusian State Medical University, Minsk, Belarus; [2]Department of Endocrinology, Belarusian State Medical University, Minsk, Belarus; [3]Minsk City Clinical Endocrinology Center, Minsk, Belarus

Background: Polycystic ovary syndrome (PCOS) is defined as a chronic metabolic and reproductive disease associated with cardiovascular, gynecological, psychological, and oncological risks. Its prevalence in the population ranges from 8%-21%, making it the most common endocrine disorder in women of reproductive age. The aim of the study to evaluate to evaluate the clinical characteristics of PCOS and the incidence of comorbid conditions in young women observed at the Minsk City Clinical Endocrinology Center.

Materials and Methods: A cross-sectional retrospective study was conducted, including 150 young women diagnosed with PCOS observed at the Minsk City Clinical Endocrinology Center in 2024-2025. The study included women aged 18 to 45 years with PCOS. Clinical, laboratory, and instrumental data were used.

Results and Discussion: Data from 150 women diagnosed with PCOS were analyzed. The average age of patients was 24.5 (22-29.3) years. In the structure of PCOS phenotypes, phenotype A prevailed with an incidence of 59.33% (89), phenotype B—12.67% (19), C—2% (3), D—26% (39). When assessing anthropometric data, the median BMI was 23.06 (20.2-27.1) kg/m2, while overweight was detected in 21.05% (32), obesity—in 15.13% (23). When evaluating the diagnostic criteria, menstrual cycle disorders were found in 96.67% (145) of women, with the average age of menarche being 13 (12-14) years, the maximum duration was 90 (60-150) days. Clinical hyperandrogenism was found in 24.67% (37) of patients, with hirsutism in 8% (12), alopecia in 4.67% (7), acne in 12% (18). Laboratory hyperandrogenism was detected in 68.67% (103), with a median total testosterone level of 0.6 (0.47-0.75) ng/mL. An increase in ovarian volume of more than 10 cm^3 according to pelvic ultrasound was determined in 86% (129) of the examined women, the presence of 20 or more follicles in 10.67% (16).

Conclusions: The study results allowed us to establish the frequency of PCOS phenotypes, among which the most common were phenotypes A (59.33%) and D (26%). The obtained data confirm the high frequency of PCOS complications in young patients, which indicates the advisability of updating this problem and the need to implement measures for the early detection of associated pathology.

Abstract citation ID: lvag096.1584

EP1373 - ECE_2572 - The incidence of comorbid pathology in women with PCOS

Yuliya Dydyshka[1], Catherine Shepelkevich[2], Alena Yurenia[3] and Alla Shepelkevich[1]
[1]Department of Endocrinology, Belarusian State Medical University, Minsk, Belarus; [2]Belarusian State Medical University, Minsk, Belarus; [3]Minsk City Clinical Endocrinology Center, Minsk, Belarus

Background: Polycystic ovary syndrome (PCOS) is defined as a chronic metabolic and reproductive disease associated with cardiovascular, gynecological, psychological, and oncological risks. Its prevalence in the population ranges from 8%-21%, making it the most common endocrine disorder in women of reproductive age. The aim of the study to evaluate to evaluate the clinical characteristics of PCOS and the incidence of comorbid conditions in young women observed at the Minsk City Clinical Endocrinology Center.

Materials and Methods: A cross-sectional retrospective study was conducted, including 150 young women diagnosed with PCOS observed at the Minsk City Clinical Endocrinology Center in 2024-2025. The study included women aged 18 to 45 years with PCOS. Clinical, laboratory, and instrumental data were used.

Results and Discussion: Data from 150 women diagnosed with PCOS were analyzed. The average age of patients was 24.5 (22-29.3) years. Analysis of clinical and laboratory data for assessment of comorbid conditions included glycemia values—4.9 (4.6-5.2) mmol/l; OGTT in 23.16% (22) of patients, which confirmed the presence of IGT in 13.04% (3) of women with PCOS; T2DM—in 5.33% (8), history of GDM—in 1.33% (2). The average level of total cholesterol was 5.21 (4.42-6.03) mmol/l, hypercholesterolemia was detected in 50.6% (42) of patients. The LDL level was 3.1 (2.3-3.76) mmol/l, the indicator was increased in 65.96% (31), HDL—1.77 (1.44-2.01) mmol/l, the indicator was decreased in 8% (4). The triglyceride level was 1.06 (0.78-1.69), elevated in 22.78% (18). When assessing comorbid conditions, gynecological pathology was found in 32.67% (49) of women, and a history of psychological disorders was detected in 10.67% (12).

Conclusions: The analysis of comorbid conditions in the examined patients revealed overweight in 21.05%, obesity in 15.13%, hypercholesterolemia in more than 50%, prediabetes in 4%, and type 2 diabetes in 5.33%. Combined gynecological pathology was detected in 32.67% of women, and a history of psychological disorders was found in 10.67%. The obtained data confirm the high frequency of comorbid disorders in young patients with PCOS.

Abstract citation ID: lvag096.1585

EP1374 - ECE_2753 - Analytical performance of an automated LC-MS/MS analyzer for measurements of androgens

Russell P. Grant[1], Meghan Norris Bradley[1], Michael Vogeser[2], Pieter Vermeersch[3], Sven Groesgen[4], Dustin Wier[5], Elie Fux[4], Ruediger Laubender[4], Jan Furrer[6], William A. Clarke[7], Robert Fitzgerald[8], Louise Cowie[9], Annemieke C Heijboer[10], Raymond T. Suhandynata[8], Barry J. Toole[9] and Dusanka Kasapic[6,11]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Center for Esoteric Testing, Labcorp, Burlington, United States; [2]LMU University Hospital, Institute of Laboratory Medicine, Munich, Germany; [3]Clinical Department of Laboratory Medicine, UZ Leuven, Leuven, Belgium; [4]Roche Diagnostics GmbH, Mannheim, Germany; [5]Roche Diagnostics, Indianapolis, United States; [6]Rotkreuz, Switzerland; [7]Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, United States; [8]Department of Pathology, University of California San Diego, San Diego, United States; [9]Newcastle Upon Tyne Hospitals, Newcastle Upon Tyne, United Kingdom; [10]Endocrine Laboratory, Department of Laboratory Medicine, Amsterdam UMC Location University of Amsterdam, Amsterdam, The Netherlands; [11]Roche Diagnostics Int., Rotkreuz, Switzerland

Background & Introduction: Hyperandrogenism is a common endocrine disorder in women and female adolescents, and an important diagnostic pillar for polycystic ovary syndrome (PCOS), for example. The diagnosis of PCOS is challenging and requires an accurate quantification of androgens, specifically testosterone, androstenedione, and dehydroepiandrosterone sulfate (DHEA-S). Furthermore, clinical guidelines for PCOS emphasize the necessity of measuring 17-hydroxyprogesterone (17-OHP) to rule out Non-Classic Congenital Adrenal Hyperplasia (NCCAH), a condition that clinically mimics PCOS. Frequently used immunoassays often lack specificity, due to cross-reactivity, and limited sensitivity at lower androgen concentrations. Consequently, liquid chromatography-tandem mass spectrometry (LC-MS/MS) is recommended by international guidelines for accurate steroid measurements.

Objective: The objective of this study was to evaluate the analytical performance of the selected Ionify® Steroids assays on the Cobas® i 601 analyzer, a fully automated LC-MS/MS analyzer. The evaluation focused on the precision of testosterone, androstenedione, DHEA-S and 17-OHP.

Results: Testosterone demonstrated lot-to-lot repeatability %CVs ranging from 1.7% to 3.1% and lot-to-lot reproducibility ranging from 1.9% to 3.2%. Androstenedione showed a similar performance, with lot-to-lot repeatability %CVs between 1.6% and 3.2% and reproducibility between 1.9% and 3.2%. For DHEA-S, lot-to-lot repeatability and reproducibility %CVs were below 7% for 89% (8 of 9) of the samples tested. For 17-hydroxyprogesterone, lot-to-lot repeatability and reproducibility %CVs were below 5% for all of the samples.

Conclusions: The Cobas i 601 analyzer was found to produce accurate, precise, and consistent determinations of testosterone, androstenedione, DHEA-S and 17-OHP. These results support the use of this automated LC-MS/MS system for the reliable quantification of these steroid hormones, facilitating the accurate diagnosis of biochemical hyperandrogenism.

Abstract citation ID: lvag096.1586

EP1376 - ECE_1850 - Hypertestosteronemia in a patient with cirrhosis: the interplay of iron overload and SHBG

Mohitraje Mankumare, Mahmoud Ebid, Sumudu Bujawansa and Ram Prakash Narayanan

Diabetes and Endocrine, Mersey & West Lancashire Teaching Hospitals NHS Trust, Prescot, United Kingdom

Background: Interpretation of androgen status in men with chronic liver disease can be challenging due to alterations in sex hormone–binding globulin(SHBG). Elevated total testosterone in the presence of hypogonadal symptoms may mask relative androgen deficiency. Iron overload has also been implicated in altered SHBG metabolism, even in the absence of classic HFE mutations.[1]

Case: We report a 66-year-old man with established liver cirrhosis who was referred for endocrine assessment after detection of markedly elevated total testosterone and SHBG during investigation for erectile dysfunction and fatigue.There was no history of anabolic steroid use. Family history was notable for several relatives with haemochromatosis. Initial biochemistry demonstrated raised total testosterone-49.6 nmol/L and SHBG-157 nmol/L, with luteinising hormone(LH-8.5 IU/L) and follicle-stimulating hormone-10.6 IU/L, both within reference ranges. α-fetoprotein, β-hCG and LDH were normal. Repeat testing confirmed persistently elevated testosterone(35 nmol/L) and SHBG(153 nmol/L). Calculated free testosterone was low–normal(0.256 nmol/L), consistent with symptoms suggestive of functional hypogonadism despite high total testosterone. Iron studies revealed elevated transferrin saturation-48%. Genetic testing for HFE mutations, including p.C282Y and p.H63D, was negative, and extended testing for rarer haemochromatosis-associated mutations was also unremarkable. Liver ultrasound showed stable cirrhotic changes. Given inappropriately normal gonadotropins in the context of high testosterone, pituitary imaging was performed. MRI demonstrated a 3×3×2 mm non-enhancing hyperintense lesion, potentially consistent with incidental microadenoma, requiring surveillance only. Testicular ultrasound was normal. Eerectile dysfunction was managed with phosphodiesterase-5 inhibition.

Discussion & Conclusions: This case illustrates the complex interaction between chronic liver disease, SHBG, iron metabolism, and androgen status. Liver disease is a well-recognised cause of elevated SHBG, resulting in disproportionately high total testosterone despite reduced bioavailable androgen levels. Emerging evidence suggests that iron overload may further increase SHBG, even in the absence of pathogenic *HFE* mutations.[1] Consequently, reliance on total testosterone alone may be misleading in this population. Assessment should prioritise free or bioavailable testosterone to avoid under-recognition of clinically significant androgen deficiency and prevent misdiagnosis or inappropriate management.

Reference

1. Gautier A, Lainé F, Massart C, et al. Liver iron overload is associated with elevated SHBG concentration and moderate hypogonadotrophic hypogonadism in dysmetabolic men without genetic haemochromatosis. *Eur J Endocrinol*. 2011;165(2): 339-343. https://doi.org/10.1530/eje-11-0215

Abstract citation ID: lvag096.1587

EP1377 - ECE_1891 - Erectile dysfunction as a manifestation of MEN2B: a key indication for preimplantation genetic testing

Erik Bényei[1,2], David Ralph[3] and Marta Korbonits[1]

[1]Centre for Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom; [2]Department of Internal Medicine and Oncology, Faculty Of Medicine, Semmelweis University, Budapest, Hungary; [3]Miskolc, Hungary

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: MEN2B is a rare, autosomal dominant tumour syndrome where approximately 95% of cases are caused by the *RET* M918T mutation, which arises *de novo* in over 90% of patients. In addition to the classical endocrine manifestations—medullary thyroid carcinoma (MTC) and phaeochromocytoma—MEN2B is associated with a broad spectrum of non-endocrine phenotypic features, including marfanoid body habitus, involvement of the peripheral nervous system, such as tumours derived from neural crest cells, as well as motor and sensory neuropathies. Preimplantation genetic testing is an option for patients with MEN2B.

Case Presentation: A 14-year-old boy with a past medical history notable for severe constipation and multiple ganglioneuroma resections from the lips and oral cavity was referred to ophthalmology due to prominent bilateral corneal nerves, raising suspicion of MEN2B. Physical examination revealed a marfanoid habitus with a body mass index of 12.7 kg/m^2. His calcitonin level was 310 ng/l [<11], metanephrins were normal. The patient underwent total thyroidectomy with central lymph node dissection, and histopathological examination confirmed the diagnosis of MTC. Genetic testing identified a *RET* M918T mutation. During subsequent follow-up, the patient had measurable, but stable calcitonin levels and biochemical and imaging assessments showed no evidence of phaeochromocytoma. Eyelid "shaving" for small ganglioneurinomas was performed as needed. At 17 years of age, the patient reported absence of prior or current erections and inability to ejaculate. Endocrinological examination confirmed normal testosterone and gonadotrophin levels. Pharmacological treatment with phosphodiesterase type 5 inhibitors were unsuccessful. Following referral to urology, nocturnal penile tumescence testing was performed and demonstrated complete absence of erections. Intracavernosal alprostadil injections failed to produce clinical improvement. Implantation of an inflatable penile prosthesis is a possible further option. A literature search suggested that out of 22 familial MEN2B kindreds, the disease was transmitted by the father only in 6 occasions. Erectile dysfunction most likely contributes substantially that—in familial cases of MEN2B—the disease is predominantly passed on by females. A mouse model of MEN2B shows infertility of male mice, while normal sperm was present in the testis. Systematic evaluation of neuropathy and erectile function in male patients with MEN2B is warranted.

Conclusions: Neurological involvement in MEN2B may include severe erectile dysfunction. This devastating neurological manifestation which may affect male offspring could be a key consideration for preimplantation genetics as part of genetic counselling for patients with MEN2B planning to start a family.

Abstract citation ID: lvag096.1588

EP1379 - ECE_2030 - Reproductive outcomes and hormonal control in adolescents and adults with congenital adrenal hyperplasia: implications for transition care

Ruta Navardauskaite[1,2], Marija Kurenkoviene[1], Rimantas Uktveris[3] and Kristina Jariene[4]
[1]*Department of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania; ;* [3]*Department of Radiology, Lithuanian University of Health Sciences, Kaunas, Lithuania;* [4]*Department of Obstetrics and Gynecology, Lithuanian University of Health Sciences, Kaunas, Lithuania*

Background: Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency requires lifelong management and careful transition from pediatric to adult endocrine care. Suboptimal hormonal control during adolescence and early adulthood may predispose patients to gonadal adrenal rest tumors (TARTs/OARTs), compromised fertility. However, real-world data integrating hormonal control, gonadal imaging, and reproductive outcomes across the transition period remain limited.

Objective: To evaluate hormonal control and reproductive health in adolescents and adults with CAH and to identify clinically relevant implications for structured transition care.

Methods: This cross-sectional, single center study (2018-2023) included patients with genetically or clinically confirmed 21-hydroxylase deficiency who were followed at a national tertiary referral center. Detailed analysis focused on patients aged ≥14 years ($n = 35$; 18 males, 17 females), covering the transition from pediatric to adult care. Hormonal evaluation included 17-hydroxyprogesterone (17-OHP), testosterone, DHEA-S, progesterone, LH, and FSH. All males underwent systematic testicular ultrasound screening for TARTs, and semen analysis was offered to men ≥18 years. Females underwent pelvic ultrasound and menstrual cycle assessment. Hydrocortisone dosing was analyzed. Non-parametric statistics and Spearman correlations were applied.

Results: Only 31.4% of patients achieved recommended 17-OHP targets, indicating widespread suboptimal hormonal control during the transition period. In line with this finding, TARTs were detected in 10/18 males (55.6%), predominantly advanced-stage lesions. Semen analysis ($n = 8$) revealed severe spermatogenic impairment in all cases (6 azoospermia, 2 oligozoospermia). Ovarian adrenal rest tumors were identified in 2/17 females (11.8%). Menstrual irregularities were observed in 35% of women. Four women had achieved pregnancy, including two via assisted reproductive techniques. In females, 17-OHP strongly correlated with testosterone ($r = 0.804$, $P < .001$) and DHEA-S ($r = 0.657$, $P = .004$). In males, hydrocortisone dose correlated positively with LH ($r = 0.538$, $P = .032$), suggesting glucocorticoid-related modulation of the hypothalamic–pituitary–gonadal axis.

Conclusions: Adolescents and young adults with CAH frequently exhibit inadequate hormonal control and a high burden of reproductive complications, particularly TARTs and severe spermatogenic failure. These findings underscore the critical need for structured transition programs incorporating routine gonadal imaging, fertility counseling, and individualized treatment strategies to preserve reproductive health during the vulnerable transition and early adulthood.

Abstract citation ID: lvag096.1589

EP1380 - ECE_2463 - Bone mineral density in young adults with Turner syndrome—a single expert center experience

Ralitsa Robeva[1], Desislava Yordanova[2], Silvia Vandeva-Kalvacheva[1], Iva Stoeva[3,4], Alexander Shinkov[1] and Atanaska Elenkova[1]
[1]*Department of Endocrinology, USHATE "Acad. Iv. Penchev", Faculty of Medicine, Medical University-Sofia; Expert Center for Rare Endocrine Diseases—USHATE "Acad. Iv. Penchev", Sofia, Bulgaria;* [2]*Sofia, Bulgaria;* [3]*Screening and Functional Endocrine Diagnostics, USHATP "Prof. Dr. Iv. Mitev", Sofia, Bulgaria;* [4]*Faculty of Medicine, University "Assen Zlatarov", Burgas, Bulgaria*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Bone mineral density in reproductive-aged women with Turner syndrome (TS) is usually lower compared to that of healthy women because of estradiol deficiency, X-chromosome monosomy, additional genetic, hormonal, and environmental factors.[1] Nevertheless, the data on bone health in adult TS patients from various ethnic groups are still limited.

Aim: The present study aims to investigate spine bone mineral density in Bulgarian women with TS, thereby exploring different hormonal factors that may contribute to the lower bone mass.

Materials and Methods: Spinal (L1-L4) BMD (Z-score) was investigated in 34 TS patients (age 18-49 years). The possible associations with different hormonal factors and therapies were studied.

Results: the spinal BMD Z-score of TS women varied between −4.12 and +1.1, with a median of −1.31. It was not associated with the karyotype, age, age of diagnosis or the presence of autoimmune thyroiditis of the TS women ($P > .05$). However, it was positively related to patients' body mass index ($r = 0.401$, $P = .019$), and estradiol levels ($r = 0.436$, $P = .018$). No low-energy fractures were experienced by the women in the group. Testosterone, dehydroepiandrosterone-sulphate, 25-OH vitamin D, thyroid-stimulating hormone and prolactin levels were not related to the BMD ($P > .05$), while follicle-stimulating hormone (FSH) levels tended to be inversely associated with spinal Z-score ($r = −0.351$, $P = .053$). Women treated with estrogens for more than two years had significantly higher BMD Z-score than others (−0.5 vs −2.1, $P = .012$), while past growth hormone treatment did not influence the BMD Z-score (−1.3 vs −1.4, $P = .580$) significantly. A total of 3 of 18 TS individuals (16.67%) remained with lower bone density (Z-score <−2.0) despite the good adherence to long-lasting hormone replacement therapy.

Conclusions: the long-lasting estrogen-replacement therapy leading to normal estradiol and FSH levels is crucial for the bone density in young adults with TS. Additional genetic or environmental factors might be associated with poor bone health in some TS women despite adequate hormonal treatment. Further studies are needed to identify the best therapeutic approach for bone health improvement in women with TS.

Keywords Turner syndrome, BMD, spinal Z-score, osteodensitometry

Reference

1. Itonaga T, Koga E, Nishigaki S, Kawai M, Sakakibara H, Hasegawa Y. A retrospective multicenter study of bone mineral density in adolescents and adults with Turner syndrome in Japan. *Endocr J*. 2020;67(10):1023-1028. https://doi.org/10.1507/endocrj.EJ20-0083

Abstract citation ID: lvag096.1590

EP1383 - ECE_3514 - Mangement considerations in adult presentation of 46,XX congenital adrenal hyperplasia in individuals raised as male

Ashani Wickramarachchi[1,2] and Jeremy W Tomlinson[1]
[1]*Oxford, United Kingdom;* [2]*Oxford Center for Diabetes, Endocrine and Metabolism, Oxford University Hospital, Oxford, United Kingdom*

Congenital adrenal hyperplasia (CAH) is a steroidogenic enzyme disorder most caused by 21-hydroxylase deficiency, with a variable clinical presentation. Adult diagnosis is more frequently recognised in individuals assigned female sex at birth. We describe two rare cases of 46,XX CAH in individuals raised as male, both diagnosed later in life following incidental imaging findings revealing internal female reproductive organs. Patient 1, born in the 1930s and raised as male, underwent hypospadias repair at 15 years of age and lived in a stable marital relationship with an adopted child. Imaging performed for unrelated indications incidentally identified bilateral adrenal hyperplasia and a rudimentary uterus, prompting further endocrine and genetic evaluation at the age of 75 years. Adrenal biopsy was consistent with CAH, and chromosomal analysis confirmed a 46, XX karyotype. A failed short Synacthen test led to initiation of glucocorticoid replacement, though interestingly, he never had features of adrenal insufficiency. Following appropriate counselling, the patient chose not to receive the results of chromosomal analysis. He died at the age of 83 from unrelated causes. Patient 2 was raised and lived as male and was diagnosed at 40 years of age with CAH due to compound heterozygous mutations in the 21-hydroxylase enzyme, with a confirmed 46,XX karyotype. Pelvic imaging demonstrated an involuted postmenopausal-type uterus with bilateral ovaries and a patent endocervical canal, alongside male-typical external genitalia. After discussion regarding the uncertain malignant potential of retained internal reproductive organs exposed to prolonged androgen excess, the patient opted for surveillance rather than surgical intervention. Glucocorticoid replacement was initiated following a failed Synacthen test; however, adherence was suboptimal, influenced by concerns regarding testosterone suppression. Disclosure of the diagnosis and karyotype resulted in significant psychological distress, fertility-related concerns, depression, and suicide attempts. These cases illustrate the complex clinical, ethical, and psychosocial challenges associated with late-diagnosed CAH in adulthood. Delayed diagnosis, particularly in individuals raised in eras without newborn screening, may result in long-standing endocrine, reproductive, and psychological consequences. The discordance between chromosomal sex, internal reproductive anatomy, and lived gender identity underscores the importance of patient-centred care, sensitive communication, and respect for autonomy, including decisions regarding disclosure of genetic information. Multidisciplinary management involving endocrinology, genetics, psychology, and specialist services for disorders of sex development is essential to optimise long-term outcomes.

Abstract citation ID: lvag096.1591

EP1384 - ECE_3130 - Glycogen storage disease type III presenting with hypogonadotropic hypogonadism and infertility: a rare case report

Naciye Guduk Sirvan[1], Selin Tekin[2], Alperen Onur Işler[2], Suleyman Nahit Sendur[2], Rahşan Göçmen[3], Onur Keskin[4], Hasan Ozen[5], Alev Ozon[6], Can Ebru Kurt[7] and Selcuk Dagdelen[2]
[1]*Internal Medicine, Hacettepe University Hospital, Ankara, Türkiye;* [2]*Endocrinology, Hacettepe University Hospital, Ankara, Türkiye;* [3]*Radiology, Hacettepe University Hospital, Ankara, Türkiye;* [4]*Gastroenterology, Hacettepe University Hospital, Ankara, Türkiye;* [5]*Pediatric Gastroenterology, Hacettepe University Hospital, Ankara, Türkiye;* [6]*Pediatric Endocrinology, Hacettepe University Hospital, Ankara, Türkiye;* [7]*Neurology, Hacettepe University Hospital, Ankara, Türkiye*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Glycogen storage disease type III (GSD III) is a rare autosomal recessive metabolic disorder caused by mutations in the AGL gene, leading to a defect in the glycogen debranching enzyme. It primarily affects the liver and skeletal muscle, with childhood manifestations like hepatomegaly, fasting hypoglycemia, and elevated transaminases. Endocrine complications are exceptionally rare and the coexistence of hypogonadotropic hypogonadism and infertility has been scarcely reported. In this case report, we present a male patient with genetically confirmed GSD type III who developed hypogonadotropic hypogonadism and infertility, emphasizing the importance of recognizing multisystem involvement in metabolic diseases.

Case Presentation: A 28-year-old man with a known diagnosis of glycogen storage disease type III since childhood was admitted with infertility and decreased libido. Physical examination revealed short stature, reduced facial and body hair, and small testes. Laboratory studies showed markedly low total testosterone (78 ng/dL), low luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels, but normal prolactin and thyroid hormone levels, consistent with hypogonadotropic hypogonadism. Liver enzyme levels were persistently elevated (AST 154 U/L, ALT 132 U/L), and ultrasonography of the abdomen revealed hepatomegaly. Serum triglyceride levels were elevated as well. Scrotal ultrasonography demonstrated bilateral testicular atrophy, and semen analysis confirmed azoospermia. Magnetic resonance imaging (MRI) of the pituitary gland demonstrated pituitary stalk hypoplasia. Genetic testing reconfirmed homozygous *AGL* mutation consistent with GSD type III. Testosterone replacement therapy was begun, leading to significant improvement in libido, energy, and general well-being. The patient was referred for reproductive counseling for assisted fertility options.

Conclusions: This case highlights an uncommon endocrine manifestation of glycogen storage disease type III, in which chronic metabolic decompensation and hepatic dysfunction, possibly related to infundibular hypoplasia, may contribute to secondary hypogonadotropic hypogonadism and infertility. Recognition of endocrine complications in GSD is crucial for timely hormonal replacement and fertility counseling. Adult survivors of GSD should be followed up in multidisciplinary care settings to monitor and manage late-onset endocrine and metabolic complications effectively.

Abstract citation ID: lvag096.1592

EP1386 - ECE_2443 - Reproductive characteristics of adult Turner syndrome patients—a single center experience

Ralitsa Robeva[1], Sesil Kedikova[2], Diana Hristova[3], Yuri Hranov[3], Desislava Yordanova[4], Iva Stoeva[5,6] and Atanaska Elenkova[1]

[1]Department of Endocrinology, USHATE "Acad. Iv. Penchev", Faculty of Medicine, Medical University-Sofia, Expert Center for Rare Endocrine Diseases—USHATE "Acad. Iv. Penchev", Sofia, Bulgaria; [2]Acibadem City Clinic University Hospital "TOKUDA", Sofia, Bulgaria; [3]Department of Obstetrics and Gynecology, Faculty of Medicine, Medical University-Sofia, University Obstetrics and Gynecology Hospital "Maichin dom", Sofia, Bulgaria; [4]Sofia, Bulgaria; [5]Screening and Functional Endocrine Diagnostics, USHATP "Prof. Dr. Iv. Mitev", Sofia, Bulgaria; [6]Faculty of Medicine, University "Assen Zlatarov", Burgas, Bulgaria

Background: Turner's syndrome is a genetic condition associated with significantly diminished ovarian follicular reserve.[1] Nevertheless, up to 20% of women with TS might have spontaneous menarche, and up to 12% of them achieve pregnancies in the developed countries.[1,2] However, data about the fertility of TS patients in different regions across Europe are still lacking.

Aim: The present study aims to investigate the reproductive history of Bulgarian patients with Turner syndrome (TS) and to identify gaps in the care for women with TS.

Materials and Methods: 74 patients with TS (age: 18-59 years) have been investigated. The prevalence of menstrual disturbances, live births, and hormone replacement therapy was studied in the group.

Results: The prevalence of primary amenorrhea was 87.8% (36/41) in monosomic 45, XO patients, 37.5% (6/16) in women with structural X abnormalities, and 47.1% (8/17) in mosaic TS individuals ($P < .001$). Spontaneous menarche was observed in 24 patients at a median age of 14.6 years. Among women with spontaneous menarche, all but two developed secondary amenorrhea in adolescence. Only two patients retained regular menstrual cycles in adulthood, both with non-monosomic forms of TS. The first one entered menopause at the age of 30 years, while the other retained a regular menstruation pattern at the age of 19 years, with still normal follicle-stimulating hormone (FSH) and anti-mullerian hormone (AMH). Only one of the patients gave birth to a healthy child after egg donation and pregnancy complicated with gestational diabetes and preeclampsia. No spontaneous pregnancies occurred in the investigated group. A total of 45 (61.6%) of the 73 amenorrheic patients had received regular HRT. Late TS diagnosis or poor adherence to therapy were observed in other women.

Conclusions: Only 2.7% of Bulgarian TS patients who have reached adulthood retain regular menstruation; moreover, pregnancies in the TS group are very rare. Social and financial support is needed for patients with TS in developing countries to allow access to modern assisted reproductive technologies. More efforts should be taken by medical specialists to improve adherence to HRT in adult women with TS.

Keywords Turner syndrome, pregnancy, menstrual disturbances, HRT, fertility

References

1. Porcu E, Cipriani L, Damiano G. Reproductive health in Turner's syndrome: from puberty to pregnancy. *Front Endocrinol (Lausanne)*. 2023;14:1269009. https://doi.org/10.3389/fendo.2023.1269009
2. Bryman I, Sylvén L, Berntorp K, et al. Pregnancy rate and outcome in Swedish women with Turner syndrome. *Fertil Steril*. 2011;95(8):2507-2510. https://doi.org/10.1016/j.fertnstert.2010.12.039

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1593

EP1387 - ECE_3572 - Gonadal function in sickle cell disease: data from a tertiary center

Kalliopi Pantelia[1], Aggeliki Kyriakou[1], Angeliki Angelidou[1], Vasiliki Antonopoulou[1], Angelos Theocharis[1], Aikaterini Kapama[1], Kanella Kantreva[1], Loukia Evliati[2], Chrysa Kalkana[2], Marinella Tzanela[1] and Georgia Ntali[1]
[1]*Department of Endocrinology "D. Ikkos"- Diabetes Center-EndoERN-Evangelismos General Hospital, Athens, Greece;* [2]*Thalassaemia and Sickle Cell Unit, Evangelismos General Hospital, Athens, Greece*

Introduction: Sickle cell disease (SCD) results from a structural hemoglobin abnormality, causing chronic hemolytic anemia and recurrent vaso-occlusive events that lead to ischemia and organ dysfunction. Gonadal dysfunction has been reported in both sexes, but data remain limited. Treatments such as chronic transfusions and hydroxyurea may impair gonadal function.

Aim: To evaluate gonadal function of patients with sickle cell disease.

Patients and Methods: This retrospective study included 42 patients with SCD (27 women, 15 men) followed at the Mediterranean Anemia and Sickle Cell Disease Unit of Evangelismos General Hospital in Athens. 35/42 patients had sickle cell–thalassemia. Data included age at menarche, menstrual characteristics, age at menopause for women and serum testosterone levels for men and hydroxyurea use (HU) during reproductive age.

Results: We identified 27 women and 15 men with sickle cell disease. Mean age at menarche (±SD) was 13.7 (±1.6) years, with most women reporting normal cycles. Mean age at menopause (±SD) was 46.3 (±5) years. 1/27 women (4%) had hypothalamic amenorrhea. 3/27 (11%) were diagnosed with premature ovarian insufficiency and 1/27(4%) reported early menopause. Mean menopause age was similar in women exposed and unexposed to HU. No cases of hypogonadism were identified in men. Mean testosterone (±SD) was 575 (±254) ng/dL; 14/15 men had received HU.

Conclusions: Patients with SCD showed a mild delay in menarche compared with the average age in Greece (12.3-12.4 years), as well as an earlier age at menopause (average age of menopause in Greece 48.7-49.1 years). Menopause age does not appear to be influenced by hydroxyurea exposure during reproductive age. Despite literature reports of hypogonadism in up to 24% of male patients with SCD, no such cases were observed in our cohort. Data on gonadal function in SCD, particularly in sickle cell–thalassemia, remain scarce and warrant further investigation.

SCD PATIENT DATA	
Patients with SCD	**42**
Women	**27/ 42**
Men	**15/ 42**
Patients with HbSβ	**35/ 42**
WOMEN	
Mean age (SD)	**54,1** (11,7)
Mean age: menarche [*N* = 26] (SD)	**13,7** (1,6)
Mean age: menopause [*N* = 17] (SD)	**46,3** (5)
SCD + HU [*N* = 7] (SD)	**46,1** (6)
SCD without HU [*N* = 10] (SD)	**46,4** (4,5)
MEN	
Mean age (SD)	**52,5** (10,3)
Mean serum testosterone [ng/dL] (SD)	**575** (254)
Men with low testosterone	**0/15**
Men receiving HU	**14/15**

Abstract citation ID: lvag096.1594

EP1388 - ECE_1762 - Overlapping cognitive presentations of Andropause and Alzheimer's disease: two case reports

Akriti Karki[1], Elizabeta Mukaetova-Ladinska[2] and Ali Al Jumaah[3]
[1]*University Hospitals of Leicester NHS Trust, Leicester, United Kingdom;* [2]*Leicester, United Kingdom;* [3]*Endocrinology Department, University Hospitals of Leicester NHS Trust, Leicester Cancer Research Centre, University of Leicester, Leicester, United Kingdom*

Background: Andropause, a prevalent hormonal disorder in aging men, is clinically described as late onset hypogonadism. Diagnosed based on clinical manifestations of testosterone deficiency. (TD) Testosterone declines after the age of 30, reducing at a rate of 0.2%-1% per year in total testosterone (TT). According to the International society of sexual medicine, TD is defined as TT <8 nmol (231 ng/dl). It is associated with sexual, musculoskeletal, cognitive symptoms and reduced quality of life. Evidence of testosterone role upon cognitive function remains limited. Men with early-onset Alzheimer's disease alongside memory impairment may also have significant changes in mood and motivation, including apathy, depression, and irritability. This warrants further investigation of co-existing testosterone deficiency.

Case Reports: Mr A, a 64-year-old man with confirmed Alzheimer's disease (AD) presented with total testosterone <8 nmol/L. AD diagnosis was supported by CSF biomarkers (elevated phosphorylated tau and reduced amyloid-β42:40 ratio) and FDG-PET findings consistent with AD. Testosterone therapy increased levels to 13.3-17.2 nmol/L and was associated with improvements in mood, cognition, and behaviour. Subsequent initiation of donepezil 5 mg provided additional memory benefit. Mr. B, a 65-year-old man, presented with an 18-month history of progressive cognitive difficulties, including date confusion, task forgetting, word-finding difficulties, and functional errors, with limited insight. He also reported apathy, anhedonia, sensory hypersensitivity, sleep disturbance, and increased appetite. Cognitive testing showed preserved global cognition (SDTP 7/7; RUDAS 30/30) with selective memory impairment on ACE-III (81/100), and low total testosterone (7.2 nmol/L). Brain MRI demonstrated age-related involutional changes without features consistent with Alzheimer's disease. CSF findings awaited. His apathy improved with memantine 20 mg mane.

Discussion: The overlapping symptoms between andropause and Alzheimer's disease (AD) are commonly overlooked. Both can have

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

detrimental impacts, resulting in low mood, poor memory, anhedonia, and reduced quality of life. Studies have highlighted the protective role of testosterone against AD, including its involvement in tau protein cleavage and prevention of beta-amyloid–induced neuronal death. Cohort studies have reported that individuals with higher testosterone-to–sex hormone–binding globulin ratios are associated with improved visual and verbal memory and slower longitudinal memory decline.

Learning Points

- Testosterone deficiency is common, under-recognised, and can contribute to cognitive, mood, and behavioural symptoms in older men.
- Hypogonadism represents a potentially reversible and treatable factor, even alongside neurodegenerative disease.
- Routine testosterone assessment may aid holistic management and optimise outcomes through endocrine—neurology collaboration.

Abstract citation ID: lvag096.1595

EP1389 - ECE_2499 - Robertsonian translocation (13;14) and endocrine dysfunction: implications for recurrent pregnancy loss

Kalyani Nagarajah[1,2,3]
[1]Aneurin Bevan Health Board, Endocrinology, Endocrinology, Newport, United Kingdom; [2]Aneurin Bevan, Endocrinology and Diabetes, Endocrinology, Newport, United Kingdom; [3]Aneurin Bevan, Endocrinology and Diabetes, Newport, United Kingdom

Recurrent pregnancy loss often involves male factor infertility, where structural chromosomal variants like Robertsonian translocations play a critical role. These balanced rearrangements, notably rob(13;14), disrupt meiotic segregation, leading to spermatogenic impairment and unbalanced gametes that compromise embryo viability.[1,2] Updated global consensus statements advocate systematic karyotyping alongside endocrine profiling in subfertile males to enable precision reproductive strategies.[3,4] A 33-year-old male underwent assessment after his partner's repeated first-trimester losses during fertility treatment. He reported no chronic illnesses or medications. Initial semen evaluation confirmed oligospermia. G-banded karyotyping disclosed a Robertsonian translocation t(13;14), cytogenetically denoted 45,XY,der(13;14)(q10;q10). Endocrinological workup demonstrated subnormal gonadotrophins and testosterone diagnostic of hypogonadotropic hypogonadism; however, sellar MRI revealed no anatomical defects. Reproductive counselling encompassed gonadotrophin supplementation alongside preimplantation genetic testing for structural rearrangements (PGT-SR) to prioritise euploid embryo transfer. Carriers exhibit oligozoospermia, teratozoospermia, and elevated aneuploidy rates in embryos, driving reproductive failure.[1,2,5] Cohort analyses validate PGT-SR integration within IVF protocols, yielding superior implantation rates and miscarriage reduction through euploid selection.[2,4,5] Sporadic reports link Robertsonian carriers to isolated gonadotrophin deficiency, postulating contiguity effects on HPG axis loci or cryptic gene disruptions.[6] Harmonised AUA/ASRM–EAU frameworks mandate holistic genitourinary phenotyping—cytogenetics plus serial hormone assays—to stratify risk and tailor adjunctive therapies.[3,4] This presentation exemplifies synergistic genetic–endocrine perturbation of male gametic competence and gestational success. Males in recurrent loss cohorts warrant protocolised genetic–hormonal scrutiny, especially with seminal compromise. This paradigm shift underpins PGT-SR deployment, hormone repletion, and expectant management, maximising term delivery while curtailing iterative grief.[1-6]

References

1. Bandyopadhyay R, et al. Review: Robertsonian translocation (13;14) and its clinical manifestations. *Fertil Steril*. 2025.
2. Chen Y, et al. Chromosomal abnormalities in couples with infertility and recurrent miscarriage. *Reprod Genet*. 2024.
3. American Urological Association (AUA) and American Society for Reproductive Medicine (ASRM). Updates to Male Infertility Guidelines. *J Urol*. 2024.
4. European Association of Urology (EAU). Male Infertility Guidelines. 2025.
5. Benn P, Merrion K. Chromosome segregation of human nonhomologous Robertsonian translocations. *Eur J Hum Genet*. 2024;33(6):711-717. https://doi.org/10.1038/s41431-024-01693-w
6. Baghdasaryan E, Turner R, Abnous O, Valles-Ayoub Y, Robinson M. Normosmic hypogonadotropic hypogonadism, pituitary hypoplasia, and testicular microlithiasis in 45,XY Robertsonian translocation. *Genet Mol Med*. 2024;5(1):1-3.

Abstract citation ID: lvag096.1596

EP1390 - ECE_2565 - From recurrent ovarian torsion of enlarged ovaries in childhood to PCOS diagnosis in adolescence: case series

Zuzanna Aurast[1,2] and Karina Kapczuk[1]
[1]Division of Gynaecology, Department of Gynaecology, Poznan University Of Medical Sciences, Poznań, Poland; [2]Doctoral School, Poznan University Of Medical Sciences, Poznań, Poland

Introduction: Polycystic ovary syndrome (PCOS) is a common endocrine-metabolic disorder in women of reproductive age. The etiology of the syndrome is complex and not fully known. Pediatric and adolescent populations present a challenge for physicians to make an accurate diagnosis due to an overlap between physiological features during puberty and symptoms and diagnostic criteria of PCOS established by the European Society of Human Reproduction and Embryology (ESHRE) 2023. Ovarian torsion in childhood is mostly caused by an adnexal mass; however, almost 50% of patients do not present a focal ovarian lesion, and the cause of oversized ovaries in childhood is not fully known. We present two cases of patients with enlarged ovaries and recurrent ovarian torsion in the prepubertal period, who were diagnosed with PCOS in adolescence.

Case Presentation: Case 1: Following two episodes of left ovarian torsion without mass (at age 4.2 and 4.7 years, respectively), the girl underwent ovariopexy. The third episode of torsion took place at age 6.3. From the age of 5.3 to 9.3, the mean ovarian volume (OV) increased from 3.3 cm^3 to 12 cm^3, despite the girl being prepubertal. She had menarche at age 15.2 years.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Following menarche, she presented with functional abnormal uterine bleeding for more than 2 years, but no hyperandrogenism. At the age of 17.3, the mean OV was 23 cm^3, markedly elevated LH, impaired glucose tolerance and insulin resistance were found, and the patient was classified as being at risk for PCOS. Case 2: The girl had her first episode of left ovarian torsion without mass in prepuberty, at age 9.8, and the second, followed by ovariopexy, in early puberty (Tanner 2) at age 10.8. Mean OV (after resolution of oedema) was 8.5 cm^3. The third episode of torsion occurred at the age of 12. Mean OV 3 months after surgery was 13.4 cm^3. She had menarche at age 13.3. Since the second year after menarche, she presented with oligomenorrhea. No hyperandrogenism was found, but the patient had markedly elevated LH. Mean OV was 13.6 cm^3 at age 17.5 and 17 cm^3 at age 21.3. She was diagnosed with PCOS.

Conclusions: Ultrasound criteria of polycystic ovarian morphology (PCOM) in adolescence are not currently defined and therefore not included in diagnostic criteria of PCOS in this age group. However, increased OV in childhood and adolescence might be the early manifestation of a high risk for PCOS. Long-term follow-up is essential for these patients to enable early, personalized management.

Abstract citation ID: lvag096.1597

EP1391 - ECE_3025 - Xeroderma pigmentosum: an underrecognized cause of premature ovarian insufficiency

Doha Dahmani, Aziouaz Fatima and Benkacem Mariem
Endocrinology and Metabolic Diseases Department, Mohammed VI University Hospital, Tangier, Morocco

Introduction: Xeroderma pigmentosum (XP) is a rare autosomal recessive disorder caused by mutations affecting one of seven genes involved in the DNA repair pathway, leading to hypersensitivity to the deleterious effects of ultraviolet (UV) radiation on DNA. From a gynecological and endocrine perspective, women with XP appear to be at increased risk of developing premature ovarian insufficiency (POI). We report the case of a 29-year-old woman with XP who presented with secondary amenorrhea, in whom investigations revealed POI.

Case Report: A 29-year-old woman with xeroderma pigmentosum diagnosed in childhood presented with secondary amenorrhea of one year's duration. Menarche occurred at the age of 13 years, with regular menstrual cycles until the age of 24 years, followed by the onset of oligo-spaniomenorrhea and subsequently secondary amenorrhea associated with hot flashes from the age of 28 years. Hormonal evaluation revealed hypergonadotropic hypogonadism with low estradiol and markedly elevated FSH and LH, associated with a severely reduced ovarian reserve (AMH <0.01 ng/mL), consistent with premature ovarian insufficiency. Karyotype analysis was normal.

Discussion: This case highlights a rarely described association between xeroderma pigmentosum, a DNA repair–deficiency disorder, and premature ovarian insufficiency, highlighting the essential role of genomic stability in preserving normal ovarian function. The ovaries, due to their high proliferative activity, exhibit particularly high expression levels of the XPC gene, likely reflecting an increased requirement for correction of replication errors and repair of endogenous DNA damage. Murine models of XP demonstrate reduced reproductive performance, associated with increased apoptosis of germ cells. Merideth et al. (2019) evaluated 60 women with xeroderma pigmentosum and found that 31% of these patients had experienced menopause, with 78% meeting criteria for premature menopause; the median age at menopause was 29.5 years, approximately 20 years earlier than in the general population.

Conclusions: Awareness of the increased risk of premature menopause in women with xeroderma pigmentosum warrants early surveillance to detect declining ovarian reserve and to guide reproductive management. When indicated, initiation of hormone replacement therapy is essential to prevent skeletal and cardiovascular complications.

Abstract citation ID: lvag096.1598

EP1393 - ECE_3719 - Return of "menses" after menopause: un unusual cause

Kalliopi Bilariki[1], Youssef El Cadhi[2], Jennifer Lerouge[2], Noemie Bertrand[3], Sarra El Younsi[1], Jean-Noël Barjon[1] and Etienne Justinien[1]
[1]*Endocrinology, Compiegne Noyon Intercommunal Hospital Center, Compiegne, France;* [2]*Chamant, France;* [3]*Private practice (General practicioner), Chantilly, France*

Introduction: Postmenopausal bleeding most frequently reveals uterine lesions. We report a case of a postmenopausal bleeding leading to the diagnosis of an ovarian Leydig cell tumour.

Observation: A 57-years-old obese woman, reporting menopause since the age of 49, is seen in July 2023 at the endocrinology outpatient clinic for evaluation before bariatric surgery. Laboratory tests reveal iron deficiency, The patient is at that time asymptomatic. She is addressed in Gastroenterology and Gynecology for evaluation and workup. Gastroscopy reveals a gastritis and coloscopy reveals a diverticulosis. At this time, a first episode of uterine bleeding reveals a thick endometrium. She has an hysteroscopy and biopsies, as well as two pelvic ultrasounds, referred as normal. The patient is finally allowed to undergo a sleeve gastrectomy in March 2024. She now reports "regular menses". We suspect that previous amenorrhea was related to obesity and not menopause. This hypothesis is consistent with the biology: FSH 16 U/L, LH 10.13 U/l et Oestradiol 2046 pmol/l. Surprisingly, the patient provides us with previous (2019) data: FSH 47 U/l LH 36 U/l. She now develops hirsutism, which is intriguing in the context of weight loss following sleeve gastrectomy. Further laboratory tests reveal an hyperandrogenism: elevated D4-androstenedione and testosterone but normal DHEAS levels, indicating an ovarian rather than adrenal origin. New ovarian ultrasound reports normal left ovary and fails to visualize right ovary. A Pelvic MRI reveals a 2 cm right ovarian mass. Ca-125 and HE4 are in normal ranges. The patient undergoes hysterectomy and bilateral annexectomy in January 2025.

Pathology: Leydig cell benign ovarian tumour, 17 × 14 mm, ki67 2%. Symptoms improved rapidly: regression of hirsutism and recurrence of postmenopausal hot flushes that had disappeared for some years. Serum androgen returned to low normal ranges, estradiol became undetectable while FSH and LH rose again. In december 2025 the patient remains asymptomatic.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Discussion: Leydig cell tumours account for 0,1%-0,2% of ovarian neoplasms. There is a delay of up to 5 years from onset of symptoms to diagnosis. Most typically, it is the clinical hyperandrogenism (severe hirsutism and virilization) that motivates workup and leads to diagnosis. In the great majority of cases already described, estrogen effects are not prominent. They are probably inhibited in the context of severe hyperandrogenism. In our case, androgen elevation was quite moderate and didn't inhibit estrogenic effects (postmenopausal bleeding), leading to investigations and a more rapid diagnosis.

Abstract citation ID: lvag096.1599

EP1394 - ECE_1225 - Impact of daylight saving time transitions on global searches for menstrual health terms

Christos Savvidis, Vasiliki Tsiama, Stella Proikaki, Konstantinos Belis, Efthymia Kallistrou, Dimitra Ragia, Dimitra Motsiou and Ioannis Ilias
Dept of Endocrinology, Hippokration Hospital, Athens, Greece

Introduction: Daylight Saving Time (DST) shifts disrupt sleep and circadian rhythms, potentially influencing menstrual cycles via hormonal dysregulation. This study investigates worldwide Google Trends for menstrual terms ("Menstrual," "Menstrual cycle," "Menstruation," "Menses," "Menstrual period") from 2004-2025, across three algorithmic periods (2004-2015, 2016-2021, 2022-2025). The aim was to assess search elevations during DST entry (spring: Mar–June) and exit (winter: Nov–Jan) vs rest-of-year as proxies (via concerns) for DST-related menstrual disorders.

Materials and Methods: Google Trends data were retrieved for relative search volumes (RSVs) related to menstrual terms ("menstrual," "menstruation," "menstrual cycle," "menstrual period," "menses") in the European Union (EU) and North America (US + Canada) from January 2004 to November 2025. Data were segmented into three periods to account for Google algorithm changes: 2004-2015, 2016-2021, and 2022-2025. To evaluate potential Daylight Saving Time (DST) effects, months were categorized as: 0 (baseline), 1 (spring transition: April-June for EU, March-May for North America), and 2 (fall transition: November-January for both regions). Time series analysis was performed using ARIMA models to assess trends, seasonality, and differences in RSVs across periods, with model selection based on AICc, BIC, and residual diagnostics. Statistical significance was set at $P < .05$.

Results: Median RSVs across terms showed variability by region and timeframe. ARIMA modeling revealed significant drift and coefficients indicating temporal increases in RSVs only in the EU during 2004-2015 (eg, for "menstrual": ARIMA(4,1,4), drift 0.312, $P < .001$; time period coefficient 1.289, $P < .001$), with no comparable effects in North America or later EU periods. Spring and fall transitions correlated with RSV peaks in early EU data.

Discussion/Conclusions: This analysis suggests a potential indirect association between DST transitions and increased Google searches for menstrual issues in the EU from 2004-2015, possibly reflecting circadian disruptions affecting menstrual regularity, as proxied by search behavior. No such patterns were observed in North America or subsequent EU periods, which may relate to algorithm shifts. Limitations include the ecological nature of search data and lack of individual-level confounders. Future studies should incorporate clinical data to validate DST's impact on menstrual health. In conclusion, early EU data hint at DST-related menstrual perturbations, warranting physician awareness during transition periods.

Abstract citation ID: lvag096.1600

EP1398 - ECE_1115 - Longitudinal effects of Eurycoma longifolia extract and multivitamin supplementation on reproductive hormone profiles in infertile men: a randomized controlled trial

Seso Sulijaya Suyono[1,2,3], Dewi Lestari[3] and Raymond Rubianto Tjandrawinata[4]
[1]Gladiool IVF Centre, Andrology, Andrology, Magelang, Indonesia; [2]Sadewa IVF Centre, Andrology, Andrology, Daerah Istimewa Yogyakarta, Indonesia; [3]Pharmacology, Universitas Kristen Duta Wacana, Daerah Istimewa Yogyakarta, Indonesia; [4]School of Bioscience, Technology and Innovation, Universitas Katolik Indonesia Atma Jaya, Jakarta, Indonesia

Background: Herbal supplements and antioxidants are widely used in male infertility, yet their endocrine effects remain inconclusive. Eurycoma longifolia has been traditionally used for its androgenic properties and has been proposed to influence androgen regulation within the hypothalamic–pituitary–gonadal axis; however, controlled data on reproductive hormone dynamics are limited.

Objective: To evaluate the longitudinal effects of Eurycoma longifolia extract, multivitamins, and their combination on serum testosterone and follicle-stimulating hormone (FSH) levels in infertile men.

Methods: In this randomized controlled trial, 90 infertile men aged 20-45 years with baseline serum testosterone levels of 350-600 ng/dL were randomized to receive Eurycoma longifolia extract, multivitamins (vitamin C, vitamin E, and β-carotene), or their combination for 12 weeks. Serum testosterone was measured at baseline, 6 and 12 weeks, while FSH was assessed at baseline and 12 weeks. Hormonal changes were analyzed using repeated-measures and paired statistical methods, as appropriate. Safety and tolerability were assessed.

Results: Eighty-three participants completed the trial. At baseline, mean serum testosterone levels were significantly lower in the multivitamin group, while baseline FSH levels were comparable across groups. No statistically significant changes in serum testosterone were observed at either 6 or 12 weeks across the intervention groups. However, a consistent upward trend in serum testosterone was observed in the combination group (1% and 8% at 6 and 12 weeks, respectively). Changes in serum FSH at 12 weeks were not statistically significant in any group compared with baseline, although a numerical increase was noted in the multivitamin group. All interventions were well tolerated, with no serious adverse events reported.

Conclusions: In this randomized trial, daily supplementation with Eurycoma longifolia, multivitamins, or their combination was safe but did not result in statistically significant changes in serum testosterone or FSH levels over 12 weeks. Given the observed longitudinal variability in serum testosterone, repeat hormonal assessment prior to treatment initiation should be considered. Further studies incorporating larger cohorts and stratified endocrine phenotyping are warranted.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1601

EP1400 - ECE_1757 - Impact of maternal obesity and gestational GLP-1 receptor agonist exposure on fetal hypothalamic development

Hadley Johnson[1], Matthew B. A. Higgins[1], Ameera Cunningham[1], Denise S. Fernandez-Twinn[1,2], Susan Ozanne[1,2] and Laura Dearden[1]
[1]University of Cambridge, Institute of Metabolic Science, Cambridge, United Kingdom; [2]MRC Metabolic Diseases Unit, Institute of Metabolic Science, Cambridge, United Kingdom

Given the societal shift to an obesogenic environment, it remains unknown why some individuals are more predisposed to gaining weight than others. Understanding this variability requires examining the biological basis of weight-regulation behaviours at the genetic and developmental levels. *In utero* programming allows maternal hormones and nutrient availability to shape the developing fetal brain, altering long-term gene expression in hypothalamic appetite circuits. Semaglutide, a GLP-1 receptor agonist (GLP-1RA), mimics endogenous GLP-1 to enhance insulin secretion, delay gastric emptying, increase satiety, and influence hypothalamic pathways. Although not recommended during pregnancy due to preclinical findings of growth restriction and pregnancy loss in rodents, an increasing number of women are conceiving while on the medication, possibly because of interactions such as reduced oral contraceptive effectiveness and increased fertility of women with obesity. There are concerns about the effects of gestational GLP-1RA exposure on fetal neurodevelopment that warrant further investigation. This project investigates whether semaglutide exposure during critical developmental windows alters hypothalamic development by examining GLP-1 receptor expression in embryonic hypothalamic cells, assessing effects on neuronal growth, and evaluating changes in metabolic protein expression within key hypothalamic nuclei. By addressing critical gaps in our understanding of gestational GLP-1RA exposure, this research aims to clarify whether semaglutide can modulate fetal hypothalamic development in ways that may influence lifelong metabolic outcomes.

Abstract citation ID: lvag096.1602

EP1402 - ECE_2190 - Plasticity of the circadian chronotype in healthy female individuals over the course of their menstrual cycle

Manon Torres and Achim Kramer
AG Chronobiologie—Achim Kramer, Berlin, Germany

The circadian clock (~24 hours) is an endogenous system that regulates daily changes in a multitude of physiological functions, including sleep, metabolism, and cognitive functions. In mammals, the endocrine system is closely linked to the circadian clock, with strong rhythmic expression of circadian genes and proteins in both the central nervous system and peripheral glands, resulting in well-known daily pulses of hormone secretion.

Studies conducted mainly on rodents strongly suggest that female estrus (or the menstrual cycle in humans) has a reciprocal influence on the circadian clock, with ovarian steroid hormones (ie, estrogen and progesterone) capable of altering the rhythmic expression of core circadian genes in both the central clock and peripheral tissues. However, due to technological limitations, it remains unclear whether in human too circadian clock is altered in response to the female cyclic fluctuation of ovarian hormones.

Recently developed in our laboratory, the HairTime test estimates a person's internal circadian chronotype (ie, predicted Dim Light Melatonin onset or "pDLMO") from a single sample of hair follicles. This test accurately reflected the known diversity of chronotypes among individuals (from early risers to night owls), and its precision allowed us to observe the plasticity of the human chronotype under the influence of environmental factors such as work schedule.

In this study, we propose to apply the HairTime assay to evaluate the plasticity of the chronotype in healthy female individuals over the course of their menstrual cycle. We present here the overview of this new study and preliminary results from first participants.

Abstract citation ID: lvag096.1603

EP1404 - ECE_3141 - Are DHEA-S levels associated with miscarriages in females with Ehlers–Danlos syndrome?

Jan Domański[1,2,3], Ivan Rychlik[4], Aleksandra Żuk-Łapan[1,2], Bernadetta Kałuża[1,2] and Edward Franek[1,5]
[1]Department of Internal Medicine, Endocrinology, and Diabetology, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland; [2]Students Scientific Group of the Medical University of Warsaw at the Department of Internal Medicine, Endocrinology, and Diabetology, National Medical Institute of the Ministry of the Interior and Administration, Medical University of Warsaw, Warsaw, Poland; [3]Doctoral School of the Medical University of Warsaw, Medical University of Warsaw, Warsaw, Poland; [4]Third Faculty of Medicine, Department of Internal Medicine, Charles University, and Královské Vinohrady University Hospital, Prague, Czech Republic; [5]Polish Academy of Sciences, Department of Human Epigenetics, Mossakowski Medical Research Institute, Warsaw, Poland

Background: Ehlers–Danlos syndrome is a group of genetic conditions involving abnormal connective tissue synthesis and structure and characterized by varied, subtype-dependent symptom severity and varied location, predominantly presenting as joint hypermobility and skin hyperextensibility, musculoskeletal abnormalities, and internal organ frailty, which may result in miscarriages, which are more prevalent in affected females than in the general population. The purpose of this study was to evaluate adrenal hormone levels in female patients with Ehlers–Danlos syndrome as part of miscarriage risk assessment.

Material and Methods: We assessed adrenal hormone levels and conducted imaging diagnostics in 30 female patients with classic and hypermobile Ehlers–Danlos syndrome. The patients were divided into two groups: group 1—patients with no history of miscarriage ($n = 21$) and groups 2—patients with a history of miscarriage ($n = 9$).

Results: The patients from the two compared groups differed significantly in terms of DHEA-S levels (237.00 ± 90.42 vs 147.81 ± 88.98 [μg/dl], $P = .021$); however, they did not differ in terms of ACTH (21.91 ± 14.04 vs 23.12 ± 11.33 [pg/mL], $P = .651$), cortisol (14.78 ± 6.39 vs 15.84 ± 5.01 [μg/dl], $P = .511$), androstenedione (1.97 ± 0.78 vs 1.62 ± 1.07 [ng/mL], $P = .118$), 17-OH-progesterone (1.28 ± 0.74 vs 1.24 ± 0.38 [ng/mL], $P = .667$), sodium (141.62 ± 2.44 vs 140.89 ± 1.90 [mmol/L], $P = .61$), or potassium (4.71 ± 0.39 vs 4.51 ± 0.32 [mmol/L], $P = .147$) levels. Univariate regression

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

analysis showed a significant correlation between DHEA-S levels and the risk of miscarriage (OR 0.988 [0.976-0.999]; $P = .035$). Conversely, such parameters as ACTH (1.007 [0.949-1.069]; $P = .814$), cortisol (OR 1.032 [0.902-1.181]; $P = .648$), androstenedione (OR 0.589 [0.21-1.651]; $P = .314$), 17-OH-progesterone (OR 0.891 [0.256-3.098]; $P = .856$), sodium (OR 0.865 [0.608-1.23]; $P = .419$), or potassium (OR 0.212 [0.02-2.216]; $P = .195$) levels showed no such correlation.

Conclusions: DHEA-S levels in female patients with hypermobile or classical Ehlers–Danlos syndrome may affect the risk of miscarriage. These patients' adrenal function should be assessed to reduce the risk of miscarriage.

Abstract citation ID: lvag096.1604

EP1405 - ECE_3843 - Assessment of adropin effects on proliferation and PCNA levels in porcine granulosa cells

Jakub Chatys, Alicja Łapa, Patrycja Kurowska and Agnieszka Rak
Faculty of Biology, Institute of Zoology and Biomedical Research, Laboratory of Physiology and Toxicology of Reproduction, Jagiellonian University, Kraków, Poland

Granulosa cell proliferation is essential for ovarian follicle growth and oocyte development. Adropin is a peptide hormone involved in the regulation of energy homeostasis and lipid metabolism. Our previous studies have demonstrated that adropin is expressed in the porcine ovary; however, its role in ovarian physiology remains poorly understood.

The aim of this study was to evaluate the effect of adropin on the proliferation of porcine granulosa cells and the expression of proliferating cell nuclear antigen (PCNA). Granulosa cells were isolated from ovarian follicles collected on days 10-12 of the estrous cycle and seeded in 96-well plates at a density of 50 000 cells per well. After 24 hours of preincubation in M199 medium supplemented with 10% fetal bovine serum (FBS), cells were treated with adropin at concentrations of 0.1, 1, 10, and 100 nM for 48 hours. Cell proliferation was assessed using a BrdU incorporation assay, while cell viability was evaluated by alamarBlue. PCNA mRNA and protein levels were analyzed by quantitative real-time PCR and Western blotting, respectively. Statistical analysis was performed using one-way ANOVA in GraphPad Prism 8.1 ($n = 5$).

We demonstrated that adropin reduced granulosa cell proliferation at all tested concentrations and significantly decreased cell viability at 1 and 10 nM. Furthermore, adropin significantly downregulated *PCNA* gene expression at 1, 10, 100 nM, and reduced PCNA protein levels at all tested doses (0.1-100 nM).

These findings indicate that adropin inhibits granulosa cell proliferation, which may negatively impact folliculogenesis and potentially contribute to impaired fertility.

Abstract citation ID: lvag096.1605

EP1408 - ECE_3453 - Are hypothyroidism and autoimmune thyroiditis associated with an increased risk of miscarriage in females with Ehlers–Danlos syndrome?

Michalina Andrzejak[1,2], Ivan Rychlik[3], Jan Domański[1,2], Aleksandra Żuk-Łapan[1,2], Jędrzej Jedliński[1,2], Bernadetta Kałuża[1,2] and Edward Franek[1,2,4]
[1]*Department of Internal Medicine, Endocrinology, and Diabetology, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland;* [2]*Warsaw, Poland;* [3]*Third Faculty of Medicine, Department of Internal Medicine, Charles University, and Královské Vinohrady University Hospital, Prague, Czech Republic;* [4]*Department of Human Epigenetics, Polish Academy of Sciences, Mossakowski Medical Research Institute, Warsaw, Poland*

Background: Ehlers–Danlos syndrome is a group of genetic conditions involving abnormal synthesis of connective tissue, particularly collagen, characterized by polymorbidity and an increased risk of pregnancy and delivery complications. Uncontrolled hypothyroidism increases the risk of miscarriage. The aim of this study was to assess the risk of miscarriage in women Ehlers–Danlos syndrome and concomitant hypothyroidism.

Material and Methods: Thyroid hormone levels were assessed in 30 females with classical or hypermobile Ehlers–Danlos syndrome. The patients were divided into two groups: Group 1—patients with no history of miscarriage ($n = 21$) and Group 2—patients with a history of miscarriage ($n = 9$).

Results: The two groups differed neither in terms of hypothyroidism rates (19.05% vs 22.22%, $P = .87$), or the levels of thyroid stimulating hormone (2.13 ± 1.18 vs 2.09 ± 1.83 [μIU/mL], $P = .59$), free triiodothyronine (3.37 ± 0.62 vs 3.41 ± 0.74 [pg/mL] $P = .89$), free thyroxine (1.35 ± 0.25 vs 1.33 ± 0.17 [ng/dl], $P = .80$), or thyroid peroxidase antibodies (34.58 ± 110.11 vs 40.26 ± 38.12 [IU/mL], $P = .121$). Conversely, they differed in terms of autoimmune thyroiditis rates (9.52% vs 44.44%, $P = .03$) and thyroglobulin antibody levels (21.46 ± 23.33 vs 64.97 ± 81.48, $P = .03$). Univariate logistic regression analysis showed no correlation between hypothyroidism (OR 1.21 [0.18-8.22], $P = .84$) and an increased risk of miscarriage; however, such correlation was observed in the case of autoimmune thyroiditis (OR 7.6 [1.07-54.09], $P = .04$).

Conclusions: Autoimmune thyroiditis in females with Ehlers–Danlos syndrome was shown to increase the risk of miscarriage.

Abstract citation ID: lvag096.1606

EP1410 - ECE_1202 - Individualized endocrine care in non-binary individuals: efficacy, safety, and long-term outcomes of microdosing and selective hormone modulators

Ipsita Mishra
IMS & SUMII, Phulnakhara, Soul Balance, Diabetes and Endocrine Centre of Excellence, Endocrinology, Diabetes and Metabolism, Cuttack, India

Background: Current gender-affirming hormone therapy (GAHT) guidelines are optimized for binary outcomes (full masculinization or feminization), leaving a critical evidence gap for the growing population of non-binary and gender-diverse (NBGD) individuals who seek partial physical changes. These non-traditional therapeutic goals often necessitate the off-label use of low-dose, intermittent GAHT ("microdosing"), or Selective Estrogen Receptor Modulators (SERMs). This study aimed to evaluate the efficacy, safety, and impact on long-term health markers in a cohort of NBGD individuals receiving individualized hormone protocols.

Methods: This retrospective cohort study analysed data from 180 NBGD adults over a median follow-up period of 3.5 years

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

.The cohort was stratified into three groups:Group A(Microdosing MHT;$N = 95$;Natal Sex—Female;Low dose testosterone;25 mg/week);Group B(Microdosing FHT;$N = 65$;Natal Sex—Male;Low dose Estradiol;1 mg/day [oral]);Group C(SERM Protocol;$N = 20$; Natal Sex—Male;SERM ± GnRH Agonist; Raloxifene 60 mg/day).Primary Outcome: Change in patient-reported psychosocial outcomes (Gender Congruence Scale (GCS) and Quality of Life (QoL) scores).Secondary Outcomes: Physical changes, Bone Mineral Density (BMD), lipid panels, and HbA1c.

Results: The mean age of the cohort was 31.2 ± 6.8 years.Baseline BMD T-scores were: Group A (LS T-score: −0.4 ± 0.9); Group B (LS T-score: −0.2 ± 1.0); Group C (LS T-score −0.5 ± 0.8). HbA1c and lipid profiles were comparable across groups and within the normal range.Both GCS and QoL scores demonstrated a statistically significant improvement across all groups from baseline to final follow-up ($P < .001$). Microdosing MHT(Group A) achieved initial voice deepening (75%) and facial hair growth (45%) in 88% of patients.Microdosing FHT (Group B) resulted in mild breast development (A-cup or small B-cup) in 70% of patients.The SERM Protocol (Group C) successfully achieved fat redistribution and skin softening with minimal/no palpable breast tissue in 95% of cases.Group A and C maintained stable BMD.Group B demonstrated a statistically significant, albeit small, decrease in Lumbar Spine BMD (−0.015 g/cm^2, $P = .045$) in patients who maintained Estradiol levels below 100 pmol/L while achieving adequate Testosterone suppression.No major cardiovascular or thromboembolic events were recorded.

Conclusions: Microdosing and selective hormone modulator regimens represent a safe and effective strategy for achieving individualized, non-binary gender affirmation goals, resulting in significant improvements in GCS and QoL. While metabolic and cardiovascular profiles remained largely stable, the data highlights a risk of bone demineralization in a subset of Microdosing FHT patients, particularly those whose Estradiol levels are insufficient to provide skeletal protection.

Abstract citation ID: lvag096.1607

EP1411 - ECE_2838 - Spontaneous pregnancy in turner syndrome mosaicism: a case report

Satik Shahbazyan[1,2], Irina Muradyan[1], Bayburdyan Gayane[1] and Yelena Aghajanova[1]
[1]Yerevan, Armenia; [2]Endocrinology, Yerevan State Medical University after Mkhitar Heratsi, Yerevan, Armenia

Introduction: Turner syndrome (TS) is a chromosomal disorder caused by partial or complete loss of one X chromosome. Although infertility is typical, mosaic forms may preserve ovarian function and, in rare cases, achieve spontaneous pregnancy.

Case Presentation: A 26-year-old woman presented for pregnancy planning. Diagnosed with TS at age 12, karyotyping showed mosaicism: 45,X (29), 47,XXX (15), and 46,XX (9). She had self-induced regular menstrual cycles from 14. She was treated with levothyroxine for subclinical hypothyroidism and received one year of growth hormone therapy, reaching a height of 152 cm. At the age of 15, pelvic ultrasound revealed bilateral ovarian follicles. At age 26, she was consulted by endocrinologist; hormonal results were normal (AMH 1.45 ng/mL), no cardiac or renal anomalies were found. Reproductive endocrinologist confirmed spontaneous pregnancy. Non-invasive prenatal testing (NIPT) indicated high risk for monosomy X. Genetic counseling and amniocentesis with FISH testing were recommended for confirmation.

Discussion: Spontaneous conception in TS is rare but can occur in mosaic forms containing 46,XX or 47,XXX lines. These women may experience normal puberty and menstruation, as in our case. However, pregnancies are high-risk due to possible cardiovascular complications, notably aortic dissection, and increased fetal chromosomal anomalies. Preconception cardiac evaluation is essential. NIPT is a valuable screening tool, but positive results should be verified through invasive tests like amniocentesis or Chorionic Villus Sampling (CVS). This case demonstrates that natural conception in mosaic TS is possible, emphasizing the need for multidisciplinary monitoring.

Conclusions:

- Spontaneous pregnancy in mosaic TS is rare but possible.
- Preconception and cardiovascular evaluations are essential.
- NIPT is useful for screening but must be confirmed by amniocentesis or CVS.
- Multidisciplinary management including endocrinology, cardiology, obstetrics, and genetics is recommended.
- Further research is needed to create clear, evidence-based guidelines for monitoring and managing spontaneous pregnancy in TS mosaicism, since current advice is mostly based on small case reports and expert opinion.
- This case shows how the reproductive care of women with TS mosaicism is changing and emphasizes the need to update clinical practice as new genetic and obstetric knowledge emerges.

Abstract citation ID: lvag096.1608

EP1413 - ECE_3372 - Comparative effects of oral versus transdermal menopausal hormone therapy on key lipid parameters: a scoping review

Erin Edwards, Mia Evans, Ralph Akyea, Barbara Iyen, Nadeem Qureshi and Yana Vinogradova
Medical School, University of Nottingham, Nottingham, United Kingdom

Background: Menopausal Hormone Therapy (MHT) is commonly used as an approach to alleviate vasomotor symptoms in both peri- and post-menopausal women. While MHT is known to have an influence on lipid profile, it remains unclear how lipid effects vary by route of administration—specifically between oral and transdermal therapy.

Objectives: This scoping review aimed to map and synthesise the current evidence comparing the effects of oral and transdermal MHT on key lipid parameters in peri- and post-menopausal women.

Methods: This review followed the PRISMA-ScR guidelines. A comprehensive search using three databases—MEDLINE, EMBASE and APA PsycINFO was conducted, limited to papers published in the last 10 years. Studies were included if they reported lipid outcomes following oral and transdermal MHT use in peri- or post-menopausal women (and outcomes stratified by route). Title, abstract, full-text screening and data charting were performed by 2 independent reviewers. Data was extracted from eligible studies independently, and charted by study characteristics, MHT route, follow-up duration and lipid outcomes.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Results: After screening 2493 studies, a total of 6 studies met the criteria and were therefore included in this review. Studies were conducted across a wide geographical range, and there was large heterogeneity in study design, population characteristics and outcomes reported. Across included studies, oral therapy was associated with more consistent lipid outcomes, whereas with transdermal therapy, findings showed more variability.

Conclusions: Current evidence suggests that there is greater consistency in lipid profile effects with oral compared to transdermal MHT, however this is limited by heterogeneity and limited comparative data. This field lacks research on long-term effects on MHT, and effects across a broader age range. This review highlights the need for more controlled head-to-head trials comparing the effects of oral and transdermal MHT on lipid profile.

Abstract citation ID: lvag096.1609

EP1416 - ECE_3099 - Fertility and reproductive outcomes in adults with congenital adrenal hyperplasia: data from a single-center cohort

Malgorzata Bobrowicz[1], Zuzanna Roszkowska[2], Karolina Palys[2], Hanna Mruzek[2] and Urszula Ambroziak[1]
[1]Warsaw, Poland; [2]Student Scientific Club "Endocrinus" Affiliated to the Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, Poland

Background: Congenital adrenal hyperplasia (CAH) is a lifelong endocrine disorder with well recognized implications for reproductive health. Although considerable progress in our understanding of the issues of fertility and reproductive health has been made, regional differences in the patients' management may influence the results in different cohorts. The aim of our study was to assess fertility, parenthood, and pregnancy-related outcomes in a cohort of adult patients with CAH, with a focus on clinically relevant sex-specific aspects.

Methods: We conducted a cross-sectional analysis of adult patients with CAH followed at a tertiary endocrine center. Demographic characteristics, sex, parenthood status, and pregnancy history were obtained from patient-completed surveys. Reproductive outcomes were analyzed descriptively and stratified by sex where applicable.

Results: The cohort included 37 adults with CAH (31 women [83.8%] and 6 men [16.2%]). Eleven patients reported having children (29.7%), while 23 reported no offspring (62.2%); parenthood status was unavailable in 3 cases (8.1%).

Among patients who provided information on attempts to conceive ($n = 11$), 10 (90.9%) reported active attempts to achieve pregnancy, while 1 (9.1%) reported no attempts. Reported time to conception ranged from immediate conception to 7 years; due to heterogeneous reporting formats, calculation of mean or median time to conception was not feasible.

Among women with CAH who reported childbirth ($n = 11$), Cesarean section was the predominant mode of delivery, occurring in 8 cases (72.7%). Pregnancy- or delivery-related complications were reported in 5 women (45.5%). Only 2 partners (18.2%) underwent genetic testing prior to conception.

Among 31 women with CAH, four (12.9%) reported at least one miscarriage. No cases of recurrent miscarriage (three or more pregnancy losses) requiring extended diagnostic work-up were reported.

Conclusions: In this cohort of adults with CAH, fewer than one-third reported parenthood despite most being of reproductive age. Pregnancy outcomes were characterized by a high rate of Cesarean section and a substantial burden of pregnancy-related complications. Although recurrent miscarriage was not observed, sporadic pregnancy loss was reported in a notable proportion of women.

The low uptake of partner genetic testing prior to conception highlights gaps in preconception counseling and genetic risk assessment. Overall, these findings underscore the need for structured, multidisciplinary reproductive care for adults with CAH, integrating endocrine management with obstetric, genetic, and psychosocial support to optimize fertility and pregnancy outcomes. Further research on this topic is warranted.

Abstract citation ID: lvag096.1610

EP1418 - ECE_2655 - Testosterone-induced cardiomyopathy: a reversible cause of nonischemic cardiomyopathy

Humera Tabassum[1,2,3], Samyukta Ravi[1,2,3], Grishma Sheth[1,3], Sathya Jyothinagaram[1,2] and Karyne Vinales[1,2]
[1]Endocrinology, University of Arizona College of Medicine, Phoenix, United States; [2]Phoenix VA Healthcare System, Phoenix, United States; [3]Endocrinology, Medicine, Banner—University Medical Center Phoenix, Phoenix, United States

Background: Testosterone replacement therapy (TRT) is increasingly prescribed for male hypogonadism. Large, randomized trials support cardiovascular noninferiority of physiologic TRT when appropriately indicated and monitored. However, supraphysiologic testosterone exposure has been associated with adverse myocardial remodeling, primarily described in anabolic-androgenic steroid use. Reports of cardiomyopathy associated with prescribed TRT remain rare and limited to isolated case reports, suggesting this entity may be underrecognized despite potential reversibility.

Case Presentation: A 54-year-old male presented for endocrine evaluation due to concern for testosterone-induced cardiomyopathy. He had been treated for presumed hypogonadism at a men's health clinic for seven years without documentation of a comprehensive endocrine evaluation prior to initiation of therapy. He was asymptomatic, and premature ventricular contractions were incidentally identified during anesthesia for a minor surgical procedure.

The patient received intramuscular testosterone 190 mg weekly for seven years, resulting in persistently supratherapeutic testosterone levels (total testosterone 1033 ng/dL, free testosterone 198 pg/mL, bioavailable testosterone 398 ng/dL).

Cardiac evaluation demonstrated progressive systolic dysfunction. Transthoracic echocardiography showed a left ventricular ejection fraction (LVEF) of 50% in 2022, declining to 45% in early 2024. Cardiac magnetic resonance imaging revealed globally reduced systolic function with LVEF 37% and right ventricular ejection fraction of 30%, mild ventricular enlargement, and no late gadolinium enhancement, arguing against ischemic or infiltrative cardiomyopathy. Coronary computed tomography angiography showed no obstructive coronary artery disease. Holter monitoring demonstrated a premature ventricular contraction burden of 9%. Comprehensive genetic testing revealed no pathogenic variants associated with cardiomyopathy.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Management and Outcome: Given concern for testosterone-induced cardiomyopathy, testosterone therapy was gradually tapered and discontinued, and anastrozole was stopped. Following cessation, the patient demonstrated spontaneous recovery of the hypothalamic–pituitary–gonadal axis without pharmacologic intervention. Repeat laboratory testing showed luteinizing hormone 8.5 mIU/mL, follicle-stimulating hormone 5.5 mIU/mL, total testosterone 307 ng/dL, and free testosterone 53.8 pg/mL.

Follow-up transthoracic echocardiography demonstrated normalization of left ventricular systolic function with LVEF 55%-60% and normal right ventricular function.

Conclusions: This case illustrates testosterone-induced cardiomyopathy as a rare but potentially reversible cause of nonischemic cardiomyopathy associated with prolonged supraphysiologic testosterone exposure. Recovery of endogenous testosterone production and normalization of systolic function following testosterone withdrawal support a causal relationship. This case underscores the importance of appropriate diagnostic evaluation prior to initiating TRT and the need for cardiovascular monitoring during long-term therapy.

Abstract citation ID: lvag096.1611

EP1419 - ECE_3961 - Progressive bilateral gynecomastia associated with hyperestrogenemia, hypogonadotropic hypogonadism, and pituitary microadenoma

Andi Alfian[1,2], Tri Tarigan[1], Dicky Tahapary[1] and Wismandari Wisnu[1]

[1]*Faculty of Medicine, Division of Endocrinology, Department of Internal Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia;* [2]*Faculty of Medicine, Department of Internal Medicine, Universitas YARSI, YARSI Hospital, Jakarta, Indonesia*

Introduction: Gynecomastia is a benign proliferation of male breast glandular tissue caused by an imbalance between estrogenic and androgenic activity. While often physiological during puberty, persistent or progressive gynecomastia in adults warrants evaluation for endocrine disorders, testicular pathology, pituitary disease, systemic illness, medication effects, or hereditary predisposition. Hyperestrogenemia accompanied by suppressed gonadotropins is uncommon and raises concern for primary estrogen excess, increased peripheral aromatization, or central hypothalamic–pituitary dysfunction. We report a rare case of progressive bilateral gynecomastia in a young male with marked hyperestrogenemia, hypogonadotropic hypogonadism, and a pituitary microadenoma, with a possible familial component.

Case Description: A 21-year-old male presented with a five-year history of progressively enlarging, symmetrical breast tissue, initially painless but later intermittently tender, causing significant psychosocial distress. He denied headaches, visual disturbances, sexual dysfunction, nipple discharge, or systemic symptoms. Pubertal development was spontaneous and complete. His older brother exhibited similar breast enlargement, suggesting a possible hereditary pattern.

Physical examination revealed a body mass index of 21.6 kg/m^2 and bilateral symmetric breast enlargement with firm glandular tissue consistent with true gynecomastia. Testicular volume was normal (20 mL bilaterally) without masses. External genitalia and secondary sexual characteristics were normal.

Laboratory evaluation demonstrated persistently elevated estradiol (98-115 pg/mL), markedly suppressed FSH (0.25 mIU/mL), low-to-normal LH (2.4-5.7 mIU/mL), borderline elevated prolactin (18-21 ng/mL), and low normal testosterone (4.19-5.76 ng/mL). Thyroid, liver, and renal function were normal. Breast ultrasonography confirmed diffuse glandular proliferation. Dynamic pituitary MRI revealed a 0.3×0.2 cm left-sided microadenoma with delayed enhancement. Testicular and adrenal imaging were unremarkable, reducing the likelihood of peripheral estrogen-secreting tumors.

The constellation of findings indicated progressive true gynecomastia associated with hyperestrogenemia, disproportionate gonadotropin suppression, hypogonadotropic hypogonadism, and a pituitary microadenoma of uncertain functional significance, within a possible familial context. Management considerations included hormonal monitoring, selective estrogen receptor modulators, genetic evaluation, reproductive counseling, and surgical options if symptoms persisted.

Conclusions: This case illustrates a rare and complex presentation of progressive gynecomastia associated with hyperestrogenemia, suppressed gonadotropins, and a pituitary microadenoma, possibly within a familial context. Comprehensive endocrine andrology evaluation is essential for accurate diagnosis, individualized management, and addressing the psychosocial impact in young adults.

Abstract citation ID: lvag096.1612

EP1421 - ECE_1608 - Macrophage dynamics in polycystic ovary syndrome: unraveling immune contributions to ovarian dysfunction

Heli Jokela, Katja Eubler, Heidi Gerke and Pia Rantakari

Turku, Finland

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder characterized by androgen excess, disrupted folliculogenesis, and chronic anovulation. In addition to endocrine abnormalities, increasing evidence suggests that PCOS is associated with low-grade inflammation within the ovary. Macrophages—immune cells that regulate tissue remodeling, steroidogenesis, and inflammatory responses—are abundant in the healthy ovary and play essential roles in follicle development and ovulation. However, how ovarian macrophage populations are altered in PCOS, and whether these changes contribute to ovarian dysfunction, remain poorly understood.

Ovaries contain multiple macrophage populations with distinct developmental origins and functions. Tissue-resident macrophages arise during development and support normal tissue development and homeostasis, whereas monocyte-derived macrophages can also populate tissues under steady-state conditions but are often recruited from the circulation in response to inflammatory cues. Disruption of the balance between these populations has been implicated in chronic inflammatory diseases, yet their relative contributions to PCOS remain undefined. We hypothesize that altered macrophage composition and activation states contribute directly to the inflammatory and endocrine dysregulation characteristic of PCOS, which we will investigate using Letrozole and DHT-induced mouse models that recapitulate key features of the human disorder.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Both wild-type mice and fate-mapping mice will be used to identify how monocyte-derived and tissue-resident macrophages contribute to ovarian immune alterations in PCOS. Ovarian immune cells will be analyzed using complementary single-cell RNA sequencing, flow cytometry, and imaging to define macrophage composition, activation states, and localization. In parallel, archived human ovarian FFPE samples from women with PCOS and healthy controls will be analyzed to assess immune cell localization within the ovary, focusing on macrophages, to validate and extend murine findings.

This approach is expected to reveal remodeling of ovarian macrophages in PCOS, including changes in origin and inflammatory programs, providing mechanistic insight into how immune dysregulation affects ovarian function. Defining these macrophage pathways may identify targets for interventions to mitigate PCOS-associated ovarian dysfunction.

Abstract citation ID: lvag096.1613

EP1422 - ECE_1621 - Dynamic changes of metabolic parameters during pregnancy

Violeta Mladenović[1], Dragana Bubanja[1], Nebojsa Igrutinovic[1], Zeljko Ivosevic[1] and Zoran Gluvic[2,3]
[1]*Faculty of medical sciences, Univeristy of Kragujevac», University Clinical Center «Kragujevac», Serbia, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Kragujevac, Serbia;* [2]*Division of Internal medicine, Zemun Clinical Hospital Center, Dept of Endocrinology, School of Medicine, University of Belgrade, Belgrade, Serbia;* [3]*Faculty of Medicine, Department of Endocrinology, Zemun Clinical Hospital, University of Belgrade, Belgrade, Serbia*

Introduction: Pregnancy as a state of insulin resistance that can predict diabetes development in some women, usually manifests at the beginning of the third trimester, and is associated with increased risk for neonate and for mother. Serum lipids increased physiologically with gestational age in middle and late pregnancy. The establishment of reference intervals for serum lipids in pregnancy will help to distinguish abnormal serum lipid levels in middle and late pregnancy.

Aim: The aim of this study is to analyse metabolic parameters (lipids) during pregnancy.

Matherial and Methods: The research included 92 pregnant women registered in Clinic for endocrinology UCC Kragujevac that were tested who met the inclusive criteria, average age 30.8 ±4.7 years, with a range of 19 to 41 years. Of the 92 pregnant women diagnosed with vital and preferred pregnancies up to 12. gestational week, and received a signed form of the Informed Consent, 7 pregnant women had a spontaneous abortion, while 8 pregnant women gave up, so that 77 pregnant women completed the examination. The sample size included women in each trimester and 4 weeksd after delivery. The characteristics of the participants were expressed as mean ± standard deviation.

Results: It has been shown that as pregnancy progresses, the value of lipid parameters increases, especially total cholesterol and triglycerides. The highest increase was seen in the 3rd trimester of pregnancy (Figure). The average values are shown in Table.

Conclusions: The differences in the parameters of liporegulation during pregnancy is expressed in the second and third trimesters, while it does not appear in the first trimester. The highest increase in lipid parameters was demonstrated in the third trimester of pregnancy.

Keywords pregnancy, lipids

Abstract citation ID: lvag096.1614

EP1423 - ECE_2477 - Primary amenorrhea in an underweight adolescent: diagnostic and therapeutic challenges in hypogonadotropic hypogonadism

Roxana Enachescu[1] and Bogdan Pascu[1,2]
[1]*Pediatric Endocrinology, Institutul Național Pentru Sănătatea Mamei și Copilului, București, Romania;* [2]*Universitatea de Medicină și Farmacie Carol Davila, București, Romania*

Primary amenorrhea in adolescents requires careful evaluation to differentiate constitutional delay of puberty from hypogonadotropic hypogonadism, particularly in the setting of severe undernutrition.**Clinical Case:** A 16-year-old female presented with primary amenorrhea, marked underweight (BMI 15.4 kg/m^2), and delayed bone age (13.5 years). Baseline hormonal evaluation showed low gonadotropins (FSH 3.25 mIU/mL, LH 0.24 mIU/mL) and low estradiol (11.8 pg/mL). Pelvic ultrasound demonstrated a hypoplastic uterus (3.8 cm) with small ovaries, while brain MRI excluded structural hypothalamic–pituitary abnormalities. Karyotype analysis confirmed a normal 46,XX pattern. GnRH stimulation testing revealed a suboptimal gonadotropin response (FSH 12.02 mIU/mL, LH 4.87 mIU/mL) with persistently low estradiol, supporting the diagnosis of hypogonadotropic hypogonadism. Pubertal induction was initiated using transdermal estradiol (25 µg/day, subsequently increased to 37.5 µg/day). After 19 months of therapy, estradiol concentrations increased to 231 pmol/L, breast development progressed to Tanner stage 4-5, and uterine length increased from 3.8 cm to 6.3 cm, with an endometrial thickness of 8.7 mm. Gonadotropin levels remained suppressed, and nutritional status showed no significant improvement. Progestogen therapy was planned either after the onset of breakthrough bleeding or, in its absence, after approximately 2 years of continuous estrogen therapy.

Conclusions: This case highlights the importance of timely diagnosis and gradual estrogen replacement in adolescents with hypogonadotropic hypogonadism, even in the context of persistent undernutrition. A progressive pubertal induction strategy, combined with nutritional rehabilitation, is essential to support normal pubertal development and to reduce long-term reproductive and skeletal risks.

Abstract citation ID: lvag096.1615

EP1425 - ECE_3143 - The role of androgen excess in obesity and adipose tissue dysfunction in polycystic ovary syndrome

Valentina Soldat Stankovic[1], Gabrijela Malesevic[1], Snjezana Popovic Pejicic[1], Aleksandra Markovic[1] and Djuro MacUt[2,3]
[1]*Faculty of medicine, Univesity Clinical Center Republic of Srpska BAnja LUka, Internal Medicine, Endocrinology, University of Banja Luka, Banja Luka, Bosnia and Herzegovina;* [2]*Faculty of Medicine, University of Belgrade, University Clinical Centar, Belgrade, Serbia;* [3]*Clinic for Endocrinology, Diabetes and Diseases of Metabolism, Belgrade, Serbia*

Introduction: Low adiponectin levels in polycystic ovary syndrome (PCOS) are mainly attributed to obesity, which is common among these patients. In addition, evidence also suggests that

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

low adiponectin in PCOS may be associated with androgen excess in these women.

The aim: of this study was to investigate the association of adiponectin levels with body mass and androgen levels in women with PCOS.

Materials and Methods: A total of 60 women with PCOS who fulfi lled the Rotterdam diagnostic criteria from 2003 and 60 control women without PCOS, matched by age and body mass index, were recruited. We determined anthropometric parameters, metabolic and endocrine indicators, serum adiponectin and infl ammatory markers and statistically analyzed the results.

Results: Women with PCOS had signifi cantly lower levels of adiponectin ($P < .01$) compared to healthy women. Adiponectin level was inversely correlated with body mass index (BMI), waist circumference (WB), body fat mass, triglycerides, homeostasis model assessment HOMA IR, insulin AUC, glucose AUC, total testosterone, dehydroepiandrosterone sulfate (DHEAS) and free androgen index (FAI), and positively correlated with sex hormone-binding globulin (SHBG) and high-density lipoprotein cholesterol (HDL) in the PCOS group. In multivariate logistic regression, BMI and FAI were signifi cant independent determinants of the adiponectin cut-off level of 7.7 mg/mL.

Conclusions: Our results confi rm that adiponectin concentrations change according to BMI variations in women with PCOS. They also suggest a role for androgen excess in obesity and adipose tissue dysfunction in women with PCOS.

Abstract citation ID: lvag096.1616

EP1427 - ECE_2955 - Dual ovarian disorders: understanding concurrent PCOS and POI

Shebina Liz Mathews, Kabeer Katariya, Ann Francis and Cornelius Fernandez James
Diabetes and Endocrinology, Pilgrim Hospital, Boston (United Lincolnshire Hospitals NHS Trust), Boston, United Kingdom

Introduction: Polycystic ovary syndrome (PCOS) affects 6%-13% women of reproductive age, characterized by hyperandrogenism, oligo-amenorrhea, and polycystic ovarian morphology. This is traditionally regarded as pathophysiologically distinct from premature ovarian insufficiency (POI), which involves impaired ovarian function before the age of 40, characterized by amenorrhea >4 months, and FSH >25 IU/L on two occasions, four weeks apart. As these conditions are considered opposing diagnoses, their overlap presents a diagnostic challenge.

Case: A 36-year-old woman with a background of hypothyroidism and depression presented in 2021 with secondary amenorrhea, clinical hyperandrogenism (hirsutism, thinning of scalp hair), and excessive weight gain (BMI 44.9). Initial blood tests revealed: FSH 23.2 IU/L, LH 13.1 IU/L, 17-β estradiol 65 pmol/L, and testosterone 2 nmol/L (hyperandrogenism with hypoestrogenism). Repeat tests after clinic visit: FSH 48.2, LH 35.0, testosterone 2.6, SHBG 15, free androgen index (FAI) 17.3, and prolactin 314 (hyperandrogenism with possible POI). Subsequent testing: FSH 20, LH 14.8, 17-β estradiol 61, testosterone 1.8, SHBG 21, FAI 8.6, DHEA-S 13 µmol/L, 17-α hydroxy progesterone 0.8, TSH 2.4, FT4 15.2, and AMH <0.3 pmol/L. These results confirmed the diagnosis of overlapping PCOS and POI. Ovarian antibodies: negative. Cytogenetics and karyotyping: normal. DEXA: normal BMD. The patient was counselled on diagnosis, fertility implications, weight reduction strategies and fertility preservation options like oocyte cryopreservation. Subsequently, she was started on transdermal estradiol and micronized progesterone when she developed vasomotor symptoms.

Discussion: This case highlights that PCOS–POI can overlap and underscores the importance of longitudinal endocrine assessment in women with atypical PCOS presentations. Fluctuating FSH levels seen in POI due to residual ovarian function can delay the diagnosis. Persistent hyperandrogenism is not a feature of POI. Similarly, hypoestrogenism is not a feature of PCOS. Hence, a combination of persistent hyperandrogenism and hypoestrogenism should raise the possibility of an overlap syndrome. 10%-12% of POI have chromosomal abnormalities, 5% are autoimmune, remaining idiopathic. The proposed mechanisms include accelerated follicular atresia, chronic follicular arrest, and metabolic or inflammatory influences on ovarian reserve.

Conclusions: A subset of women with PCOS may have an increased risk of developing POI. Hence, PCOS is a significant (eightfold) and independent risk factor for later development of POI. Early recognition of POI in women with PCOS is essential to facilitate timely fertility counselling, consideration of fertility preservation, and appropriate initiation of HRT or lifestyle modifications to mitigate long-term risks, including osteoporosis and cardiovascular disease.

Abstract citation ID: lvag096.1617

EP1428 - ECE_2286 - Clinical profile of hypogonadism patients attending tertiary endocrine center in Nepal

Ansumali Joshi[1,2], Srijana Karmacharya[1], Puspa Dahal[1], Smriti Khadka[1], Radhika Tuladhar[1] and Sapana Yadav[1]
[1]*Kathmandu Diabetes and Thyroid Center, Lalitpur, Nepal;*
[2]*Kathmandu Diabetes and Thyroid Centre, Kathmandu, Nepal*

Hypogonadism patients' data is lacking in Nepal. We retrospectively reviewed data of all hypogonadism patients, who attended our clinic from 2010 to 2024. There was total 101 patients, male 74(73.27%) and females 27(26.73%) with M: F ratio 2.71: 1. Mean age was 29.47 ± 12.01 years, mean weight was 66.23 ± 20.75 kg and mean BMI was 25.62 ± 6.01 kg/m^2. Presenting symptoms and signs were decreased libido in 29 patients (28.71%), erectile dysfunction in 29 males (39.18%), menstrual abnormalities in 17 females (62.96%), primary amenorrhea in 7 females (25.92%), small phallus in 1 male (1.35%). Infertility was seen in 9 patients (8.91%). Small testes were seen in 8 males (10.81%). Cryptorchidism was seen in 3 males (4%). Absent secondary sexual characteristics was seen in 22 patients (21.78%). Gynecomastia was seen in 15 males (20.27%). Hypergonadotropic hypogonadism was seen in 46(45.54%) patients and hypogonadotropic hypogonadism seen in 43(42.57%) patients. Functional hypogonadism was seen in 12(11.88%) patients, and their mean BMI was 32.58 ± 9.03 kg/m^2. Anosmia was seen in 1 patient with hypogonadotropic hypogonadism. Testicular volume was 5.10 ± 3.83 mL and Stretched Penile Length (SPL) was 5.57 ± 1.95 cm. Main cause of hypergonadotrophic hypogonadism was idiopathic in 19 patients (18.81%), followed by Turner syndrome in 11(10.89%), history of orchitis in 5(4.95%), Klinefelter syndrome in 4(3.96%), premature ovarian failure in 3(2.97%), cryptorchidism in 3(2.97%) and XX syndrome in 1(0.99%). The main cause of hypogonadotropic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hypogonadism was idiopathic in 28 patients (27.72%), hypopituitarism in 5(4.95%), Nonfunctioning Pituitary adenoma (NFPA) in 4(3.96%), Hyperprolactinemia in 4(3.96%), Sheehan's syndrome in 1(0.99%) and head injury in 1(0.99%). Comorbidities were diabetes in 17 patients (16.83%), hypertension in 14 patients (13.86%) and hypothyroidism in 29 patients (28.71%). Mean testosterone level was 2.20 ± 4.21 ng/mL in male patients. Mean LH were 3.08 ± 2.84 IU/L and FSH 4.09 ± 5.38 IU/L in hypogonadotropic hypogonadism and LH were 24.74 ± 11.75 IU/L, FSH were 51.25 ± 38.53 IU/L and prolactin were 20.05 ± 26.95 ng/mL in hypergonadotropic hypogonadism.

Abstract citation ID: lvag096.1618

EP1435 - ECE_1192 - Symptomatology during the perimenopausal and menopausal phases: a cross-sectional analysis of 220 women

Shahina Ishtiaq[1,2]
[1]Obstetrics and Gynecology, Ziauddin University Hospital, South City Hospital, Karachi, Pakistan; [2]Obstetrics and Gynaecology, Ziauddin University Hospital, Karachi, Pakistan

Background: Menopause is a natural but complex transition in a woman's life, characterized by a wide range of physical, cognitive, and emotional symptoms that can significantly affect daily functioning and overall quality of life. The prevalence, pattern, and impact of these symptoms vary among individuals, making it essential to understand their nature for effective clinical management and timely interventions.

Objective: To evaluate the most common physical, cognitive, and emotional symptoms experienced by women during the perimenopausal and menopausal phases.

Materials and Methods: A cross-sectional study was conducted among 220 women aged 40-60 years in the perimenopausal or menopausal stage, recruited from outpatient clinics at Ziauddin Hospital Karachi. A structured questionnaire was used to assess physical, cognitive, and emotional symptoms. Data were analyzed by calculating frequencies and percentages for each symptom, and the mean number of symptoms per participant was determined to assess overall symptom burden.

Results: The most prevalent symptoms were hot flashes (74.1%), irregular periods (64.1%), and sleep disturbances (63.2%). Other frequently reported issues included low sexual desire (55%), poor concentration (42.3%), joint and muscle pain (39.5%), fatigue (34.5%), mood swings (33.2%), anxiety (15%), and depression (14.1%). On average, participants reported 4.35 ± 1.6 symptoms, reflecting a substantial symptom burden and the multifaceted nature of menopausal experiences.

Conclusions: Menopausal symptoms are multifaceted and vary widely among women. These findings emphasize the need for a comprehensive, patient-centered approach that addresses physical, cognitive, and emotional health to improve overall quality of life during the menopausal

Abstract citation ID: lvag096.1619

EP1436 - ECE_3264 - A case of primary hypogonadism in early life: its clinical features, approach, and management

Anton Angelo Urtula[1] and Lisa Angelica Evangelista[2]
[1]Internal Medicine, National Kidney and Transplant Institute, Quezon City, Philippines; [2]Green City Medical Center, Quezon City, Philippines

Background: Primary hypogonadism is defined by the failure of the testes to produce adequate levels of testosterone despite normal or high levels of gonadotropins. Its presentation varies according to the stage of life it develops.

Case Presentation: This is a case of a 26-year-old male who presented with ambiguous genitalia upon birth along with delayed secondary sex characteristics during puberty. On physical exam, testes were nonpalpable, penile shaft was underdeveloped, pubic and axillary hair were sparse or absent, breasts were prominent. On further testing, serum testosterone and estradiol were remarkably low, while LH and FSH were elevated. Thyroid hormones and serum cortisol were within normal levels. Other labs showed osteoporosis and dyslipidemia undue for age. Cranial imaging was nearly unremarkable. Karyotyping revealed a normal 46 XY karyotype

Outcome: The patient was prescribed with topical testosterone replacement therapy, along with statins and Vitamin D supplementation. Genetic testing and pelvic MRI were ordered for final confirmation of underlying cause.

Conclusions: This case highlights the varied presentation of primary hypogonadism, its natural history, and its approach to evaluation and treatment. Prompt work-up and management are needed to identify the primary etiology and to address its systemic manifestations.

Keywords hypogonadism, hypergonadotropic hypogonadism, testicular failure, disorders of sex development

Abstract citation ID: lvag096.1620

EP1437 - ECE_3493 - When hormones are normal: idiopathic gynecomastia in a young male

Inass Chaari[1], Ayoub Idrissi[2], Lahoussaine Abainou[3], Hamza El Jadi[4], Azzelarab Meftah[5] and Hicham Baïzri[5]
[1]Endocrinology, Diabetes and Metabolism, Avicenna Military Hospital, Marrakech, Morocco; [2]Endocrinology, Diabetology and Metabolic Diseases, Avicenna Military Hospital, Marrakech, Morocco; [3]Endocrinology, Diabetes and Metabolism, Oued Eddahab Military Hospital, Agadir, Morocco; [4]Marrakech, Morocco; [5]Endocrinology, Diabetes and Metabolism, Avicenna Military Hospital, Marrakech, Morocco

Gynecomastia, defined as the benign proliferation of glandular breast tissue in males, represents a frequent clinical presentation in the endocrine clinic. While often physiological during puberty due to transient hormonal fluctuations, its persistence into late adolescence and young adulthood necessitates a rigorous diagnostic approach to exclude underlying pathologies.

We present the case of a 31-year-old male presenting with a one-year history of progressive, bilateral, and painless breast enlargement . The patient reported no history of medication use, anabolic steroid consumption, or exposure to phytoestrogens. Physical examination confirmed the presence of firm, concentric subareolar tissue without signs of galactorrhea, nipple retraction, or lymphadenopathy. Testicular volume and secondary sexual characteristics were appropriate for Tanner Stage V.

Breast ultrasound revealed gynecomastia.Laboratory investigations showed normal testosterone levels (3.16 ng/mL), FSH

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

at 1.15 IU/L, LH at 2.84 IU/L, 17β-estradiol at 30 pg/mL, and normal prolactin levels.. Tumor markers (β-hCG and α-fetoprotein) were negative, and thyroid, hepatic, and renal functions were normal. Scrotal ultrasonography revealed no occult malignancies.

Idiopathic cases account for approximately 25% to 50% of gynecomastia presentations. In young adults, the condition is hypothesized to result from an increased sensitivity of breast tissue to circulating estrogens or a localized imbalance in the aromatase enzyme activity within the breast microenvironment. While the biochemical profile remains unremarkable, the psychological impact on young patients is often profound, frequently requiring a multidisciplinary approach involving endocrinologists, psychologists, and plastic surgeons.

This case highlights the clinical paradox of idiopathic gynecomastia, where significant physical changes occur despite a normal hormonal milieu. Management should prioritize patient reassurance and monitoring,

Abstract citation ID: lvag096.1621

EP1438 - ECE_2797 - Recognising turner syndrome in primary care- an adolescent presenting with primary amenorrhea

Christina Lymniati, Katerina Papadopoulou, Aggeliki Mela and Charalampos Tsentidis
Endocrinology, Diabetes Mellitus and Metabolism Department, General Hospital of Nikaia Piraeus "AG. Panteleimon", Piraeus, Greece

Aim: To describe the diagnostic pathway and early management of an adolescent presenting with primary amenorrhea in a primary care setting, highlighting the recognition of clinical features suggestive of Turner syndrome (TS) and the importance of timely referral for specialized endocrine assessment.

Methods: A 14-year-and-10-month-old girl was referred from the emergency department to endocrinology following incidental detection of subclinical hypothyroidism. Clinical evaluation included anthropometric assessment, pubertal staging, dysmorphology examination, hormonal profiling, pelvic ultrasonography, bone age determination, and cytogenetic analysis. Findings were interpreted according to current international guidelines for the evaluation of primary amenorrhea and the management of TS.

Results: The patient presented with short stature (3rd percentile), Tanner stage I pubertal development, and multiple dysmorphic features (webbed neck, micrognathia, shield chest, widely spaced nipples, cubitus valgus). Laboratory evaluation demonstrated hypergonadotropic hypogonadism (FSH 74.1 μIU/mL, LH 11.8 μIU/mL, estradiol <11.8 pg/mL), low IGF-1, and mildly elevated TSH. Pelvic ultrasonography revealed a hypoplastic uterus and non-visualized ovaries. Bone age corresponded to 13 years. Karyotype confirmed monosomy X (45,X), establishing the diagnosis of Turner syndrome.

Given the delayed diagnosis and limited remaining growth potential, the patient was submitted for approval of growth hormone (GH) therapy and simultaneously initiated on low-dose transdermal 17β-estradiol for pubertal induction. A structured titration plan was established, with gradual escalation of estrogen dosing and planned introduction of cyclic progesterone following the first breakthrough bleed. Multidisciplinary follow-up was arranged to address cardiovascular, metabolic, reproductive, and psychosocial aspects of TS.

Conclusions: Primary amenorrhea, particularly when accompanied by short stature and dysmorphic features, should prompt evaluation for Turner syndrome. Early recognition in primary care is crucial for optimizing long-term outcomes. Concurrent initiation of GH and estrogen therapy in late-diagnosed patients supports both growth potential and appropriate pubertal development. Lifelong, multidisciplinary management is essential due to the broad spectrum of comorbidities associated with TS.

Abstract citation ID: lvag096.1622

EP1439 - ECE_3455 - Body weight strongly influences the metabolic phenotype in women with polycystic ovary syndrome

Sabrina Marville[1], Nelly Pitteloud[2] and Adelina Ameti[2]
[1]*Université de Lausanne, Lausanne, Switzerland;* [2]*Division of Endocrinology, Diabetes & Metabolism, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland*

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, affecting approximately 10%. It is characterized by ovulatory dysfunction, hyperandrogenism and/or polycystic ovarian morphology on ultrasound. Beyond reproductive manifestations, PCOS is associated with an increased burden of metabolic abnormalities, including insulin resistance and dyslipidaemia.

Objective: To describe the clinical, hormonal and metabolic characteristics of women with PCOS followed in our centre and to compare normal-weight and obese phenotypes.

Methods: This retrospective study was based on the Endocrinology, Diabetes and Metabolism (EDM) database at Lausanne University Hospital (CHUV). PCOS was defined by Rotterdam criteria after exclusion of secondary causes. Women on treatments likely to interfere with hormonal/metabolic parameters at the time of assessment (eg, oral contraceptives, metformin/GLP-1 receptor agonists, spironolactone) were excluded.

For group comparisons, normal-weight (BMI <25 kg/m^2) and obese women (BMI ≥30 kg/m^2) were analysed; overweight women were excluded. Clinical, hormonal and metabolic data were collected. Sex steroids were measured by mass spectrometry, while other biochemical parameters were measured using immunoassays.

Results: Ninety-nine women were included. Phenotype A (hyperandrogenism + ovulatory dysfunction + polycystic ovarian morphology) and phenotype B (hyperandrogenism + ovulatory dysfunction) predominated (57.6% and 21.2%), and polycystic ovarian morphology was present in 79.8%.

For group comparisons, 24 normal-weight and 53 obese women were analyzed. Menstrual disturbances did not differ between groups (oligomenorrhoea 70.8% vs 67.9%; amenorrhoea 12.5% vs 15.1%; regular cycles 12.5% vs 17.0%; all $P > .05$). Acne was more frequent in normal-weight women (75.0% vs 35.8%, $P = .003$). Obese women had significantly higher fasting glucose, fasting insulin and HOMA-IR (8.21 ± 7.85 vs 2.01 ± 0.85, $P = .003$). Dyslipidemia was more prevalent in obese women (66% vs 19.6%, $P < .001$), with higher triglycerides ($P = .001$), lower HDL-cholesterol ($P < .001$), higher LDL-cholesterol ($P = .01$) and a higher triglyceride/HDL ratio ($P < .001$). SHBG concentrations were significantly lower in obese women (25.79 ± 12.33 vs 69.36 ± 61.81 nmol/L, $P < .001$), whereas total testosterone,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

androstenedione and DHEA-S levels were similar between groups (all $P > .05$).

Conclusions: Obesity is strongly associated with a worse metabolic profile in women with PCOS, characterised by marked insulin resistance and dyslipidaemia, while circulating androgen concentrations are broadly comparable across weight categories. These findings highlight the central metabolic impact of adiposity and support systematic cardiometabolic screening and weight-focused management in PCOS.

Abstract citation ID: lvag096.1623

EP1441 - ECE_1387 - Prader–willi syndrome—from diagnosis to substitution therapy

Mirjana Bojic[1], Anja Stanic[1], Ivona Risovic[1,2], Tamara Dojcinovic[1,2] and Aleksandra Markovic[1,2]
[1]*University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina;* [2]*Faculty of medicine, University of Banja Luka, Banja Luka, Bosnia and Herzegovina*

Prader–Willi syndrome is a rare genetic disorder involving chromosome 15, characterized by hypotonia, a characteristic facial appearance (reduced bifrontal diameter), convergent strabismus, and intellectual disability. In boys, it is usually accompanied by cryptorchidism and a hypoplastic scrotum.

We present the case of a patient who initially consulted a urologist due to priapism, after which further endocrinological evaluation was recommended. Hormonal testing revealed elevated estradiol levels with low testosterone levels, while clinical examination showed obesity and cryptorchidism. Due to cryptorchidism, urological treatment was performed, followed by repeat endocrinological evaluation, after which testosterone replacement therapy was initiated. This led to a reduction in body weight, voice deepening, development of male-pattern body hair, and overall clinical improvement. Review of the patient's medical documentation revealed that genetic testing had been performed at birth and the diagnosis of Prader–Willi syndrome had already been established; however, appropriate therapy had not been initiated at that time.

This case highlights the importance of early detection and appropriate long-term follow-up by an endocrinologist, as this enables timely initiation of adequate substitution therapy as well as prompt urological surgical intervention when indicated.

Abstract citation ID: lvag096.1624

EP1443 - ECE_3074 - Implementing U.S.-validated AI practices in healthcare: AI-based clinical decision support with personalized nutrition planning for polycystic ovary syndrome in Republic of Georgia

Mariam Pailodze[1,2] and Salome Kalandadze[1,3]
[1]*Caucasus Medical Centre, Tbilisi, Georgia;* [2]*David Tvildiani Medical University, Tbilisi, Georgia;* [3]*Endocrinology, Caucasus Medical Center, Tbilisi, Georgia*

Background: Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder associated with metabolic dysfunction, insulin resistance, and significant long-term health risks. Nutrition and lifestyle modification are core components of PCOS management; however, in low-resource health care systems, including Georgia, access to structured, personalized nutritional counseling remains limited. In high-income settings such as the United States, artificial intelligence (AI)–based clinical decision support and nutrition platforms have demonstrated feasibility and effectiveness in metabolic disease management. Their applicability in lower-resource, culturally distinct healthcare systems has not been systematically evaluated.

Objective: To explore the feasibility and implementation strategy of adapting U.S.-validated AI-based nutrition decision-support models for outpatient PCOS care within the Georgian health care system, with a focus on physician supervision, patient trust, and cultural acceptability.

Methods: This mixed-methods implementation study consists of three phases: (1) a scoping review of U.S.-validated AI nutrition and lifestyle interventions used in outpatient metabolic and endocrine care; (2) a cross-sectional survey assessing Georgian women with PCOS regarding attitudes toward AI-assisted healthcare, trust, and cultural dietary preferences; and (3) a pilot outpatient intervention in which AI-generated personalized nutrition plans are reviewed and approved by physicians prior to patient use. Feasibility, acceptability, and early clinical signals (diet adherence, patient satisfaction, and selected metabolic indicators) will be assessed.

Expected Impact: This project aims to generate the first evidence-based framework for trustworthy, culturally adapted AI-enabled nutrition care for PCOS in Georgia. Findings will inform scalable strategies for integrating AI into low-resource primary care systems while preserving clinician oversight and strengthening the doctor–patient relationship.

Abstract citation ID: lvag096.1625

EP1446 - ECE_2942 - Finasteride for treatment of androgenic male alopecia since puberty: case report

Fedir Laniush and Alina Urbanovych
Endocrinology, State Non-Profit Enterprise "Danylo Halytsky Lviv National Medical University", University Clinic State non-profit enterprise "Danylo Halytsky Lviv National Medical University", Lviv, Ukraine

Background: Androgenic male alopecia is a condition affecting millions of men worldwide inducing significant psychological distress and a strong desire for an early intervention and leading to an increase in off label usage of the drugs among adolescents.

Clinical case: A 21-year man visited an endocrinologist to check his hormones. He has a history of 7-year Finasteride applying because of a fear of losing his hair. He had been taking Finasteride since the age of 14 when he had first noted losing his hair. He had a history of androgenic alopecia since his older brother also started losing his hair during puberty. The patient did not attend endocrinologist previously and found information about Finasteride on internet. During these years he had been checking his hormones on his own. During examination: the hair growth is preserved and there were no signs of alopecia of any kind. Laboratory data: total testosterone 30,1 nmol/L (4.10-32.92); sex hormone-binding globulin 36.7 nmol/L (14.8-95); the free testosterone index 82.01% (14.55-94.64); estradiol 25.6 pg/mL; luteinising hormone (LH) 2.56 U/L (1.24-8.62); follicle-stimulating hormone (FSH) 3.52 U/L (1.27-19.26); prolactin 9.5 ng/mL (2.64-13.13). Patient was absolutely satisfied with his sex life and did not express any symptoms off loss of libido or erectile dysfunction.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusion: Finasteride is one of the among approved drugs for the treatment of androgenic alopecia in men aged 18 and older and benign prostatic hyperplasia (BPH). Despite the food and drug administration (FDA's) approval for usage of Finasteride in adults, off-label usage in adolescents is increasing in the recent times, primarily due to online misinformation and the psychological impact of early hair loss. Several studies have been done to show that patient's treated with Finasteride had an increase rate of development for high grade prostate cancer. The other side effects of these drug include impotence, decreased libido, decreased volume of ejaculate, gynecomastia, depression and mood changes, allergic reactions, and the most challenging Post—Finasteride syndrome which is characterised by side effects persisting after stoppage of the drug. Although Finasteride is designed to reduce hair loss but it's effect are temporary upon discontinuing the drug the hair loss resumes leaving behind distress and dissatisfaction. The usage of this drug among adolescents need more further investigations and research works

Abstract citation ID: lvag096.1626

EP1905 - ECE_3337 - In vitro endometrium of insulin resistant women with polycystic ovary syndrome

Anja Dekanski[1], Gustaw Eriksson[1], Tanja Turunen[1], Timotej Strmen[2], Tina Gorsek Sparovec[1], Angelica Lindén Hirschberg[3], Elin Chorell[2], Nayere Taebnia[1] and Elisabet Stener-Victorin[1]

[1]*Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden;* [2]*Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden;* [3]*Department of Women's and Children's Health, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden*

Introduction: Endometrial dysfunction in polycystic ovary syndrome (PCOS) can lead to reduced fertility, miscarriage, and higher endometrial cancer risk. Additionally, our recent PCOS endometrial single-cell atlas shows cell type specific transcriptomic disease signatures. *In vitro* endometrial systems mirroring the PCOS tissue of origin is crucial for future mechanistic insight and novel target testing. We hypothesized that PCOS-associated endometrial disease features can be preserved in primary human endometrial epithelial organoids (EEOs) and single-layer stromal cells, under optimized conditions.

Methods: We established and characterized EEOs ($n = 4$ PCOS; $n = 4$ controls) and stromal cells ($n = 6$ PCOS; $n = 6$ controls) from proliferative phase endometrial biopsies of women with and without PCOS. Women with PCOS were hyperandrogenic and insulin resistant. Both cell systems were differentiated with 10 nM estradiol and 1 uM progesterone. EEOs and stromal cells were collected for bulk RNA sequencing and stained for typical differentiation markers. In stromal cells, we also performed lipidomics using liquid chromatography coupled to quadrupole time-of-flight mass spectrometry, and cellular bioenergetics using Seahorse XFe96. Additionally, we used a PCOS-like anovulatory hormonal environment and a healthy hormonal environment with estrogen, progesterone and androgen levels fluctuating. We tried EEO stimulation in these hormonal environments in both a static and microfluidic setting.

Results: In the initial EEO set-up very few transcriptomic differences were captured between PCOS and Control origin cells. In stromal cells, progesterone receptor staining was reduced, and maximal respiration trended lower in PCOS. Differentially expressed genes (DEGs) in stromal cells included upregulation of fibro activation protein (*FAP*) gene and downregulation of *CARD16*. Lipidomics analysis showed PCOS stromal cells uniquely accumulated insulin-resistance-associated ceramides during differentiation. At day 14, PCOS stromal cells had significantly elevated C20-ceramide and reduced cardiolipins. Fluctuating hormonal environment and the microfluidics setting were able to recapitulate more of the transcriptomic differences between PCOS and Control in EEOs.

Conclusions: Preliminary data shows that in the static hormonal environment *in vitro*, that does not closely recapitulate neither the normal menstrual cycle nor the PCOS irregular menstrual cycle, the EEOs lose most of their PCOS phenotype *in vitro*, while stromal cells retain more of it. Mimicking the PCOS-like and healthy-like hormonal environment and using microfluidics exacerbated transcriptomic differences in EEOs. Stromal cells from women with PCOS had DEGs related to proliferation and inflammation, and lipid dysregulation associated with metabolic dysfunction. In the next steps we are establishing co-culture systems to combine EEOs and stroma, but also adipose and endometrial cells.

Abstract citation ID: lvag096.1627

EP1906 - ECE_3543 - Cell type-specific endometrial dysfunctions across the menstrual cycle in polycystic ovary syndrome

Tanja Turunen[1], Congru Li[1], Riikka Arffman[2], Gustaw Eriksson[1], Tina Gorsek Sparovec[1], Ulla Saarela[2], Angelica Lindén Hirschberg[3], Terhi Piltonen[2] and Elisabet Stener-Victorin[1]

[1]*Karolinska Institutet, Solna, Sweden;* [2]*Medical Research Center, Department of Obstetrics and Gynecology, Research Unit of Clinical Medicine, University of Oulu and Oulu University Hospital, Oulu, Finland;* [3]*Department of Women's and Children's Health, Department of Gynecology and Reproductive Medicine, Karolinska Institutet and Karolinska University Hospital, Solna, Sweden*

Polycystic ovary syndrome (PCOS) affects 11%-13% of reproductive-aged women and is characterized by hyperandrogenism, polycystic ovarian morphology, and menstrual irregularities. It is a major cause of anovulatory infertility and affected women have an increased risk of implantation failure and miscarriage, likely due to endometrial dysfunction. Recently, we published the first PCOS Endometrial Cell Atlas (PECA 1.0), which revealed cell-type-specific disease signatures in proliferative-phase endometrium. Here, we comprehensively characterize how different cell types and their transcriptomic signatures evolve across the menstrual cycle in PCOS by establishing PECA 2.0. Endometrial biopsies were obtained, after informed consent, from women with and without PCOS who had similar age and BMI ($P > .05$ two-tailed Welch's t-test). Combined with the PECA 1.0 study (12 PCOS, 5 controls), our current single-nuclei (sn) RNA-seq dataset of 62 samples covers proliferative (7 PCOS, 7 controls), early secretory (6 PCOS, 3 controls), mid-secretory (7 PCOS, 5 controls), and late secretory phases (4 PCOS, 3 controls), as well as the anovulatory state (3 PCOS). Libraries were prepared from snap-frozen biopsies using Chromium GEM-X technology v 4.0 (10X Genomics). After data quality control, the final PECA 2.0 dataset included 998 832 high-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

quality nuclei: 625 593 from PCOS and 373 239 from control endometrium. We identified four main clusters: epithelial ($n = 478$ 789), stromal ($n = 453$ 832), immune ($n = 55$ 708), and endothelial cells ($n = 10$ 503). Reintegration revealed 11 epithelial, 7 stromal, 5 endothelial, and 16 immune cell subpopulations. The proliferative phase PCOS endometrium has a decreased proportion of proliferative stromal cells (56.26%) compared to controls (92.96%; Mann-Whitney U, adj. $P = .124$; Levene's test, adj. $P = .018$). Moreover, disrupted decidualization was demonstrated by a decreased proportion of decidualized stromal cells in PCOS late secretory phase samples (45.77%) compared to controls (59.98%; Mann-Whitney U, adj. $P = .124$; Levene's test, adj. $P = .011$). Levene's test results indicate significantly greater variability in these cell proportions in PCOS samples. The PCOS Endometrial Cell Atlas across the menstrual cycle, PECA 2.0, maps cellular heterogeneity and reveals transcriptomic signatures of endometrial dysfunction in PCOS at high resolution. This resource provides a foundation for developing precise diagnostic tools, targeted therapies, and preventive strategies to improve endometrial health.

Abstract citation ID: lvag096.1628

EP1907 - ECE_1821 - Development of a immunodeficient prenatal mouse model of polycystic ovary syndrome for evaluation of new therapeutics

Camille Gauthier[1], Haojiang Lu[1], Sara Torstensson[1], Luzi Sophie Schuchmann[1], Eva Lindgren[1], Claes Ohlsson[2], Anna Benrick[3] and Elisabet Stener-Victorin[1]
[1]*Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden;* [2]*Sahlgrenska Academy University Hospital, Gothenburg, Sweden;* [3]*Physiology, Sahlgrenska Academy, Gothenburg, Sweden*

Polycystic ovary syndrome (PCOS) affects ~10% of women and is the leading cause of anovulatory infertility, diagnosed by hyperandrogenism, irregular cycles, and/or a polycystic ovarian morphology. While PCOS is strongly associated with cardiometabolic comorbidities. Current treatments are symptom-based, with no targeted treatments available. A major obstacle in developing therapies is the immune response is leading to the production of anti-drug antibodies, which neutralize drug activity and alter efficacy. We aimed to establish a PCOS mouse model on an immunodeficient background to enable preclinical testing of novel therapeutics without immune interference.

Both wild-type (C57BL/6NTac, WT) and B cells deficient mice (C57BL/6NTac-Igh-Jem1Tac, KO) were used to generate prenatal androgenized (PNA) models. The PNA mode was induced by daily dihydrotestosterone (DHT) injections in pregnant dams at embryonic days 16.5, 17.5, and 18.5. Reproductive traits of F1 mice were assessed, including anogenital distance (AGD), a marker of in utero androgen exposure, puberty onset (vaginal opening), estrous cyclicity (vaginal smears measured at P70-P82 and P126- P138). Sex steroids, as well as AMH and FSH, were quantified in serum at P186 using LC/MS, ELISA, and Milliplex immunoassays, respectively. Metabolic traits were analyzed by EchoMRI (at P84, P112, P154), and glucose and insulin tolerance tests were performed at P147, P175 in F1 mice. Data were analyzed using the Mann–Whitney U test.

PNA mice on both WT and KO backgrounds exhibited delayed puberty onset ($P < .0001$, $P = .0015$), increased AGD ($P = .0036$, $P < .0001$), disrupted estrous cyclicity (diestrus block, both $P < .0001$), and anovulation ($P = .0027$, $P < .001$). Androgen levels were unchanged, but both WT and KO PNA mice showed elevated AMH levels ($P = .0252$, $P = .022$), and WT PNA mice exhibited lower FSH levels compared to controls ($P = .0431$). Body weight and composition were similar across groups, although KO-PNA mice displayed increased subcutaneous and visceral fat at sacrifice P186 ($P = .0252$, $P = .0214$). Glucose and insulin tolerance did not differ significantly between WT and KO mice.

In conclusion, B cell deficient PNA mice recapitulate key reproductive PCOS hallmarks, despite lacking adaptive immune system. Typical metabolic alterations were attenuated, with increased fat depots in KO mice as the only metabolic feature retained. Nevertheless, this PCOS-like model provides a robust platform for evaluating PCOS therapeutics while minimizing confounding effects from immune-mediated drug clearance.

Abstract citation ID: lvag096.1629

EP1908 - ECE_2152 - Twelve-month clinical outcomes following transvaginal ultrasound-guided ovarian ablation in women with PCOS-related infertility: the ULTRA trial

Saad Amer[1], Margaux Jegaden[2], Christine Wyns[3], Mostafa Metwally[4], Kanna Jayaprakasan[5], Herve Fernandez[6], Candice Autin[7], Marwa Fakhreldin[8], Christina Hawley[9] and Karl Hansen[10]
[1]*Academic Unit of Translational Medical Sciences, University of Nottingham, Derby, United Kingdom;* [2]*Clinique de la Muette, Paris, France;* [3]*Cliniques Universitaires Saint-Luc, Bruxelles, Belgium;* [4]*University of Sheffield and Sheffield Teaching Hospitals, Sheffield, United Kingdom;* [5]*University Hospitals of Derby & Burton NHS Foundation Trust, Derby, United Kingdom;* [6]*Hôpital Bicêtre, Le Kremlin-Bicêtre, France;* [7]*Chu Saint-Pierre, Brussel, Belgium;* [8]*Department of Women's and Children's Health, The Hewitt Fertility Centre, Liverpool Women's NHS Foundation Trust, Centre for Women's Health research, University of Liverpool, Member of Liverpool Health Partners, Institute of Life Course and Medical Sciences, Liverpool, United Kingdom;* [9]*May Health, Menlo Park, United States;* [10]*University of Oklahoma College of Medicine, Oklahoma City, United States*

Background: Laparoscopic ovarian drilling(LOD) is widely accepted as an effective second line treatment for infertility associated with polycystic ovary syndrome(PCOS). However, laparoscopy is an invasive procedure that requires general anaesthesia and carries significant risks. Furthermore, there is no standardization of the LOD technique among surgeons. In contrast, the Anavi™ System(CE Mark, May Health) has been designed to deliver a precisely calculated amount of ovarian ablation via a less invasive route without general anaesthesia. This transvaginal ultrasound (TVUS) approach therefore transforms an invasive surgical procedure to an office-based technique similar in ovarian access to the well-established oocyte retrieval. Here we report clinical outcomes of participants at 12-months following intervention

Methods: The ULTRA trial is a multicenter feasibility study that included two parallel single-arm studies conducted in Europe(EU; six centres) and the United States (US; one centre). The trial included women with anovulatory infertility associated with PCOS resistant to first line ovulation induction with Clomiphene citrate and/or Letrozole (CC/LETZ). All participants

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

were treated with TVUS-guided ovarian ablation using the May Health System. The first five participants in Europe underwent laparoscopy concurrent with the ovarian ablation. The remaining participants only underwent the TVUS-guided ovarian ablation procedure under sedation. Participants completed 3- and 6-month clinical assessment and 9- and 12-month telephone assessment.

Results: A total of 32 participants (27 EU, 5 US) were treated with TVUS-guided ovarian ablation. Feasibility and safety results of this trial have previously been reported. A total of 26 participants (81%) were evaluable at 12-months and included in this analysis. The mean [SD] age was 32.4 [3.4] years, BMI was 29.6 [5.0] kg/m^2 and 69% self-identified as white, 15% black and 15% other. Of those completing the 12-month follow-up, 20 (77%) ovulated including thirteen (50%) during the first three months post procedure and seven additional participants between three and 12 months after restarting CC/LETZ. A total of 12 (46%) participants conceived at least once within the 12-months post-procedure. Of those, ten conceived naturally (7 with and 3 without the restart of first-line ovulation induction medication). One participant conceived following IUI.

Conclusions: These preliminary data suggest that the previously reported clinical efficacy of TVUS-ovarian ablation using the Anavi System may be sustained at 12 months. Therefore, this may offer a potentially effective office-based second line ovulation inducing procedure for PCOS. A larger randomized study is currently in progress (REBLANCE; NCT06206746).

Abstract citation ID: lvag096.1630

EP1449 - ECE_3573 - Graves' disease unmasked by pancreatitis and delirium in a patient with panhypopituitarism

Mariana De Griné Severino[1], Carolina Peixe[1], Catarina Isabel Lopes[1], Mariana Lopes-Pinto[1], Mariana Agapito Fonseca[1], Marta Vaz Lopes[1], Miguel Duarte[1], Teresa Alegria Neto[1], Maria Inês Alexandre[1,2], Ana Palha[3] and Ema Lacerda[1,2]

[1]Serviço de Endocrinologia, ULS Santa Maria, Lisboa, Portugal; [2]Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal; [3]Serviço de Endocrinologia, ULS São José, Lisboa, Portugal

Introduction: Graves' disease typically presents with adrenergic symptoms, weight loss, goiter and ophthalmopathy; however, severe systemic and neuropsychiatric manifestations may predominate and delay diagnosis. Hypercalcemia is an uncommon but recognized complication of thyrotoxicosis and, in rare cases, may precipitate acute pancreatitis. Diagnostic recognition is particularly challenging in patients with hypopituitarism receiving levothyroxine replacement, in whom TSH is unreliable, and symptoms overlap with pituitary hormone deficiencies or intercurrent illness.

Clinical case: A 38-year-old woman with history of panhypopituitarism following craniopharyngioma resection was admitted to the emergency department due to nausea, vomiting and acute behavioral changes for the previous 15 days, progressing to hyperkinetic delirium requiring intensive sedation. At admission, she was afebrile, tachycardic (HR 113 bpm) and hypertensive (BP 155/138 mmHg). Her chronic medication included desmopressin, levothyroxine 25 mcg, hydrocortisone, bisoprolol and escitalopram.

There were no recent therapeutic changes and she denied alcohol or illicit drug consumption. Initial blood tests showed marked hypercalcemia (Ca 14.3 mg/dL, corrected for albumin), liver dysfunction (AST 159 U/L, ALT 264 U/L, BilT 4.39 mg/dL, GGT 52 U/L) and a raised amylase of 206 U/L (RV 13-53); serum sodium was normal (Na 140 mmol/L). Abdominal imaging excluded biliary obstruction and showed diffuse pancreatic enlargement with stranding of surrounding fat and peripancreatic exudates, consistent with pancreatitis. Hypercalcemia-induced pancreatitis was presumed and treatment with intravenous fluids and pamidronate was started. Brain CT and MRI showed no structural abnormalities.

The etiologic investigation of hypercalcemia revealed low PTH (12.3 pg/mL) with thyroid tests revealing thyrotoxicosis (FT4 5,84 ng/dL and FT3 7,51 ng/dL), with positive TRAbs 5,73 U/L and US findings consistent with Graves' disease (diffuse increased vascularity). Levothyroxine was stopped and thiamazole initiated, resulting in gradual psychosis improvement and normalization of calcium levels, pancreatic enzymes and liver tests over the following week. Both hypercalcemia and delirium were attributed to hyperthyroidism.

Conclusions: In patients with hypopituitarism, Graves thyrotoxicosis may be overlooked due to nonspecific symptoms and reliance on TSH. Monitoring FT4/FT3 trends and recognition of red flags such as unexplained hypercalcemia/pancreatitis and severe neuropsychiatric symptoms are essential for timely diagnosis and management. Notably, three years later, this patient was readmitted with recurrent behavioural changes and hyperkinetic delirium and further investigation revealed decompensated hyperthyroidism once again, highlighting the need for sustained vigilance for atypical presentations of Graves' disease in patients with hypopituitarism.

Abstract citation ID: lvag096.1631

EP1450 - ECE_3915 - Severe amiodarone-induced thyrotoxicosis: therapeutic plasma exchange as a bridge to urgent thyroidectomy

Ana Luísa Barbosa[1], Patricia Ferreira[1], Juliana Gonçalves[1], Mafalda Canudas Costa[1], Joana Lopes[2], Vítor Fernandes[2], Carlos Grijó[3], Ana Margarida Fonseca[3], Cristina Fernandes[4], Cláudio Silva[5], Patrícia Martins[2], Isabel Tavares[2], Marta Borges Canha[1], Jorge Pedro[1], Joana Queirós[1] and Ana Varela[1]

[1]São João Local Health Unit, Department of Endocrinology, Diabetes and Metabolism, Porto, Portugal; [2]São João Local Health Unit, Department of Nephrology, Porto, Portugal; [3]São João Local Health Unit, Department of Internal Medicine, Porto, Portugal; [4]São João Local Health Unit, Department of General Surgery, Porto, Portugal; [5]São João Local Health Unit, Infectious Diseases Intensive Care Unit, Porto, Portugal

Background: Amiodarone-induced thyrotoxicosis (AIT) is a condition with high cardiovascular mortality and presents with significant therapeutic challenges. In severe cases refractory to conventional medical therapy, therapeutic plasma exchange (TPE) followed by urgent total thyroidectomy should be considered.

Case presentation: Case 1: A 62-year-old man with severe ischaemic heart failure (HF) and atrial fibrillation (AF) on long-term amiodarone was admitted to the intensive care unit (ICU) for

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

acute myocardial infarction. He presented with overt thyrotoxicosis and was diagnosed with AIT. Treatment with methimazole and prednisolone was initiated and progressively titrated up to 40 mg/day and 70 mg/day, respectively. Despite a transient initial partial response, the patient developed persistent severe thyrotoxicosis and presented with cardiac deterioration and septic shock. Approximately 60 days after admission, two sessions of TPE were performed, resulting in significant biochemical improvement. The patient subsequently underwent total thyroidectomy. He died two days later due to multiorgan failure.

Case 2: A 48-year-old man with a history of HF, AF and AIT diagnosed three months earlier and treated with methimazole and prednisolone was hospitalized for acute left lower limb ischaemia. He underwent urgent revascularization, followed by cardiovascular instability and exacerbated thyrotoxicosis. Despite maximal medical therapy (methimazole and prednisolone up to 60 mg/day), severe thyrotoxicosis and hemodynamic instability persisted. TPE was initiated with biochemical improvement after three sessions, enabling total thyroidectomy without major perioperative complications, with favourable clinical outcome.

Case 3: A 37-year-old woman with a history of complex congenital valve disease and AF on amiodarone therapy was admitted to the ICU for thyroid storm complicated by AF with rapid ventricular response and hemodynamic instability. Treatment with propylthiouracil (500 mg followed by 200 mg orally every 4 hours), propranolol (80 mg orally every 4 hours) and intravenous hydrocortisone (300 mg bolus followed by 100 mg every 8 hours) was started. Given the lack of clinical response to medical therapy, TPE was initiated, with biochemical improvement after three sessions. Urgent total thyroidectomy was subsequently undertaken, complicated by postoperative hemodynamic instability requiring extracorporeal membrane oxygenation, but with gradual recovery thereafter.

Discussion: These cases illustrate severe, refractory AIT associated with marked cardiac instability and life-threatening complications in which rapid hormonal control is essential. In all patients, TPE allowed partial biochemical and clinical stabilisation, enabling urgent thyroidectomy. These cases highlight the importance of timely recognition of treatment failure and early consideration of TPE as a bridge to definitive surgical treatment, as delays in definitive therapy may be fatal.

Abstract citation ID: lvag096.1632

EP1451 - ECE_2813 - Management challenges of lenvatinib in elderly patients with advanced radioiodine-refractory DTC: a case of fatal Takotsubo syndrome

Gianluca Cera[1], Pietro Locantore[1], Erika Motolese[1], Alessandro Romano[1], Laura Crispino[1], Luisa Lener[1], Andrea Corsello[2], Rosa Maria Paragliola[3] and Alfredo Pontecorvi[1]

[1]Roma, Italy; [2]Division of Endocrine Surgery, Ospedale Isola Tiberina —Gemelli Isola, Rome, Italy; [3]Departmental Faculty of Medicine, Unicamillus-Saint Camillus International University of Health Sciences, Rome, Italy

Background: Lenvatinib is an effective therapy for advanced radioiodine-refractory differentiated thyroid cancer (DTC), although various adverse effects frequently complicate clinical management. We present the case of an 84-year-old woman affected by DTC alongside comorbidities including severe COPD, hypertension, chronic venous insufficiency, and depression.

Case presentation: At age 78, the patient underwent total thyroidectomy for a TIR5 (Bethesda VI equivalent) thyroid nodule. Histopathology revealed a multifocal papillary thyroid carcinoma (left lobe: 2.2 cm; right lobe: 1 cm), classic subtype, featuring 25% solid and 25% “tall cell” components, endovascular emboli, and positive excision margins (pT2m R1). Post-surgery, she received radioactive iodine therapy (March 2019, 100 mCi); stimulated thyroglobulin was 2.6 ng/mL with negative antibodies and a negative whole-body scan. Subsequent endocrinological follow-up was performed at an external facility.

In May 2023, the patient presented with an anterior neck mass, dysphonia, and dyspnea. Ultrasound and CT confirmed a 4-cm left paratracheal nodule infiltrating the trachea, internal jugular vein, and sternocleidomastoid muscle, and encasing the common carotid artery. Genetic testing via tru-cut biopsy identified BRAF V600E and TERT-promotor (c.1-124C>T; c.1-146C>T) mutations. Given her clinical status and a recent COPD hospitalization, strict active surveillance was initiated, showing stable disease until October 2024. At that time, CT imaging demonstrated locoregional and distant progression: the neck mass reached 6.6 cm with jugular occlusion and infiltration of the trachea, carotid artery, and subclavian vessels, alongside new sternal and bilateral pulmonary metastases.

On December 10, 2024, the patient began lenvatinib at a reduced dose (10 mg qd). Treatment was complicated by weight loss (−8 kg; −16%), lower limb edema and ulcers, palmar-plantar erythrodysesthesia, and hypertension (all CTCAE grade G2). In March 2025, CT showed a mixed response: stable neck and lung disease but new hepatic lesions. Lenvatinib was increased to 14 mg qd without worsening adverse events.

Four weeks later, the patient was admitted for a femoral neck fracture following a fall. Lenvatinib was suspended, but orthopedic treatment was delayed by the onset of Takotsubo syndrome and severe cardiorespiratory failure. Despite intensive care, cardiocirculatory arrest occurred, leading to the patient’s death.

Discussion: This case underscores the difficulty of balancing oncologic goals with iatrogenic risks in elderly, fragile patients. Takotsubo syndrome in patients receiving lenvatinib has been noted in two case reports and may be precipitated by coronary endothelial dysfunction induced by VEGF inhibition. A multidisciplinary approach, including cardio-oncological evaluation, remains fundamental for managing fragile patients.

Abstract citation ID: lvag096.1633

EP1452 - ECE_2760 - Quality of life in Graves’ orbitopathy: a patient-centered perspective

Katarzyna Wojciechowska-Durczyńska[1], Przemysław Śliwka[2], Joanna Hofman[2], Kinga Krawczyk-Rusiecka[1], Renata Stawerska[1] and Arkadiusz Zygmunt[2]

[1]Department of Pediatric and Adult Endcrinology, Medical University of Lodz, Lodz, Poland; [2]Department of Endocrinology and Metabolic Diseases, Polish Mother’s Memerial Hospital Research Institute, Lodz, Poland

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Graves' orbitopathy (GO) is the extrathyroidal manifestation of Graves' disease, characterized by inflammation and remodeling of orbital tissues. In addition to visual manifestations, GO is associated with significant psychosocial consequences that adversely affect patients' quality of life (QoL). Previous studies have demonstrated that both functional visual impairment and altered appearance contribute to reduced QoL. Disease advancement, smoking, age, and sex have been shown to influence clinical course of disease too. Despite the clinical importance of QoL in GO management, correlations between QoL surveys and biochemical, demographic, and treatment-related variables remain insufficiently defined. This study aimed to characterize QoL surveys in patients with GO and to analyse their associations with demographic, clinical, biochemical, and lifestyle factors.

Materials and Methods: Eighty-seven (patients with GO were enrolled. QoL was assessed using the Polish version of the GO-QOL (Graves' Ophthalmopathy Quality of Life) questionnaire, comprising eight physiological and eight psychological questions where higher score equals lower QoL. Clinical evaluation included GO severity and activity, smoking, history of thyroidectomy and radioiodine therapy, and laboratory evaluation (TSH, fT3, fT4, TSH-receptor antibodies, anti-TPO, anti-Tg, CRP, and vitamin D levels). Correlation analyses used Pearson or Spearman methods depending on scale. Predictors were further examined via multivariable linear regression, and group differences (sex, smoking, disease advancement) via non-parametric tests.

Results: Physiological QoL (PhQoL) correlated positively with psychological QoL (PsQoL) ($r = 0.264$; $P = .018$) and summarized QoL surveys ($r = 0.774$; $P < .001$), and was associated with age ($r = 0.329$; $P = .005$), disease advancement ($r = 0.253$; $P = .035$), and smoking ($r = 0.336$; $P = .012$). PsQoL correlated with summarized QoL ($r = 0.815$; $P < .001$) and sex ($r = 0.487$; $P < .001$), being higher in females; weight correlated negatively. Biochemical variables did not significantly correlate with any QoL surveys. Regression models identified smoking and disease advancement as predictors of PhQoL and sex as the independent predictor of PsQoL. Non-parametric analyses showed significant sex differences for PsQoL ($P < .001$) and summarized QoL ($P = .037$) and higher PhQoL among smokers ($P = .013$). Advancing disease was associated with higher PhQoL ($P = .048$) but not PsQoL ($P = .325$).

Conclusions: In patients with GO, impairment of QoL is predominantly determined by demographic and clinical factors rather than by biochemical thyroid function or autoantibody profiles Female sex emerged as the principal determinant of PsQoL, whereas smoking and disease advancement primarily affected PhQoL and overall QoL outcomes. These findings support the routine incorporation of structured QoL assessment into GO management and indicate that patient-reported outcomes may reflect adaptive functional and psychosocial processes in addition to objective disease severity

Abstract citation ID: lvag096.1634

EP1453 - ECE_2038 - Detection of pathogenic variants in cytologically benign thyroid nodules

Vlasta Kuklikova[1,2], Katerina Vyhnalova[1], Olivia Cillikova[1], Marie Rodová[1], Karolina Dobiasovska[1], Karolina Hrckulakova[1], Eliska Vaclavikova[1], Jitka Carkova[1], Barbora Bulanova[1], Josef Vcelak[1], Petra Pačesová[3], Zdenek Novak[3] and Bela Bendlova[1]

[1]Department of Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic; [2]Department of Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic; [3]Department of Clinical Endocrinology, Institute of Endocrinology, Prague, Czech Republic

Background: Molecular genetic analysis, together with sonographic and cytological examination, is an integral part of the care provided to patients with suspicious thyroid nodules (primarily Bethesda III/IV) in the Institute of Endocrinology in Prague. Within the scope of our research, we were interested in the genetic background also in cases of Bethesda II when the nodules were highly suspicious on sonography. The aim of this study was to highlight pathogenic variants in the cytologically benign nodules.

Methods: In total of 876 cytologically benign fine needle aspiration biopsy (FNAB) samples were analyzed. First, DNA for the most common mutation V600E in the *BRAF* gene using allele specific Real Time PCR was analyzed. *BRAF*-positive samples were screened for *TERT* mutations and *BRAF*-negative samples were analyzed for other 12 genes by next generation sequencing (Thyro-ID panel). Thyro-ID-negative samples were subjected to detection of 23 fusion genes including *ALK*, *BRAF*, *GLIS3, NTRK1*, *NTRK3*, *PPARG*, *RET* genes using Real Time PCR. Samples suspected of medullary thyroid carcinoma for *RET* and *RAS* mutations were tested.

Results: A total of 85 pathogenic variants were detected—*BRAF* mutations in 14 patients, *RAS* mutations in 33 patients (11 *HRAS*, 8 *KRAS*, 14 *NRAS*), *RET* mutation in one patient, fusion genes in five patients (three *PAX/PPARG*, one *RET/PTC1*, one *ETV6/NTRK3*) and mutations in other genes in 32 patients. From our cohort of cytologically benign FNAB samples, in 71 patients post-surgical histopathological evaluation has been known. In 17 patients, malignant tumor was histopathologically proven—12 papillary thyroid carcinomas (five with *BRAF* mutation, three with fusion genes) and five follicular thyroid carcinomas (one with *NRAS* mutation, one with fusion gene, one with *TSHR* mutation).

Conclusions: We detected pathogenic variants in 9.7% cytologically benign thyroid nodules including mutations with almost 100% probability of malignancy. This study does not support routine analysis of all cytologically benign samples, but in certain cases of highly sonographically suspicious nodules, it may be beneficial.

Supported by AZV NU21-01-00448 and MH CZ RVO 00023761.

Abstract citation ID: lvag096.1635

EP1454 - ECE_1899 - Biotin: pitfalls beyond the known

Kaushiki Kirty[1,2] and Bilal Jajah[1]

[1]Endocrine and Diabetes, Darlington Memorial Hospital, Darlington, United Kingdom; [2]Darlington United, Darlington Memorial Hospital, United Kingdom

Introduction: We present a patient, referred with deranged and changing thyroid functions, ranging from central hypothyroidism to Grave's thyrotoxicosis over a 10 year period. She was eventually found to be having assay interference from biotin; unusually

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

however,the biotin was being absorbed accidentally from the skin,not oral supplements

Case details: A 42 year old lady was referred to the thyroid clinic with deranged thyroid functions and atrial fibrillation in February 2024.

Her past medical history was significant for being investigated for features suggestive of central hypothyroidism when she was being evaluated for obesity in 2016. At the time she had a normal MRI pituitary and normal pituitary profile.The thyroid functions subsequently normalised without treatment. She was discharged from the thyroid clinic with no very satisfactory explanation for her abnormal thyroid functions.On this episode, apart from the atrial fibrillation, this lady did not have any other features suggestive of thyrotoxicosis.

Her thyroid hormone levels were inconsistent and unusual with a suppressed TSH, elevated FT3 and low FT4 levels. TRAB and TPO antibodies were negative. The thyroid uptake scan showed a mildly elevated uptake. Repeat TFT's showed a similar picture. Assay for antibody interference was negative

Patient was questioned regarding the use of biotin supplements and she denied taking any. However, she subsequently remembered that she gives biotin supplements to her horses, mixing in the powder in their feed with bare hands, a habit of 10 years, when she got the horses. The presumptive diagnosis of biotin interference with assay was made and she was advised to use gloves when mixing biotin supplements. Following this, her thyroid functions gradually normalised and has been normal since then.

Discussion: While it is well known by now that biotin causes assay interference with all the anterior pituitary hormones, we believe this is the first instance where biotin absorption from normal skin caused deranged thyroid functions. Literature review suggests that biotin is well absorbed from both intact and damaged skin reaching levels up to 38% higher than baseline in patients with atopic dermatitis and 12% higher than baseline in patients with intact skin. While not much literature exists measuring blood levels of biotin which cause assay interference, nevertheless based on this case it would seem that skin absorption, either deliberate or accidental, should be kept in mind .This highlights the importance of close and meticulous questionings when faced with inconsistent TFT's with high suspicion of assay interference.

Abstract citation ID: lvag096.1636

EP1455 - ECE_2905 - Impact of strain ratio elastography on risk stratification of thyroid nodules with indeterminate cytology

Letizia Meomartino[1], Marco Zavattaro[2], Gloria Selvatico[1], Sara Garberoglio[1], Mauro MacCario[1], Gianluca Aimaretti[1] and Loredana Pagano[1]

[1]Endocrinology, Diabetology and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [2]Division of Endocrinology, Department of Translational Medicine, University of Eastern Piedmont, Novara, Italy

Background: Thyroid nodules with indeterminate cytology account for approximately 20% of cytological results and are classified as TIR3A (ROM 10%-15%) and TIR3B (ROM 15%-30%) according to the 2014 SIAPEC-IAP system. In this setting, cytology alone does not allow a definitive diagnosis, consequently, many patients are still referred for diagnostic surgery, despite the majority of these nodules proving to be benign on histological examination. This study aimed to evaluate the role of strain ratio elastography (SR), in malignancy risk stratification of indeterminate thyroid nodules and its predictive value within this category of nodules.

Materials and Methods: This retrospective, observational, single-center study consecutively enrolled 167 patients with TIR3A or TIR3B cytology and available definitive histology. For each patient, demographic data, presence of thyroiditis, ultrasound features, elastographic pattern, SR calculated both in comparison with the surrounding thyroid parenchyma (SR_par) and with the prethyroid musculature (SR_mus), and histological outcomes were collected.

Results: The median age was 53 years and most patients were female (77.2%). The majority of nodules were classified as (89.2%), and 61.7% of nodules were benign at histological examination. A high prevalence of thyroiditis was observed (37%).

A significant association emerged between higher SR values and risk of malignancy. The cut-off value identified in our study was 1.55 for both SR_par and SR_mus, showing high diagnostic performance and accuracy (SR_par: sensitivity 87.9%, specificity 92.7%, accuracy 90.8%; SR_mus: sensitivity 81.8%, specificity 85.3%, accuracy 83.9%). Logistic regression analysis showed an approximately six-fold and four-fold increased risk per unit increase, respectively for SR_par and SR_mus. Integration of SR with EU-TIRADS further improved malignancy prediction.

Conclusions: Strain ratio elastography represents a valuable complementary tool for risk stratification of thyroid nodules with indeterminate cytology, especially when combined with EU-TIRADS. Defining an SR cut-off value, both relative to the thyroid parenchyma and to the prethyroid musculature, extends the applicability of the technique even when adjacent thyroid tissue is unavailable. Nevertheless, standardization of image acquisition remains essential to ensure reproducibility, and population-specific cut-offs should be considered.

Abstract citation ID: lvag096.1637

EP1457 - ECE_3005 - Factors associated with recurrence and persistent disease in subacute thyroiditis—a retrospective observational study of 370 patients

Halil Durantas, Neslihan Koray Fedai, Ceren Karaçalık Ünver, Oğulcan Boz, İlknur Ozturk Unsal, Bekir Ucan, Sema Hepşen and Erman Cakal

Endocrinology and Metabolism, University of Health Sciences, Ankara Etlik City Hospital, Ankara, Türkiye

Objective: Although subacute thyroiditis (SAT) is generally a self-limiting disease, recurrence and persistent disease pose significant challenges in clinical management. This study aimed to investigate clinical, laboratory, and treatment-related factors associated with recurrence, persistent disease, and permanent hypothyroidism in patients with SAT.

Materials and Methods: This retrospective study included 370 adult patients diagnosed with SAT who were followed for at least six months after treatment. Patients were treated with nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids (CS).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Recurrence was defined as the reappearance of typical clinical symptoms, inflammatory markers, and ultrasonographic findings after treatment completion. Persistent disease was defined as the absence of clinical and laboratory improvement despite at least six weeks of CS therapy. Permanent hypothyroidism was defined as persistence of the hypothyroid phase for at least six months with a continued requirement for levothyroxine replacement therapy.

Results: Recurrence occurred in 57 patients (16.4%), while persistent disease was identified in 22 patients (6.0%). Recurrence was significantly more frequent in patients treated with CS compared with those receiving NSAIDs (18.4% vs 8.7%, $P = .010$). At diagnosis, patients with recurrence more frequently exhibited unilateral thyroid involvement on ultrasonography (36.8% vs 20.3%, $P = .036$) and were less likely to present with overt biochemical hyperthyroidism (75.4% vs 88.3%, $P = .010$). These patients had higher thyroid-stimulating hormone (TSH) levels and lower free thyroxine (fT4) levels at baseline ($P = .004$ and $P = .005$, respectively). Hyperthyroidism and inflammatory markers were also more pronounced during treatment and at treatment completion (all $P < .001$). In multivariate analysis, lower baseline fT4 levels, unilateral ultrasonographic involvement, and initiation of CS therapy were independently associated with recurrence. ROC analysis demonstrated modest predictive value of baseline TSH and fT4/ULN ratios for recurrence. Persistent disease was characterized by higher baseline TSH levels, lower fT4 levels, longer treatment duration, and higher cumulative CS doses. Permanent hypothyroidism developed in 39 patients (10.5%) and was significantly more common in patients with persistent disease and in those treated with NSAIDs ($P < .001$ for both).

Conclusions: Initial unilateral involvement, milder hyperthyroidism, and CS therapy were associated with recurrence in SAT. Persistent disease and NSAID therapy were associated with permanent hypothyroidism. These findings highlight the heterogeneity of SAT and may facilitate early identification of high-risk patients, enabling closer monitoring and more individualized treatment strategies to optimize long-term outcomes.

Abstract citation ID: lvag096.1638

EP1458 - ECE_3956 - Performance of core needle biopsy following non-diagnostic or indeterminate fine-needle aspiration in thyroid nodules

Paula Sprovera, Bruna Pimentel, Margarida Oliveira, Catarina Gama and Catarina Saraiva
Hospital Egas Moniz, Lisboa, Portugal

Background: Thyroid nodules are increasingly diagnosed, often incidentally. Although most are benign, the possibility of malignancy requires accurate assessment. Fine-needle aspiration (FNA) is the standard first-line diagnostic tool, but 15%-30% of results are inconclusive. Core needle biopsy (CNB) has emerged as a valuable alternative in such cases.

Objective: To assess the diagnostic performance of CNB in thyroid nodules with prior non-diagnostic or indeterminate FNA and its role in reducing unnecessary surgeries.

Methods: We conducted a retrospective study of 126 patients who underwent ultrasound-guided CNB between 2018 and 2023 after inconclusive FNA (Bethesda I or III). CNB results were categorized as non-diagnostic, benign, indeterminate, or malignant. Surgical outcomes and follow-up data were analyzed to evaluate CNB's diagnostic accuracy.

Results: Of the 126 nodules, 63.4% were benign, 2.38% malignant, 26.19% indeterminate, and 7.93% non-diagnostic. CNB was diagnostic in 65.08% of cases. Surgery was performed in 31 patients (24.6%), mostly due to indeterminate or non-diagnostic CNB. Histology confirmed benign disease in 58.06% and malignancy in 32.2% of surgical cases. CNB showed 100% sensitivity, 27.8% specificity, 100% negative predictive value, and 43.5% positive predictive value. No complications were observed.

Conclusions: CNB is a safe, reliable, and effective second-line diagnostic tool in thyroid nodules with inconclusive FNA.

Abstract citation ID: lvag096.1639

EP1459 - ECE_2961 - Unusual metastasis of renal cell carcinoma to thyroid

Eleana Zisimopoulou[1], Georgios Christantoniou[2], Maria Boudina[1], Chrysanthi Balodimou[1], Constantina Philippidou[1], Charalampos Papadopoulos[1], Nektaria Georgiadou[1] and Alexandra Chrisoulidou[1]
[1]*Endocrinology, Theageneio anti-cancer hospital, Thessaloniki, Greece;* [2]*Theageneio Anti-Cancer Hospital, Thessaloniki, Greece*

Renal cell carcinoma (RCC) metastatic to the thyroid gland is a rare entity.

We report two cases of RCC who developed metastatic lesions of the thyroid, discovered after thyroidectomy for nodular thyroid disease.

Two patients are discussed below, a 69-year old female (patient 1) and a 74-year old male (patient 2) (Table 1). In both cases the original RCC was of clear cell type. Pathology tumor stage was pT2a and pT1a respectively, with no angiolymphatic invasion noted.

Both patients had been followed-up for thyroid nodular disease and had been submitted to fine needle aspiration (FNA) of the thyroid nodules (3.7 and 4.4 cm respectively), which later identified as metastases from RCC. Suspicious ultrasonographic characteristics of the metastatic thyroid lesions were undulating outline of the nodule (patient 1) and central calcifications (patient 2). Interestingly, in both cases FNA cytology did not identify malignancy as both FNA results were category II by Bethesda grading system. Patient 1 had no other metastatic lesions in contrast to patient 2, who was already diagnosed with polymetastatic renal cell carcinoma at the time of the thyroidectomy. Both patients underwent, during follow-up, FDG-PET scans with poor metabolic activity in the thyroid.**Conclusions:** The thyroid gland represents an unusual site for metastatic disease in RCC. Thyroid ultrasonography, FNA and FDG-PET can be used for risk stratification and therapeutic decisions. Unfortunately, no specific features exist in the evaluation of thyroid disease in patients with extra-thyroid cancer.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Table 1 Characteristics of the RCC patients with thyroid metastases.

	Age	Sex	Stage	Time of RCC diagnosis	History of thyroid disease	Thyroid Ab's	PET-SUV in thyroid lesions	Thyroid surgery	Size of metastatis
1	69	F	pT2a	2013	TND	(-)	3.6	2017	3.9 cm 0.9 cm PTC
2	74	M	pT1a	2008	TND	(-)	No uptake	2025	4.5 cm

Abbreviations: Ab's, autoantibodies; PET, positron emission tomography; PTC, papillary thyroid cancer; RCC, renal cell carcinoma; TND, nodular disease.

Abstract citation ID: lvag096.1640

EP1460 - ECE_3350 - Calcium gluconate stimulation testing in risk stratification of medullary thyroid carcinoma in patients with basal hypercalcitoninemia: a case series

Alexandra Dulugiac[1], Vlad Radulescu[1,2], Beatrice Cristea[1], Ioana Maria Posea[1], Maria Tudorache[1], Roxana Boanta[1], Dumitru Ioachim[1] and Corin Badiu[1,2]
[1]*Adult Endocrinology, Endocrinology IV, National Institute of Endocrinology "C.I Parhon", Bucharest, Romania;* [2]*Endocrinology, Endocrinology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*

Introduction: Basal hypercalcitoninemia in patients presenting thyroid nodules represents a diagnostic challenge, as elevated calcitonin could be associated with medullary thyroid carcinoma (MTC), C-cell hyperplasia, or benign thyroid disease in addition to other benign extra-thyroid conditions. Calcium gluconate stimulation testing is performed to improve diagnostic accuracy, although optimal cut-off values remain debated.

Objective: The diagnostic value of the calcium gluconate stimulation testing is assessed by correlating the stimulated calcitonin levels with the thyroid pathology of surgical specimen.

Methods: Four patients presenting thyroid nodules and persistent basal hypercalcitoninemia were analyzed in a tertiary endocrine center. A calcium gluconate stimulation test (25 mg/kg intravenously) was performed, and the calcitonin level was measured at baseline and at 2, 5, and 10 minutes post-infusion. Peak stimulated calcitonin levels were correlated with ultrasound findings, surgical indication, and post-thyroidectomy histopathology.

Case descriptions: Case 1: A 53-year-old male, smoker, with multinodular thyroid disease and basal calcitonin ~27 pg/mL showed a stimulated calcitonin of 355 pg/mL at 2 minutes. The histopathologic exam revealed a low-grade medullary thyroid microcarcinoma (pT1a) associated with C-cell hyperplasia, with negative lymph nodes and clear surgical margins.

Case 2: A 57-year-old male with basal calcitonin ~53 pg/mL had a stimulated calcitonin of 423 pg/mL at 2 minutes. Histopathological result confirmed early-stage medullary thyroid carcinoma (pT1a).

Case 3: A 40-year-old female, former smoker, with basal calcitonin ~24 pg/mL, had a stimulated response 806 pg/mL calcitonin at 2 minutes. Histopathology showed diffuse C-cell hyperplasia with multinodular goiter and an incidental papillary microcarcinoma.

Case 4: A 40-year-old female, with multinodular goiter and basal calcitonin ~32 pg/mL, had a stimulated calcitonin of 481 pg/mL, peaking at 2 minutes. Total thyroidectomy showed a benign multinodular goiter, with calcitonin normalizing after the surgery.

Results: All patients showed stimulated calcitonin values >285 pg/mL, with the maximum response observed at 2 minutes after calcium administration, followed by a progressive decline. They were submitted to total thyroidectomy and central compartment neck dissection. Two patients were diagnosed with medullary thyroid carcinoma, one had C-cell hyperplasia, and one had benign multinodular goiter.

Conclusions: Calcium gluconate stimulation testing significantly improves risk stratification in patients with basal hypercalcitoninemia and thyroid nodules. In this series, stimulated calcitonin levels exceeding 285 pg/mL, particularly at 2 minutes, were associated with underlying C-cell pathology, ranging from C-cell hyperplasia to early-stage medullary thyroid carcinoma.

Abstract citation ID: lvag096.1641

EP1462 - ECE_1117 - Thyroid hormone metabolism and cardiac adaptation in aortic stenosis

Iulia Alexandra Pirga[1,2]
[1]*University of Medicine and Pharmacy, Craiova, Romania;* [2]*Medicover, Craiova, Romania*

Background: Aortic stenosis (AS) is characterized by chronic left ventricular pressure overload leading to concentric remodeling, metabolic stress, and progressive functional decline. Beyond structural adaptation, AS induces systemic neurohormonal and metabolic changes, including alterations in thyroid hormone conversion. While thyroid-stimulating hormone (TSH) reflects central regulation, free triiodothyronine (FT3) and the FT3/FT4 ratio more accurately represent peripheral thyroid hormone activity and myocardial metabolic efficiency. These parameters may therefore provide insight into the metabolic phenotype and functional reserve of patients with AS.

Methods: Our cross-sectional study included 71 patients with echocardiographically confirmed AS. Thyroid function parameters (TSH, FT3, and FT4) were analyzed in relation to clinical severity (NYHA functional class), metabolic reserve (hemoglobin), and hemodynamic severity (mean transvalvular gradient). Correlation and multivariable analyses were performed to explore the association between thyroid metabolism and disease burden.

Results: FT3 levels correlated inversely with NYHA class ($\rho = -0.355$, $P = .0047$), suggesting that patients with lower FT3

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

values experienced greater symptomatic limitation and reduced exercise tolerance. The FT3/FT4 ratio showed a similar negative correlation with NYHA class ($\rho = -0.320$, $P = .012$) and a positive correlation with mean transvalvular gradient ($\rho = 0.506$, $P = .016$), remaining an independent predictor after adjustment for age and sex. FT3 also correlated positively with hemoglobin ($\rho = 0.438$, $P = .00052$), indicating that low FT3 levels reflect systemic catabolic and inflammatory stress. TSH showed no significant association with any clinical or echocardiographic parameters.

Conclusions: In AS, reduced peripheral T4-to-T3 conversion reflects impaired metabolic adaptation to chronic cardiac stress rather than primary thyroid dysfunction. The FT3/FT4 ratio can be used as a sensitive biomarker, linking myocardial energetic demand, systemic metabolism and disease severity.

Keywords thyroid hormones, FT3/FT4 ratio, aortic stenosis, low T3 syndrome, deiodinase activity, cardiac metabolism, NYHA functional class

Abstract citation ID: lvag096.1642

EP1463 - ECE_1431 - Association between non-thyroidal illness syndrome and adequacy of dialysis therapy: preliminary results from bicenter observations

Aleksandra Młodożeniec[1], Małgorzata Rodzoń-Norwicz[2,3], Renata Orłowska-Florek[2,4], Krystyna Tęcza[5], Piotr Młodożeniec[6], Krzysztof Gargasz[7] and Agnieszka Gala-Bladzinska[2,4]

[1]Nephrology and Endocrinology with Nuclear Medicine Laboratory and Dialysis Center, Clinic of Internal Medicine, State Hospital 2, Rzeszow; [2]Nephrology and Endocrinology with Nuclear Medicine Laboratory and Dialysis Center, Clinic of Internal Medicine, State Hospital 2, Rzeszów, Poland; [3]Department of Human Physiology, Faculty of Medicine, University of Rzeszów, Rzeszów, Poland; [4]Department of Nephrology and Endocrinology, Faculty of Medicine, University of Rzeszów, Rzeszów, Poland; [5]Department of Nephrology and Dialysis, Dystrict Hospital John Paul II, Kolbuszowa, Poland; [6]ProVital Medical Center, Rzeszów, Poland; [7]Faculty of Medicine, Data Processing Laboratory, Natural and Medical Center for Innovative Research, University of Rzeszów, Rzeszów, Poland

Introduction: Non-thyroidal illness syndrome (NTIS) occurs in patients with severe illnesses, and the exact underlying mechanism remains unknown.[1]. Available studies emphasize the importance of routine screening for thyroid function in patients with end-stage renal disease (ESRD). However, the direct association between NTIS and the adequacy of dialysis therapy has been rarely investigated.

Objective: This study aimed to assess the association between NTIS and the quality of dialysis therapy.

Methods: We examined the prevalence of NTIS in patients with ESRD and its implications on dialysis parameters (Kt/V ratio[2]) from two independent dialysis centers in the Podkarpackie region of Poland. Patients with a history of thyroid or pituitary disease and those taking medications that could interfere with the hypothalamic–pituitary–thyroid axis were excluded. Statistical analyses were performed using STATISTICA version 13.1, with statistical significance set at $P < .05$.

Results: Of the 104 patients undergoing dialysis, 74 met the inclusion criteria and qualified for the study. Among the 74 trial participants, NTIS was identified in 37 (50%). The median age was 65 years and 15 patients (40,5%) were women. This study revealed that patients with NTIS had lower mean Kt/V ratios compared with patients in euthyroid. Preliminary results are presented in Table 1.

Conclusions:

1. NTIS is common in patients with ESRD.
2. The NTIS predicts worse dialysis therapy results in patients with ESRD.

Table 1 Comparison of selected parameters between euthyroid and NTIS groups in patients with ESRD.

Patients with ESRD ($n = 74$)			
Variables	**Euthyroid ($n = 37$)**	**NTIS ($n = 37$)**	***P*-value**
Demographics, *n* (%) or median (min-max)			
Age [year]	68 (18-89)	65 (18-88)	$P = .5^{*}$
Body weight (kg)	77 (38-116)	75 (29-108)	$P = .8^{*}$
Female sex	14 (37,8%)	15 (40,5%)	$P = .8^{\#}$
Laboratory parameters, median (min-max)			
Ca	2,2 (1,6-2,6)	2,1 (1,7-3,1)	$P = .3^{*}$
P	1,7 (0,8-3,7)	2,0 (0,8-5,6)	$P = .4^{*}$
PTH	314,5 (23,7-1606)	359 (35-1773)	$P = .6^{*}$
Kt/V ratio	1,1 (0,7-1,8)	1,0 (0,6-1,4)	$P = .03^{*}$

References

1. Sciacchitano S, Capalbo C, Napoli C, et al. Nonthyroidal illness syndrome: to treat or not to treat? Have we answered the question? A review of metanalyses. *Front Endocrinol (Lausanne)*. 2022;13:850328. https://doi.org/10.3389/fendo.2022.850328.
2. Chen YK, Chu CS, Niu SW, et al. The prognostic value of URR equals that of Kt/V for all-cause mortality in Taiwan after 10-year follow-up. *Sci Rep*. 2023;13(1):8923. https://doi.org/10.1038/s41598-023-35353-8

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1643

EP1464 - ECE_2144 - Quality of life in patients with hyperthyroidism

Zvezdana Jemuovic[1], Sandra Pekic Djurdjevic[1], Dragana Miljic[1], Mirjana Doknic[1], Marko Stojanovic[1], Olga Djajic[2], Ivana Cekic[1], Ivan Jevtic[1], Boris Kurcubic[1], Jelena Bajic[1] and Marina Nikolic Djurovic[1]
[1]*Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Center of Serbia, Belgrade, Serbia;* [2]*General Hospital Uzice, Uzice, Serbia*

Introduction: It has been shown that patients with hyperthyroidism (HT) have a worse quality of life (QoL) compared to the general population, especially in the domains of mental health, vitality and social functioning. After successful treatment, many patients experience an improvement in their quality of life, but some symptoms may last longer, especially those related to mental health.

Aim: To investigate QoL in patients with HT on thyrosupressive therapy

Methods: Case control study with 30 HT patients (mean age 52.37 ± 10.52) on thyrosupressive therapy and 30 euthyroid healthy controls, matched for age, sex and educational level, were included. Measurement of TSH, FT4, anti-TPO antibodies, TSH-receptors antibodies was done. Evaluation of QoL was evaluated by QoL questionnaire—SF36. Mann-Whitney U test was used to compare means between groups.

Results: The duration of the hyperthyroidism in HT group was 16.9 ± 18.6 months. HT patients had lower TSH levels vs control (0.95 ± 1.43 vs 1.93 ± 0.98 mIU/L, $P < .001$) and higher FT4 (20.01 ± 8.46 vs 14.36 ± 2.17 pmol/L, $P = .020$). Patients in HT group reported worse physical functioning, physical role, general health, vitality, social functioning, emotional role and mental health. HT group also reported worse physical health—Dimension A (64.00 ± 18.13 vs 79.87 ± 11.93, $P < .001$), mental health—Dimension B (62.23 ± 17.81 vs 78.20 ± 13.87, $P < .001$) and Total SF35 score (64.73 ± 18.31 vs 81.07 ± 13.38, $P < .001$).

Conclusions: Patients with HT had statistically significantly worse quality of life compared to healthy control. Future studies with larger cohorts and in longer observation periods are needed to further explore quality of life in patients with hyperthyroidism during remission of the disease.

Abstract citation ID: lvag096.1644

EP1465 - ECE_1162 - Adherence to levothyroxine in adult patients with primary hypothyroidism: a cross-sectional study

Rubel Lafaurie-Noriega[1], Maria Roa-Parra[1], Miguel Ochoa-Vera[1], Juan Sarmiento-Ramón[1,2] and Edwin Wandurraga-Sánchez[2]
[1]*Universidad Autónoma de Bucaramanga—UNAB, Bucaramanga, Colombia;* [2]*Bucaramanga, Colombia*

Introduction: Primary hypothyroidism is the most common form of thyroid hormone deficiency and is more prevalent in women. The treatment of choice is thyroid hormone replacement with levothyroxine; however, a high proportion of patients do not achieve adequate control, and adherence to medication is an important factor in achieving this.

Objective: To evaluate pharmacological adherence to levothyroxine and the factors associated with it, in patients with primary hypothyroidism treated at an endocrinology center in Colombia.

Methods: Cross-sectional study of adults (≥18 years) with primary hypothyroidism undergoing treatment for ≥3 months, attending an endocrinology clinic between December 2024 and July 2025. Patients who agreed to participate signed informed consent and completed a specific data collection form, in addition to the 8-item Morisky–Green scale for levothyroxine adherence. Sociodemographic and clinical variables were assessed; Fisher's exact test, the Mann–Whitney U test, and Pearson's chi-squared test were applied. Additionally, binary logistic regression was used to calculate crude odds ratios (OR). The analysis was performed using STATA/SE v14.0. This study was approved by an Ethics Committee.

Results: 318 patients were included, with a median age of 60 years (IQR 46-73) and a higher proportion of women (82.08%). Most lived in urban areas (94.03%), and the most frequent type of social security affiliation was payroll-based contributory health insurance (78.62%). Regarding levothyroxine adherence, 52.20% showed high adherence, 25.79% moderate adherence, and 22.01% low adherence, with no significant differences according to sex. The only two variables associated with not having high adherence to levothyroxine were: government-subsidized health insurance (OR = 3.96; 95% CI 2.00-7.83; $P < .000$) and generic brands of levothyroxine compared to commercial brands (OR = 2.24; 95% CI 1.42-3.54; $P = .001$). No statistically significant differences were found in adherence for the following variables: age, educational level, marital status, socioeconomic status, daily dose of levothyroxine, presence of comorbidities, use of other medications or polypharmacy (≥ 5 medications).

Conclusions: In a predominantly female urban sample, more than half of the patients with primary hypothyroidism showed high adherence to levothyroxine, with type of health insurance and medication brand being associated factors. It is recommended to strengthen strategies aimed at improving adherence in the low- and moderate-adherence groups, as this factor directly impacts disease control.

Abstract citation ID: lvag096.1645

EP1466 - ECE_1293 - The effect of levothyroxine on thyroid function in relation to daytime sleepiness

Ivana Škrlec[1], Snježana Džijan[2,3], Marko Bebek[4], Nika Srb[5], Đorđe Pojatić[1,6], Zrinka Biloglav[7,8], Matej Burčak[1] and Darko Katalinić[1]
[1]*Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia;* [2]*Osijek, Croatia;* [3]*DNA Laboratory, Genos Ltd., Zagreb, Croatia;* [4]*UPMC Hillman Cancer Center, Zabok, Croatia;* [5]*School of Medicine, University J. J. Strossmayer Osijek, Osijek, Croatia;* [6]*Department of Internal Medicine, General County Hospital Vinkovci, Vinkovci, Croatia;* [7]*Department of Medical Statistics, Epidemiology and Medical Informatics, School of Public Health Andrija Štampar, Zagreb, Croatia;* [8]*School of Medicine, University of Zagreb, Zagreb, Croatia*

Introduction: Daytime sleepiness is common in patients with Hashimoto's thyroiditis (HT) and may reflect both thyroid

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

dysfunction and the effects of levothyroxine (LT4) replacement therapy. Data on the relationship between daytime sleepiness and biochemical markers of thyroid function during LT4 therapy are limited. This study aimed to examine the effect of LT4 replacement therapy on thyroid function biomarkers in HT patients, stratified by daytime sleepiness.

Methods: The study included 115 patients with clinically, ultrasound, and laboratory-confirmed HT treated at a single center. Daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS), and patients were categorized as having normal (ESS $\leq$ 10) or increased (ESS $\geq$ 11) daytime sleepiness. Laboratory parameters analyzed included total cholesterol, triglycerides, HDL, LDL, iron, vitamin D, TPOAb, TgAb, TSH, fT3, and fT4.

Results: The median age was 41 years (IQR 33-50), and women comprised 92.2% of the sample ($n = 106$). LT4 therapy was used by 61.7% of patients, and 28.7% reported increased daytime sleepiness. The group without LT4 therapy included 30 patients with normal ESS and 14 with increased ESS, while the group on LT4 therapy included 52 patients with normal ESS and 19 with increased ESS. Among patients with normal daytime sleepiness, those receiving LT4 had significantly higher TSH concentrations than those not receiving LT4 (12.15 [IQR 8.75-17.15] vs 8.65 [IQR 6.48-13.48] mU/L; $Z = -2.393$; $P = .017$). In the same group, patients not receiving LT4 therapy had significantly higher fT3 concentrations than those receiving LT4 therapy (5.65 [IQR 4.90-6.15] vs 5.10 [IQR 4.40-5.68] pmol/L; $Z = -2.265$; $P = .023$). Among patients with increased daytime sleepiness, no statistically significant differences in the analyzed biochemical analytes were observed with respect to LT4 therapy.

Conclusions: In patients with Hashimoto's thyroiditis and normal daytime sleepiness, LT4 therapy is associated with higher TSH and lower fT3, while in those with increased daytime sleepiness, no such differences are observed. These results suggest a complex relationship among daytime sleepiness, thyroid function, and the effects of LT4 therapy, highlighting the need for individualized monitoring and treatment. These findings can be used to generate hypotheses for larger, longitudinal studies that could confirm these observations.

Grant No: IP3-FDMZ-2025

Abstract citation ID: lvag096.1646

EP1467 - ECE_2122 - Microwave ablation as an alternative to radioiodine therapy for hyperthyroidism caused by an autonomously functioning thyroid nodule: clinical case

Aiste Stonyte[1], Ruta Dubeikaite[2], Aurimas Maclonis[2] and Raimonda Klimaite[3]

[1]Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Department of Radiology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania; [3]Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

Introduction: Microwave ablation (MWA) is advantageous for patients with autonomously functioning thyroid nodules (AFTNs) who are poor surgical candidates or wish to avoid surgery and radioiodine therapy (RAI). The procedure is well tolerated, with few major complications and mostly preserves thyroid function. In this young female with an AFTN, MWA highlights the evolving role of image-guided thermal ablation as a safe and effective therapy in selected patients and discusses its potential in the contemporary AFTN management.

Case report: A 19-year-old female patient was referred due to weight loss, palpitations, and sweating. Since 2022, she had been monitored for a thyroid nodule. In 2022, FNA of the left thyroid lobe nodule showed cystic degeneration. Thyroid scintigraphy with 99mTc demonstrated the presence of an autonomous adenoma.

Laboratory tests (2025-01-13): TSH: 0.20 (0.4-3.6 mU/L), FT4: 10.27 (7.87-20.3 pmol/L), FT3: 4.54 (3.34-5.14 pmol/L).

Thyroid ultrasound (2025-01-13): in the left lobe, a mixed nodule with septations measuring $3.9 \times 2.5 \times 3.8$ cm (volume of ~19.3 mL). Nodular thyroid, EU-TIRADS 3.

As an autonomous thyroid adenoma causing subclinical thyrotoxicosis was diagnosed, treatment was initiated. The patient was unable to comply with radiation safety requirements following radioiodine therapy. Therefore, MWA of the left thyroid lobe nodule was chosen.

MWA (2025-03-03): Under ultrasound guidance, an 18G MWA antenna ablated the left thyroid lobe nodule at 15W for 42 minutes using the "fluid-motion" technique.

Thyroid ultrasound post-MWA, follow-up: I (2025-03-04): a broad, heterogeneous post-ablation zone is seen with peripheral vascularity and fragmented vascularity at the lower pole.

II (2025-03-18): mixed nodule, markedly devascularized, measuring $3.8 \times 2.0 \times 2.9$ cm.

III (2025-06-20): The nodule decreased in size to $2.65 \times 1.49 \times 2.05$ cm. No mass is visible in the neck. The nodule is completely devascularized.

IV (2025-12-29): a nodule has decreased in size to $2.53 \times 1.43 \times 1.74$ cm (volume ~3.3 mL). The nodule is completely devascularized.

Laboratory follow-up: The thyroid hormone levels normalized after MWA. Thiamasole were discontinued.

Conclusions: MWA was an effective alternative to RAI in this 19-year-old patient with a autonomic thyroid adenoma, achieving significant nodule reduction, devascularization, and normalization of thyroid hormone levels. This case highlights MWA as a viable option for AFTN, particularly in patients ineligible for RAI and underscores the need for further studies to evaluate long-term outcomes.

Abstract citation ID: lvag096.1647

EP1468 - ECE_2504 - Hidden in plain sight: rising encounters of thyrotoxic periodic paralysis

Zachary Pierrepont[1] and Brian Lee[2]

[1]University Hospital Birmingham NHS Trust, Birmingham, United Kingdom; [2]Sandwell & West Birmingham Hospitals NHS Trust, Birmingham, United Kingdom

Background: Thyrotoxic periodic paralysis (TPP) is a rare endocrine emergency presenting with acute flaccid weakness and hypokalaemia in the setting of thyrotoxicosis. Misdiagnosis as a neurological disorder is common. We report a recent case of TPP and compare it with a previous case two years earlier in the Acute Medical Unit of the same NHS Trust.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Case Presentation: Current case: A 41-year-old Chinese man presented with sudden bilateral lower-limb weakness (power 2/5), initially treated as a stroke. Serum potassium was 2.9 mmol/L. Thyroid tests showed thyrotoxicosis. MRI spine was normal. Weakness fully resolved after potassium replacement, and antithyroid therapy was started.

In comparison, a previous 27-year-old ethnic Chinese male, had presented two years earlier with more profound paralysis (power 1/5), severe hypokalaemia (1.5 mmol/L), and ECG features of hypokalaemia. He had marked thyrotoxicosis required critical care and antithyroid therapy and radioactive iodine treatment following recovery.

Discussion: These cases demonstrate the variable severity and heterogeneous thyroid aetiology of TPP. Although uncommon, the occurrence of two cases within two years in one Trust highlights the need for greater awareness—especially given increasing international migration from regions where TPP is more prevalent.

Conclusions: In any patient presenting with acute limb weakness and hypokalaemia, TPP should be considered. We recommend urgent thyroid function testing as a routine add-on in such cases. Earlier recognition in acute settings can prevent delays in treatment and reduce morbidity.

Table 1 Comparison of two TPP cases in one NHS trust.

Feature	Case 1	Case 2 (This Report)
Initial Presentation	Sudden bilateral weakness (1/5), Guillain-Barré syndrome/spine initially suspected	Sudden bilateral weakness (2/5), stroke alert
Potassium	1.5 mmol/L	2.9 mmol/L
ECG	U waves, prolonged QTc	Normal
Thyroid function Test on admission	FT4 48 (9-20 pmol/L)	FT4 19.2
	FT3 28.4 (2.4-6.0 pmol/L)	FT3 7.2
	TSH <0.01 (0.35-4.94 miu/L)	TSH <0.008
Thyroid Aetiology	Graves' disease	Toxic nodular goitre
Thyroid Antibodies	TSH-R Ab positive	TSH-R negative
	TPO positive	TPO positive
Thyroid Ultrasound	No nodules	U2 nodules
Management	IV Potassium, antithyroid therapy, critical care	IV Potassium, antithyroid therapy
Definitive Treatment	Radioactive iodine	Planned radioactive iodine

Reference

1. Baranskaya A, Zhang Y, Lee B. Thyrotoxic periodic paralysis: a case report with patient perspective. *Acute Medicine*. 2024;23(2):91-94. https://doi.org/10.52964/AMJA.0981

Abstract citation ID: lvag096.1648

EP1470 - ECE_1560 - Late onset of slipped upper femoral epiphysis in adult as the initial presentation of undiagnosed primary hypothyroidism

Sushma Burri and Shemitha Rafique
Tunbridgewells Hospital, Tunbridgewells, United Kingdom

Background: Hypothyroidism in adults is typically characterized by symptoms such as fatigue, cold sensitivity, weight gain, and constipation. However, acquired hypothyroidism in children and adolescents can disrupt growth and development, leading to long-term complications if left undiagnosed. The condition can significantly affect height and bone maturation until puberty.

Case History: A 20-year-old male presented to the emergency department with a six-week history of worsening left hip pain. The patient, who had been highly active in sports, reported difficulty participating in activities since the age of 15. Hip pain began at 17. Initial X-ray of the left hip revealed a diagnosis of Slipped Upper Femoral Epiphysis (SUFE), a condition typically seen in boys aged 11-17 years, around puberty.

The patient had been born full-term with no significant childhood illnesses. His height was within normal limits until age 14, after which growth significantly slowed. His mid-parental height is 5′10″, and his brother is 5′9″. The patient also noted difficulty losing weight and feeling excessively cold.

Physical Examination: The patient had a puffy face, short neck, a slightly enlarged tongue (but able to close the mouth), and small hands. A thyroid examination was normal, but delayed relaxation of the ankle jerk was noted.

Investigations

- Blood Tests:
  - TSH: >100 mU/L
  - Free T4: <3.0 pmol/L
  - Cortisol: 452 nmol/L
  - TPO antibodies: 230 IU/mL
- X-ray (Hand and Wrist for Bone Age):
  - Chronological age: 20 years, 5 months
  - Bone age: Corresponds to a male skeletal age of approximately 16 years (based on the Greulich and Pyle method).

Diagnosis: Primary hypothyroidism with delayed skeletal maturation.

Management: The patient was started on Levothyroxine 200 mcg prior to surgery. He subsequently underwent left hip surgery (Left Hip Slipped Upper Femoral Epiphysis, cannulated screw pinning) when his Free T4 level had increased to >6 pmol/L. There were no complications in anaesthesia or surgery when operated with a FT4 of 6. His Levothyroxine dose was reduced to 100 mcg following surgery. He was discharged with a follow-up plan in endocrine Clinic.

Abstract citation ID: lvag096.1649

EP1473 - ECE_3737 - The relationship between iron metabolism indicators and thyroid function in adolescents

Marianna Yuskiv and Alina Urbanovych
State Non-Profit Enterprise «Danylo Halytsky Lviv National Medical University», Lviv, Ukraine

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Thyroid dysfunction may be accompanied by changes in iron metabolism, in particular, the levels of ferritin and hepcidin, a key regulator of its homeostasis. At the same time, the relationship between iron metabolism indicators and thyroid hormones in adolescents remains insufficiently studied, which determines the relevance of this research. Therefore, the aim of our research was to assess the correlations between iron metabolism markers and thyroid function indicators in adolescents.

Materials and Methods: The study involved 28 adolescents with established thyroid dysfunction. Participants were divided into 2 groups depending on the existing thyroid dysfunction: group 1—hypothyroidism on the background of autoimmune thyroiditis ($n = 16$, 57.14%, median age 14 [11.8; 15.3] years) and group 2—Graves' disease, thyrotoxicosis ($n = 12$, 42.86%, median age 12 [10.8; 15.3] years). All patients underwent determination of iron, hepcidin and ferritin levels.

Results: In adolescents with established thyroid dysfunction ($n = 28$), the median hepcidin level was 182.8 [139.5; 243.6] ng/mL (range: 91.09-394.68 ng/mL). Elevated hepcidin levels were found in 21.43% (95% CI: 8.51-38.22%) of children. The frequency of elevated hepcidin was significantly higher in children in group 2 compared to group 1—41.67% (16.54-69.40%) vs 6.25% (0.01-22.79%), $P = .02$. Reduced ferritin levels, as a marker of iron stores, were found in 42.86% (95% CI: 25.43-61.26%) of children; the median value was 14.5 [8.2; 25.8] ng/mL (min.–max.: 3.79-48.86 ng/mL). The median serum iron level in adolescents with thyroid dysfunction was 12.5 [5.8; 26.3] μmol/L (2.0-53.0 μmol/L) and in 64.29% (45.97-80.66%) of cases it deviated from the norm: in 39.29% (22.33-57.69%) it was reduced, in 25.00% (11.02-42.37%) it was increased. Iron below the norm was more often found in children of group 2—58.33% (30.60-83.46%), while elevated iron levels prevailed in group 1—37.50% (16.19-61.75%).

Conclusions: Our research demonstrated that adolescents with thyroid dysfunction had impaired iron metabolism, manifested by a decrease in ferritin in almost half of the examined and deviations in serum iron levels in most children. Elevated hepcidin levels are more often observed in children of group 2 (Graves' disease, thyrotoxicosis) and are associated with a reduced serum iron level. The identified relationships indicate the potential influence of iron metabolism regulators on thyroid function. The obtained data create the basis for further studies of the mechanisms of interaction of iron and thyroid hormones in adolescence.

Abstract citation ID: lvag096.1650

EP1474 - ECE_3620 - Epidemiology and risk factors of hearing loss in thyroid eye disease (TED)

Jason Brant[1], Vinaya Manchaiah[2], Junjie MA[3], Juan Ayala-Haedo[3], Patricia Franco[3] and Haridarshan Patel[3]
[1]*University of Wisconsin School of Medicine and Public Health, Madison, United States;* [2]*University of Colorado School of Medicine, Aurora, United States;* [3]*Amgen Inc., Thousand Oaks, United States*

Introduction: Hearing loss has not been fully evaluated in large population-based cohorts, particularly in patients with thyroid eye disease (TED). Understanding the epidemiology of hearing loss in this population is crucial for optimizing patient management and reducing the disease burden. Here we aim to describe the epidemiology and risk factors of hearing loss in patients with TED, Graves' disease, and the general population.

Methods: A retrospective cohort study using a large US claims database (2014-2019) estimated the age- and gender-adjusted cumulative incidence, incidence rates (per 10 000 person-years), and prevalence of hearing loss. Multivariable Cox regression assessed the association of hearing loss with TED (reference: general population). Machine learning methodology was used to identify predictors of hearing loss.

Results: Cohorts included 38 723 patients in TED, 171 831 in Graves' disease, and >20 million in the general population. Hearing loss was high in TED (cumulative incidence: 2.8%; incidence rate: 142.2; prevalence: 4.6%), followed by Graves' disease (cumulative incidence: 2.0%; incidence rate: 92.0; prevalence: 3.0%), and the general population (cumulative incidence: 1.6%; incidence rate: 67.6; prevalence: 2.2%). The adjusted hazard ratio for hearing loss with TED was 1.6 (95% CI: 1.5, 1.7). Top predictors included age, gender, tinnitus, dyslipidemia, and ototoxic drug use (macrolide and NSAIDs).

Conclusions: TED was associated with a significantly higher risk of hearing loss than the general population.

Abstract citation ID: lvag096.1651

EP1476 - ECE_2864 - From somatic mutation detection to the identification of potentially pathogenic germline variants in patients with radioiodine-refractory differentiated thyroid carcinoma (RAIR-DTC).

Olga Karapanou[1], Evmorfia Tzagkaraki[2], Emmanouela Linardaki[2], Georgios Kyriakopoulos[3], Grigoris Effraimidis[4,5], Marina Michalaki[6], Constantine Stratakis[2,7,8] and Katerina Saltiki[9]
[1]*Endocrine Department, 401 General Military Hospital of Athens, Athens, Greece;* [2]*Institute of Molecular Biology and Biotechnology of the Foundation for Research and Technology Hellas (IMBB-FORTH), Heraklion, Greece;* [3]*Department of Pathology, Evangelismos Hospital, Department of Biological Chemistry, Medical School, National and Kapodistrian University of Athens, Athens, Greece;* [4]*Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece;* [5]*Department of Endocrinology and Metabolic Diseases University General Hospital of Larissa, Larissa, Greece;* [6]*Division of Endocrinology-Department of Internal Medicine, School of Health Sciences, University of Patras, Patras, Greece;* [7]*Pediatrics, University of Athens Medical School, Athens, Greece;* [8]*Hospital for Endocrine Surgery Research Center, HCA Florida Healthcare, HCA Healthcare Research Institute, Tampa, FL, United States;* [9]*Endocrine Unit, Department of Clinical Therapeutics, National and Kapodistrian University, Athens, Greece*

Introduction: Certain detectable variants (pathogenic/likely pathogenic) in cancer predisposition genes, identified with a variant allele frequency (VAF) >40%, are considered potentially of germline origin and are reported in approximately 3%-17% of cases.

Methods: Comprehensive genomic tumor profiling was performed on tumor tissue sections (FFPEs Formalin-Fixed Paraffin-Embedded) from 35/42 patients with radioiodine-refractory

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

differentiated thyroid carcinoma (RAIR-DTC) within the Hellenic Network of Molecular Oncology (EDIMO). Next-Generation Sequencing (NGS) using Ion AmpliSeq technology was applied for the detection of oncogenic/potentially oncogenic single-nucleotide variants (SNVs) and insertions/deletions (Indels) across >500 genes, as well as clinically significant copy number variants (CNVs) involving large genomic regions.

Results: Variants with VAF > 40%, compatible with a potential germline origin, were identified in 21/35 patients (60%). Among these, 6 metastatic patients harboured variants in cancer predisposition genes including: *TERT* (44.34-53.42%, *N* = 4: 1 male, 3 females, of whom one with ovarian cancer and a concomitant *RAD51D* variant (44%) and one with both breast and ovarian cancer); *TSHR* (42.7%, *N* = 1); *ATM* (50.2%, *N* = 1); co-occurrence of *APC* (49.15%) and *TP53* (55.5%) in one patient. In 15/21 germline-origin variants with primarily pharmacogenomic relevance were identified (*DPYD*, *NQO1*, *CYP2D6*, VAF:42%-99%). Additionally, potentially clinically significant CNVs were detected in 6 patients (5 metastatic), involving the following genes: *CHEK2* (*N* = 2), *BRCA2* (*N* = 2), *RAD54L* (*N* = 1), *ATM* (*N* = 2), and *CHEK1* (*N* = 2).

Conclusions: NGS-based comprehensive genomic profiling of aggressive RAIR-DTC patients revealed a high prevalence of variants suggestive of germline origin in cancer predisposition genes. Confirmation of these variants in peripheral blood DNA is recommended (using Sanger sequencing for SNVs/Indels and MLPA (Multiplex Ligation-dependent Probe Amplification) for CNVs) to establish their somatic or germline origin.

Subsequent cascade screening within families enables targeted testing of relatives and individualized genetic counselling regarding the risk of additional malignancies beyond thyroid cancer. Identification of germline variants may guide surveillance strategies for early cancer detection and stratification of targeted therapeutic approaches.

Abstract citation ID: lvag096.1652

EP1478 - ECE_1860 - Potential use of predictive molecular techniques in thyroid nodules with indeterminate cytology

Selena Rodriguez Fernandez, Kevin David Díaz Gorrín, Javier Panizo Fra, Paula Pérez, Óliver Quintero Rodríguez, Ana Paola Leon Ocando, Patricia Cabrera García, Itziar Aznar Ondoño, MacArena Sánchez-Gallego Alonso and Juan Ignacio Márquez De La Rosa
Endocrinology and Nutrition, Hospital Universitario de Canarias, San Cristóbal de La Laguna, Spain

Introduction: Fine-needle aspiration biopsy (FNAB) is the diagnostic method of choice for assessing malignancy risk in thyroid nodules. The Bethesda System is the standard for cytological classification. Indeterminate categories (III and IV) represent a diagnostic challenge. In recent years, molecular testing (ThyroidPrint® or mir-THYpe®Full) has emerged as a tool to improve risk stratification in indeterminate nodules and potentially reduce unnecessary surgeries.

Objective: To evaluate the management of Bethesda III and IV nodules and the potential impact of molecular testing in avoiding unnecessary surgical procedures.

Materials and Methods: An observational, analytical, retrospective study including 87 patients with thyroid nodule cytology classified as Bethesda I, III, or IV between January 2023 and December 2024 at the University Hospital of the Canary Islands.

Results: Cytological samples from 87 patients were analyzed: 2 Bethesda I, 59 Bethesda III, and 26 Bethesda IV. A second FNAB was performed in 59 patients, yielding: 2 Bethesda I, 15 Bethesda II, 17 Bethesda III, 23 Bethesda IV, 1 Bethesda V, and 1 Bethesda VI.

Therapeutic approach: Hemithyroidectomy in 31.6%, total thyroidectomy in 24.1%, pending surgery in 3.8%, ultrasound follow-up in 32.9%, and surgical reintervention for differentiated thyroid cancer in 1.3%. Overall, 60.8% underwent surgery and 39.2% were managed conservatively. Among 25 hemithyroidectomies, 2 (8%) were malignant. Among 19 total thyroidectomies, 4 (21.1%) were malignant. Of the 17 Bethesda III nodules, 7 were surgically treated, all benign. Of the 23 Bethesda IV nodules, 18 were surgically treated, with 2 malignant outcomes.

Conclusions: Among 45 non-diagnostic or suspicious FNABs, 7 were malignant (14%). Seventy-six percent of surgeries resulted in benign pathology, suggesting that 23 hemithyroidectomies and 15 total thyroidectomies could have been avoided (cost €3500-7000 per patient). With 40 candidates for molecular testing (cost €34 400-60 000), the potential savings would be approximately €200 000 over two years. These findings highlight the need to incorporate predictive molecular techniques such as ThyroidPrint® or Mir-THYpe® in Bethesda III and IV nodules.

Abstract citation ID: lvag096.1653

EP1479 - ECE_1543 - Thyroid hormone treatment and breast cancer risk in women: a systematic review and meta-analysis of observational studies

Stylianos Kopanos[1], Jasper Feldkamp[2], Johanna Tyssen[1], Xinjun Li[3], Kristina Sundquist[4], Carolina Pape-Köhler[5], Marc Binnebösel[6], Annika Hoyer[7], Per Wändell[8] and Joachim Feldkamp[1]
[1]Medical School and University Medical Center East Westphalia-Lippe, Academic Department of General Internal Medicine, Endocrinology, Diabetes and Infectiology, Bielefeld University, Bielefeld, Germany; [2]Division of Hematology, Oncology, and Cancer Immunology, Humboldt-Universität zu Berlin and Berlin Institute of Health, Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Berlin, Germany; [3]Center for Primary Health Care Research, Lund University, Malmö, Sweden; [4]Skåne University Hospital, University Clinic Primary Care, Malmö, Sweden; [5]Klinikum Bielefeld—Rosenhöhe, Bariatric Clinic, Bielefeld, Germany; [6]Medical School and University Medical Center East Westphalia-Lippe, Klinikum Bielefeld, Academic Department of Surgery, Bielefeld, Germany; [7]Biostatistics and Medical Biometry, Medical School OWL, Bielefeld University, Bielefeld, Germany; [8]Division of Family Medicine and Primary Care, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden

Objective: Thyroid hormone treatment is the standard therapy for hypothyroidism, particularly in women. Concerns have been raised that exogenous thyroid hormone use may increase breast cancer risk, but evidence remains inconclusive. This study aimed to systematically review and synthesize observational evidence on the association between thyroid hormone treatment and breast cancer risk in women.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Design: We conducted a systematic review and meta-analysis of observational studies.

Methods: MEDLINE, EMBASE, and Web of Science were searched from January 1976 to February 2025. Eligible studies assessed breast cancer incidence in adult women receiving thyroid hormone treatment versus non-users. Pooled odds ratios (ORs) and hazard ratios (HRs) were calculated using meta-analytic models. Heterogeneity, publication bias, and certainty of evidence were assessed. PROSPERO ID: CRD42022348966.

Results: Four case-control studies including 221 254 women receiving thyroid hormone treatment and 4 385 666 controls were included. In the primary random-effects meta-analysis, thyroid hormone treatment was associated with an increased risk of breast cancer (OR 1.43, 95% CI 1.07-1.90; $I^2 = 94.3\%$). A secondary meta-analysis of five cohort studies reporting hazard ratios showed a pooled HR of 1.25 (95% CI 1.08-1.44; $I^2 = 82\%$). Funnel plots and Egger's test ($P = .054$) suggested no strong publication bias. The certainty of evidence was rated as moderate due to heterogeneity.

Conclusions: Thyroid hormone treatment is associated with a modest but statistically significant increase in breast cancer risk in women. While causality cannot be established, these findings underscore the need for careful risk–benefit evaluation, particularly in women with other breast cancer risk factors.

Abstract citation ID: lvag096.1654

EP1480 - ECE_1613 - Diagnostic performance of ACR TI-RADS in cytologically indeterminate thyroid nodules: a multicenter retrospective study

José Vicente Gil Boix[1,2], Javier Bodoque-Cubas[3], Meritxell Viñes Raczkowski[4], Iñaki Argüelles Jiménez[5], Francisco Javier Maravall Royo[1,2], Virginia Patricia Morillo Maclas[2,6], Santiago Tofé Povedano[5,7] and Agustín Ángel Merchante Alfaro[1,2]

[1]Endocrinology and Nutrition, Hospital General de Castellón, Castellón de la Plana, Spain; [2]Universidad Jaume I, Castellón de la Plana, Spain; [3]Endocrinology and Nutrition, Hospital De Tortosa Verge De La Cinta, Tortosa, Spain; [4]Endocrinology and Nutrition, Hospital Comarcal de Inca, Inca, Spain; [5]Endocrinology and Nutrition, Hospital Universitario Son Espases, Palma, Spain; [6]Hospital Clínico Universitario de Valencia, Valencia, Spain; [7]Universitat de les Illes Balears, Palma, Spain

Introduction: Cytologically indeterminate thyroid nodules (Bethesda III-IV) represent a diagnostic challenge and often lead to surgery despite a relatively low malignancy rate. The usefulness of ultrasound risk stratification systems such as ACR TI-RADS in this subgroup remains controversial.

Objective: To evaluate the diagnostic performance of ACR TI-RADS classification and individual ultrasound features for predicting malignancy in Bethesda III-IV thyroid nodules.

Methods: We performed a multicenter retrospective study including 179 patients with Bethesda III-IV thyroid nodules who underwent surgery. Nodules were classified according to ACR TI-RADS by experienced investigators. Final histopathology was used as the reference standard. Diagnostic performance was evaluated for individual TI-RADS categories and for grouped cutoffs (TR4-5 vs TR1-3 and TR5 vs TR1-4).

Results: Of the 179 nodules, 60 (33.5%) were malignant. Malignancy rates increased across TI-RADS categories, reaching 62.5% in TR5 nodules (Table 1).

Table 1 ACR TI-RADS risk of malignancy.

	Malignancy ($n = 60$)	Benign ($n = 119$)	ROM
TR1	1 (1.7)	3 (2.5)	NE
TR2	1 (1.7)	2 (1.7)	NE
TR3	14 (23.3)	45 (37.8)	23.73%
TR4	29 (48.3)	60 (50.4)	32.58%
TR5	15 (25.0)	9 (7.6)	62.50%

Abbreviations: NE, Not estimable ($N < 10$); NPV, Negative Predictive Value; PPV, Positive Predictive Value; ROM, Risk Of Malignancy.

When TR4-5 was considered suspicious for malignancy, ACR TI-RADS demonstrated high sensitivity but limited specificity, with a positive predictive value of 38.9% and a negative predictive value of 75.8%. In contrast, using TR5 as the sole cutoff markedly increased specificity and positive predictive value, at expense of sensitivity (Table 2).

Table 2 Diagnostic performance of ACR TI-RADS using different malignancy cutoffs in Bethesda III-IV nodules.

TI-RADS cutoff	Sensitivity %	Specificity %	PPV %	NPV %
TR4-5 vs TR1-3	73.3 (62.1-84.5)	42.0 (33.2-50.8)	38.9 (29.9-47.9)	75.8 (65.6-85.9)
TR5 vs TR1-4	25.0 (14.0-36.0)	92.4 (87.7-97.1)	62.5 (43.3-81.7)	71.0 (63.9-78.1)

Data in brackets represent 95% confidence intervals.

Among individual ultrasound features, irregular or lobulated margins, taller-than-wide shape, and punctate echogenic foci were significantly associated with malignancy ($P < .05$).

Conclusions: In Bethesda III-IV thyroid nodules, ACR TI-RADS shows a pronounced trade-off between sensitivity and specificity depending on the selected cutoff. TR4-5 prioritizes sensitivity and captures most malignant nodules, whereas TR5 identifies a subgroup with high certainty of malignancy. However, the overlapping malignancy risk across categories suggests that ACR TI-RADS alone is insufficient for clinical decision-making, highlighting the need for complementary diagnostic approaches.

Abstract citation ID: lvag096.1655

EP1481 - ECE_2804 - Clinical significance of anti-thyroglobulin antibody dynamics in differentiated thyroid cancer

Merve Şenay Özçalık, Deniz Türküm Atikcan, Ece Gül Köse Hamidi, Ozlem Turhan Iyidir, Asli Nar and Neslihan Başçıl Tütüncü

Endocrinology and Metabolism, Baskent University, Ankara, Türkiye

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: The prognostic value of baseline anti-thyroglobulin antibodies (anti-Tg) in differentiated thyroid cancer (DTC) remains controversial. While anti-Tg interferes with thyroglobulin measurements, its dynamic behavior during follow-up may provide clinically relevant prognostic information beyond baseline levels.

Methods: We retrospectively evaluated 62 patients with DTC diagnosed between 2000 and 2024 who had positive baseline anti-Tg levels. The mean age was 47.6 ± 14.1 years, and 77.4% were female. Patients were classified according to histopathological subtype and ATA risk stratification. Anti-Tg dynamics, including negativization at 24 months, radioactive iodine (RAI) treatment, and recurrence outcomes were analyzed. Associations between baseline anti-Tg levels, anti-Tg negativization, and long-term recurrence were assessed.

Results: Classic papillary thyroid carcinoma was the most frequent histopathological subtype (58.1%). According to ATA risk classification, 35.5% of patients were low risk, 17.7% low–intermediate risk, 25.8% intermediate–high risk, and 21.0% high risk. RAI therapy was administered to 82.3% of patients. At 24 months, anti-Tg negativization was achieved in 77.4% of cases. Lower baseline anti-Tg levels were significantly associated with anti-Tg negativization at 24 months ($P = .001$). Baseline anti-Tg levels were not independently associated with ATA risk category, histopathological subtype, or recurrence ($P > .05$). However, among 47 patients with at least 5 years of follow-up, persistent anti-Tg positivity at 24 months was significantly associated with recurrence ($P = .031$).

Conclusions: Baseline anti-Tg levels alone do not predict ATA risk classification or recurrence in differentiated thyroid cancer. In contrast, failure to achieve anti-Tg negativization at 24 months was significantly associated with recurrence during long-term follow-up. These findings highlight the importance of dynamic anti-Tg monitoring as a prognostic marker beyond static baseline measurements. However, these findings should be interpreted cautiously due to the limited number of recurrance events.

Abstract citation ID: lvag096.1656

EP1482 - ECE_3080 - The use of rapid on-site evaluation during thyroid fine needle aspiration might help improve samples representativity

Aurélien Schommers, Iulia Potorac, Pauline Delannoy, Laurent Vroonen, Daniela Betea, Sandrine Petignot, Anne-Sophie Chachati and Patrick Petrossians
Endocrinology, Université de Liège, CHU Liège, Liège, Belgium

Introduction: Thyroid fine needle aspiration (FNA) is routinely performed in thyroid nodular disease. It provides precious information about nodules' cellular constitution and can help therapeutic management, notably through the use of Bethesda classification. Unfortunately, this test encounters a significant number of non-diagnostic (class I) results, which leads to uncertainty in providing the most appropriate support and potentially increasing patients' anxiety. In our study, we were interested in appreciating the improvement of sample quality by checking the cellular content during FNA with the help of a microscope and using rapid on-site evaluation (ROSE) directly in the consultation room.

Design and Methods: We conducted a retrospective study on 297 (69 males, 228 females; mean ages 54 and 55 respectively) fine needle aspirations, made between 2017 and 2024. Ultrasound appearance according to EU-TIRADS classification were respectively 131 EU-TIRADS 3 (44%), 68 EU-TIRADS 4 (23%), and 98 EU-TIRADS-5 (33%). In group A (ROSE, 67 patients), FNA was performed by the same operator (Operator A), spreading out a drop of the sample over a microscope slide. Samples were coloured using Diff-Quick method, and cellularity was evaluated under a microscope. If the cellularity was insufficient, another aspiration was made. Group B (230 patients) comprises cases of FNA performed without microscopic quality-control by operator A and others.

Results: 9 samples were classified as non-diagnostic in group A (13%) against 118 in group B (51%), $P < .0001$. Looking at the samples taken by operator A ($n = 146$), ROSE procedure was performed in 67 cases whereas standard FNA procedure was used in 79 cases. 9 needle aspirations were classified as non-diagnostic in the first subgroup (13%) against 31 (39%) in the second one. $P < .0001$. The proportion of different EU-TIRADS nodules in groups A and B was not significantly different.

Conclusions: Our study suggests the use of microscope and ROSE during FNA might improve the yield of fine needle aspiration by reducing the number of non-diagnostic samples. This method would help reduce the overall number of repeated biopsy sessions and allow the practician to offer a more refined exploration of thyroid nodular disease.

Abstract citation ID: lvag096.1657

EP1484 - ECE_3544 - Clinical, radiological, and pathological characteristics of NIFTP: a single-center experience

Ekin Yiğit Köroğlu[1], Cevdet Aydin[2], Caglar Keskin[1], Ayşegül Aksoy Altınboğa[3], Asiye Şafak Bulut[3], Buket Altun Özdemir[4], Oya Topaloglu[2], Reyhan Ersoy[2] and Bekir Cakir[2]
[1]*Endocrinology and Metabolism Diseases, Ankara Bilkent City Hospital, Ankara, Türkiye;* [2]*Endocrinology and Metabolism Diseases, Ankara Yıldırım Beyazıt University, Ankara, Türkiye;* [3]*Medical Pathology, Ankara Bilkent City Hospital, Ankara, Türkiye;* [4]*Breast and Endocrine Surgery, General Surgery, Ankara Bilkent City Hospital, Ankara, Türkiye*

Background: Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) represents a borderline thyroid entity with indolent behavior. However, its preoperative characterization remains challenging due to overlapping cytological and radiological features with papillary thyroid carcinoma (PTC). This study aimed to comprehensively evaluate the clinical, ultrasonographic, cytological, pathological, and outcome characteristics of patients diagnosed with NIFTP.

Methods: We retrospectively analyzed 165 consecutive patients diagnosed with NIFTP between 2017 and 2023 at a tertiary referral center. Demographic data, thyroid function, autoimmunity, ultrasonographic features (EU-TIRADS, ATA risk stratification), fine-needle aspiration (FNA) cytology, surgical approach, pathological findings, and clinical outcomes were evaluated. Descriptive statistics were applied, and follow-up data were analyzed in patients with isolated NIFTP.

Results: The cohort showed marked female predominance (84.8%; female-to-male ratio 5.6:1) with a mean age of 50.0 ± 12.6 years. Most patients were euthyroid at diagnosis (69.1%),

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

while autoimmune thyroiditis was present in 26.7%. Median ultrasonographic nodule diameter was 1.8 cm, and the majority were classified as low risk by EU-TIRADS (73.3%) and ATA (73.9%). Predominant sonographic features included regular margins (83.6%), isoechogenicity (85.5%), and wider-than-tall shape (91.5%).

FNA was performed in 85.5% of patients, with indeterminate cytology (Bethesda III-V) observed in 46.8%, most commonly Bethesda III (33.3%). Nuclear atypia was the most frequent cytological feature (82.1%), with a mean of 3.25 ± 1.79 papillary carcinoma–type nuclear features per patient.

Total thyroidectomy was performed in 79.4% of cases. Median pathological tumor size was 1.2 cm, and microcarcinomas (≤1 cm) accounted for 47.3%. Concurrent PTC was identified in 41.2%, while 58.8% had isolated NIFTP. During a median follow-up of 26 months, isolated NIFTP patients ($n = 97$) demonstrated excellent outcomes with no lymph node metastasis or recurrence and a disease-free survival rate of 100%.

Conclusions: NIFTP predominantly presents with low-risk ultrasonographic features and indeterminate cytology but demonstrates excellent clinical outcomes when isolated. Awareness of its characteristic profile may help avoid overtreatment and support conservative management strategies.

Abstract citation ID: lvag096.1658

EP1485 - ECE_1032 - Determinants of radioactive iodine therapy failure in hyperthyroidism: a multivariable analysis from a UK cohort

Enam Ruf[1], Sonia Akther[1], Abdelmajid Musa[1,2], Harshal Deshmukh[3] and Mohamed Malik[1]
[1]*Diabetes & Endocrinology, Scunthorpe General Hospital, Scunthorpe, United Kingdom;* [2]*endo&diabetes, Scunthorpe General Hospital, Scunthorpe, United Kingdom;* [3]*James Cook University, South Mackay, Australia*

Introduction: Radioactive iodine (RAI) has been a cornerstone in management of hyperthyroidism since 1940s. Despite being effective therapy, a proportion of patients fail initial therapy and require repeat treatment. This study aims to identify clinical and biochemical predictors of RAI failure.

Methods: Retrospective cohort study of 764 patients treated with RAI for hyperthyroidism between 2007 and 2023 at a UK District Hospital. Univariable analyses followed by multivariable logistic regression were performed to identify independent predictors of treatment failure. Predictor variables were selected based on clinical relevance and published literature. Biochemical analysis of serial post-RAI TFTs up to 12 months were included. Categorical variables were analysed as factors with clinically relevant reference categories, and continuous variables were included as linear terms. Missing data were handled using random forest–based imputation. Results are reported as odds ratios (OR) with 95% confidence intervals (CI), with statistical significance defined as $P < .05$.

Results: Of the 764 patients included; 44 (5.76%) experienced treatment failure. Mean age was 56.6 ± 15.1 years, and 26.6% were male.

On univariable analysis; male sex was associated with increased odds of treatment failure (OR 3.29, 95% CI 1.55-6.89, $P = .001$). Longer ATD treatment duration was protective, particularly ≥13 months (13-18 months: OR 0.06, 95% CI 0.006-0.57; >24 months: OR 0.10, 95% CI 0.02-0.48). Multinodular goitre was associated with higher failure risk compared with smooth texture (OR 4.85, 95% CI 2.06-11.44, $P < .001$). Six-week post-RAI TSH was significantly lower in patients who failed treatment (Mann-Whitney U = 1481, $P < .001$).

On multivariable analysis; current smoking independently predicted treatment failure (OR 4.35, 95% CI 1.36-15.22, $P = .016$) whilst ex-smoking did not show the same relation (OR 1.62, 95% CI 0.33-7.15, $P = .53$) when compared with never smoking. Small goitre size was strongly protective compared with no goitre (OR 0.04, 95% CI 0.005-0.23, $P < .001$). Multinodular goitre texture remained independently associated with treatment failure (OR 11.48, 95% CI 2.58-62.12, $P = .002$). Autoimmune aetiology showed a borderline association with increased failure risk (OR 3.44, 95% CI 0.90-15.44). Six-week post-RAI TFTs were not independently predictive in the multivariable model, although raised TSH demonstrated a borderline protective trend.

Conclusions: This study confirms established clinical predictors of RAI treatment failure, including smoking status and multinodular goitre morphology. Importantly, suppressed 6-week post-RAI TSH emerged as a novel early biochemical marker of treatment failure, supporting its role in early risk stratification and optimisation of follow-up strategies.

Abstract citation ID: lvag096.1659

EP1487 - ECE_2528 - Etiological diagnosis of hypothyroidism after craniofacial radiotherapy

Fatma Ben Abdessalem, Taieb Ach, Imen Halloul, Wiem Saafi, Hamza Fekih, Ghada Saad and Yosra Hasni
Endocrinology, Hôpital Farhat Hached, Sousse, Tunisia

Introduction: Radiotherapy for craniofacial cancers often leads to various forms of thyroid dysfunction as a significant late complication. The aim of this study is to identify the different causes of hypothyroidism following external radiotherapy.

Materials and Methods: This was a cross-sectional study involving 22 patients treated with external radiotherapy who developed hypothyroidism during post-radiation follow-up.

Results: 22 patients—10 men and 12 women—who experienced hypothyroidism following craniofacial radiation therapy were included in the study. Of these, 21 had nasopharyngeal carcinoma and one had Hodgkin's lymphoma. Over an average of 12 months, a dose of 72 ± 2 Gray was administered. The average interval between the end of radiation therapy and the hypothyroidism diagnosis was four years. Six cases had central hypothyroidism, with an inappropriate TSH (4.5 ± 2 mIU/L) and an average FT4 level of 4.1 pg/mL. Peripheral hypothyroidism was present in 14 cases. Anti-thyroperoxidase antibody levels were ten times higher than normal in four patients. Low FT4 levels (4.6 pg/mL), inappropriate TSH levels (12 mIU/L and 0.32 mIU/L), and elevated anti-thyroperoxidase antibody titers (82 and 890 IU/mL) were found in two cases with a mixed origin.

Conclusions: Hypothyroidism is the most common thyroid disorder after radiotherapy. It may be peripheral, due to direct toxicity or autoimmune damage, or central, isolated or occurring as part of hypothalamic-pituitary injury, or mixed. Therefore, regular thyroid function monitoring is essential for the early detection of post-radiation hypothyroidism.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1660

EP1488 - ECE_2677 - Association of thyrotoxic periodic paralysis with long-term risk of incident diabetes: a population-based cohort study

Gloria Hoi-Yee Li[1], Kelvin Ho[1], Kathryn Choon-Beng Tan[2], Elaine Yun-Ning Cheung[3] and Ching-Lung Cheung[2]
[1]*Department of Health Technology and Informatics, The Hong Kong Polytechnic University, Hung Hom, Hong Kong;* [2]*Department of Pharmacology and Pharmacy, The University of Hong Kong, Pokfulam, Hong Kong;* [3]*Department of Medicine and Therapeutics, The Chinese University of Hong Kong, CUHK Medical Centre, Sha Tin, Hong Kong*

Introduction: Thyrotoxic periodic paralysis (TPP) is a rare complication of thyrotoxicosis, characterized by episodes of muscle paralysis and hypokalemia. During acute attacks, patients with TPP were observed to develop hyperinsulinemia triggered by precipitating factors such as carbohydrate load. Compared to patients with thyrotoxicosis but not TPP (simple thyrotoxicosis), those with TPP exhibited higher insulin levels even after the resolution of paralytic episodes. In this study, we aimed to evaluate the association of TPP with the long-term risk of developing diabetes.

Methods: We conducted a retrospective cohort study using a representative electronic health record database in Hong Kong. Individuals with first TPP and simple thyrotoxicosis between 2002 and 2016 were identified, and followed until the development of incident diabetes, death, or end of study on 31 December 2021. Propensity score (PS) matching was used to balance the baseline characteristics, matching each individual with TPP history with up to four individuals with simple thyrotoxicosis. Cox proportional hazards model was applied to estimate the hazard ratio (HR) for incident diabetes among individuals with TPP history compared to those with simple thyrotoxicosis.

Results: Between 2002 and 2016, a total of 631 individuals developed incident TPP, while 16 240 developed simple thyrotoxicosis. Using the PS approach, 630 individuals with TPP were matched to 1654 individuals with simple thyrotoxicosis. Over a median follow-up of more than 11 years, the incidence rate of diabetes was 11.03 per 1000 person-years (95% confidence interval [CI]: 8.72-13.77) in the TPP group and 6.6 per 1000 person-years (95% CI: 5.51-7.85) in the simple thyrotoxicosis group. In time-to-event analysis, individuals with TPP history had significantly higher risk of incident diabetes compared to those with simple thyrotoxicosis (HR = 2.25; 95% CI: 1.61-3.14; $P < .001$). Sensitivity analyses restricted to individuals with at least 10 and 15 years of follow-up time yielded similar results (10-year follow-up: HR = 2.33; 95% CI: 1.55-3.51; $P < .001$; 15-year follow-up: HR = 2.18; 95% CI: 1.54-3.09; $P < .001$).

Conclusions: Individuals with TPP history exhibited a significantly higher long-term risk of developing diabetes compared to those with simple thyrotoxicosis. Regular monitoring for diabetes may be warranted in individuals with TPP history to facilitate early detection and timely intervention.

Abstract citation ID: lvag096.1661

EP1490 - ECE_3131 - Use of liothyronine in combination with levothyroxine: real-world biochemical outcomes in a UK endocrine clinic

Muhammad Masroor Amjad[1,2], Muhammad Haroon Riasat[1], Samraiz Nafees[3], Khurram Qayyum[1], Rehmat Karim[1], Najeeb Shah[1] and Mohamed Malik[4]
[1]*Hull Royal Infirmary, Hull, United Kingdom;* [2]*Diabetes & Endocrinology, Hull Royal Infirmary, Kingston upon Hull, United Kingdom;* [3]*Scarborough General Hospital, Scarborough, United Kingdom;* [4]*Scunthorpe General Hospital, Scunthorpe, United Kingdom*

Combined Levothyroxine and Liothyronine (T4/T3) therapy in primary hypothyroidism remain a matter of debate, this study was designed to highlight the biochemical outcomes from real clinical practice.**Methodology:** Retrospective observational audit of electronic records from secondary care endocrine clinic in UK.

Participants: All adults receiving liothyronine in combination with levothyroxine for primary hypothyroidism under clinic follow up during the audit period ($n = 26$). Most participants were female (24/26, 92.3%) and aged 36-80 years, with primary autoimmune, post-radioiodine and postsurgical hypothyroidism predominating.

Interventions: Existing combination therapy was reviewed. For each patient, prior levothyroxine dose, TSH and weight were extracted together with current T4 and T3 doses, TSH, weight and duration on a stable regimen.

Main outcome measures: Primary outcome was the proportion of patients with TSH within the reference range (0.4-4.5 mU/L) on combination therapy. Secondary outcomes included TSH <0.4 or >4.5 mU/L, change in TSH and weight from monotherapy to combination therapy, time to stable TSH, and prescribed T4:T3 dose ratios.

Results: Before combination therapy, 17/26 patients (65.4%) had TSH >4.5 mU/L despite levothyroxine doses most commonly between 100 and 150 mcg daily. On combination therapy, 18/26 (69.2%) had TSH 0.4-4.5 mU/L, 4/26 (15.4%) had TSH <0.4 mU/L, and 4/26 (15.4%) had TSH >4.5 mU/L. Stable TSH was documented in 14/26 patients (53.8%); in 12/26 (46.2%) TSH remained unstable, suppressed, recently altered or showed only minimal improvement. Mean T4:T3 ratio was approximately 4:1, with wide inter-individual variability.

Conclusions: In this cohort, combination therapy was used in a small, predominantly female group with persistent biochemical abnormalities on levothyroxine alone and led to normalisation of TSH in around two thirds of patients. However, almost half did not achieve sustained biochemical stability and a sizeable minority had suppressed or elevated TSH, raising concerns in the context of guidance that does not recommend routine combination therapy and emphasises cautious dosing and regular review. These findings support tighter local criteria, more structured monitoring and clearer documentation of indications when prescribing liothyronine.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1662

EP1491 - ECE_3615 - Dose is not the answer: rethinking refractory hypothyroidism

Diana Martiniuc[1,2], Otilia-Andreea Tarcau[1], Simina Plesca[1], Ingrid-Ioana Stafie[1,2], Viviana Adam[1,2], Anca Matei[1,2], Stefana Bilha[1,2], Alexandru Florescu[1,2] and Cristina Preda[1,2]
[1]*Endocrinology, "St Spiridon" Clinical Emergency County Hospital, Iași, Romania;* [2]*"Grigore T. Popa" University of Medicine and Pharmacy, Iași, Romania*

Levothyroxine (LT4) is the first-line therapy for hypothyroidism and is available in multiple formulations, including tablets, liquid formulations, and soft-gel capsules. Persistent hypothyroidism despite apparently adequate or high LT4 doses is frequently labelled as "refractory", although this term encompasses heterogeneous mechanisms, including poor adherence, incorrect administration, and gastrointestinal disease impairing levothyroxine bioavailability. Accurate differentiation between these entities is essential, particularly in patients requiring strict TSH control.

We report three female patients referred to a tertiary endocrine centre for severe hypothyroidism despite high-dose LT4 therapy. All patients underwent a levothyroxine absorption test based on administration of the usual daily LT4 dose, with serial measurements of total and free thyroxine, according to the protocol described by Prof. Philippe Caron and colleagues. A comprehensive evaluation for gastrointestinal, autoimmune, and pharmacological causes of impaired absorption was performed. LT4 formulation and route of administration were individualized based on test results. Two patients demonstrated preserved intestinal LT4 absorption (>60%) despite marked biochemical hypothyroidism, consistent with pseudo-malabsorption, most likely related to improper administration or functional non-adherence. In both cases, therapeutic education and transition to liquid LT4 led to normalization of thyroid function tests. The third patient, with a history of total thyroidectomy for papillary thyroid carcinoma, presented with severe hypothyroidism despite high-dose LT4 and a clinical requirement for TSH suppression. She exhibited true malabsorption, associated with chronic gastritis and hypergastrinemia. A combined strategy using oral LT4 with vitamin C to enhance gastric acidification, together with temporary rectal LT4 administration, successfully restored euthyroidism. Follow-up demonstrated maintenance of biochemical control on oral LT4 alone, suggesting reversible, pH-dependent malabsorption.

Refractory hypothyroidism represents a diagnostic signal rather than a final diagnosis. The daily-dose levothyroxine absorption test is a practical and informative tool to distinguish pseudo-malabsorption from true absorption impairment and to guide individualized therapy. While most patients exhibit functional causes, a minority present with genuine, potentially reversible malabsorption, a distinction of particular importance in patients with differentiated thyroid carcinoma.

Abstract citation ID: lvag096.1663

EP1492 - ECE_3648 - Metformin in the management of thyroiddysfunction and carbohydrate metabolism disorders inpatients with diffuse toxic goiter and insulin resistance

Halyna Suslyk[1] and Orysia Lishchuk[1,2]
[1]*Endocrinology, University Clinic, Lviv, Ukraine;* [2]*Danylo Halytskyi Lviv National Medical University, Lviv, Ukraine*

Introduction: Subsequent clinical and experimental studies have shown that in thyrotoxicosis insulin interacts differently with target tissues, including the liver, muscles, adipose tissue, and endothelium. The degree of glucose intolerance and β-cell dysfunction correlates with the severity of diffuse toxic goiter. Hyperthyroidism is associated with hepatic insulin resistance, increased fasting plasma glucose, enhanced gluconeogenesis, and glycogenolysis. Thyroid hormones regulate key enzymes of carbohydrate metabolism, while metformin, a biguanide and the only insulin sensitizer approved by major diabetes associations, reduces hepatic glucose production and improves peripheral glucose uptake. Data on the effect of metformin on thyroid function remain limited.

The aim of the study was to assess carbohydrate metabolism and insulin resistance indices in patients with diffuse toxic goiter receiving metformin.

Materials and Methods: The study included 41 patients (30 women and 11 men, mean age 42.0 ± 0.9 years) with diffuse toxic goiter and insulin resistance. Examinations were performed at baseline and after 3 and 6 months of thyreostatic therapy with thyrozol combined with metformin. Thyroid function (TSH, free T4, free T3), carbohydrate metabolism parameters (glucose, HbA1c, insulin, C-peptide), and insulin resistance indices (HOMA-IR, HOMA-β, Caro index) were assessed. Statistical analysis was performed using Microsoft Excel and STATISTICA 6.0.

Results and Discussion: Thyrozol therapy led to a significant increase in TSH levels from 0.02 ± 0.00 to 1.75 ± 0.12 mMO/L ($P < .001$), with a further rise to 2.20 ± 0.03 mMO/L ($P < .05$) after adding metformin. Free T4 levels decreased from 4.46 ± 0.35 to 1.65 ± 0.06 ng/dL after thyrozol treatment and to 1.57 ± 0.05 ng/dL with combined therapy ($P < .001$). Free T3 levels also significantly decreased from 16.18 ± 1.07 to 3.48 ± 0.11 pg/mL and further to 3.28 ± 0.10 pg/mL ($P < .001$).

Combined therapy resulted in improved carbohydrate metabolism: fasting glucose decreased from 5.56 ± 0.15 to 5.20 ± 0.10 mmol/L ($P < .05$), insulin from 13.09 ± 0.54 to 11.53 ± 0.43 mMO/L ($P < .05$), and HOMA-IR from 3.30 ± 0.20 to 2.70 ± 0.14 ($P < .05$). A trend toward reduced HbA1c was observed.

Conclusions: Thyrozol therapy achieved euthyroidism in patients with diffuse toxic goiter and insulin resistance. The addition of metformin enhanced normalization of thyroid hormone levels and significantly reduced insulin resistance. Thyreostatic therapy alone did not fully eliminate insulin resistance, highlighting the benefit of combined treatment with metformin.

Abstract citation ID: lvag096.1664

EP1493 - ECE_1099 - When antithyroid drugs fail: refractory amiodarone-induced thyrotoxicosis managed with plasmapheresis and surgery

Mohammad Zaid Seegoolam, Hao Wei Tan, Amit Allahabadia, Sabapathy Balasubramanian and Miguel Debono
Diabetes and Endocrinology, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield, United Kingdom

Severe amiodarone-induced thyrotoxicosis (AIT) can be rapidly life-threatening, particularly when standard antithyroid therapy is contraindicated or ineffective.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

A 69-year-old man with a history of paroxysmal atrial fibrillation (pAF), treated with amiodarone for the past 3.5 years, presented with progressive exertional dyspnoea. Amiodarone had been discontinued by cardiology in June 2024 due to conduction abnormalities.

Initial thyroid function tests (TFTs) revealed a thyrotoxic profile showing a suppressed TSH < 0.02, FT4 > 100 and FT3:25.1. Autoantibody screening including TRAb and TgAb was negative.

Patient was commenced on carbimazole 40 mg OD (07/01/2025) subsequently escalated to 20 mg TDS (13/01/2025), and prednisolone 40 mg OD (23/01/2025) for suspected amiodarone-induced thyrotoxicosis (AIT). By late January, transaminitis was noted but therapy was continued. On 12/02/2025, with persisting hepatic dysfunction, carbimazole was reduced to 20 mg BD. Prednisolone was switched to dexamethasone 2 mg BD.

Therapy was optimised in accordance with the SPROG protocol (Sheffield Peri-operative Rapid Optimisation in Graves' disease, which comprises of Lugol's iodine, dexamethasone, cholestyramine, lithium, propranolol): with carbimazole and dexamethasone continued, bisoprolol switched to propranolol 40 mg TDS, and cholestyramine 4 g TDS added. At endocrine MDT review (14/02/2025), a switch to propylthiouracil (PTU) 150 mg TDS was recommended alongside adjunctive therapy and surgical referral. However, with worsening hepatic dysfunction (ALT 436 IU/L), PTU was discontinued and the regimen revised to Lugol's iodine 0.3 mL TDS, lithium, dexamethasone 2 mg BD, cholestyramine 4 g TDS, and maximal-dose propranolol. Despite five weeks of intensive inpatient management with the SPROG protocol and adjunctive measures, thyroid function remained abnormal (TSH < 0.02 mU/L, FT4 > 100 pmol/L).

Following haematology input, plasmapheresis was introduced as a bridging therapy to surgery. An initial course of 10 alternate-day sessions over three weeks achieved only transient biochemical improvement (FT3 5.1 pmol/L, FT4 53.2 pmol/L), with subsequent biochemical relapse. Escalation to daily plasmapheresis for a further week was required, and in total the patient received 17 sessions. This strategy enabled sufficient stabilization to permit a successful high-risk total thyroidectomy after three months of intensive therapy.

Postoperatively, the patient made a marked clinical recovery, with resolution of fatigue and breathlessness. He was commenced on levothyroxine 125 µg OD, titrated to 75 µg OD and was placed on a hydrocortisone taper, now maintained on 10 mg, 5 mg, 2.5 mg for secondary adrenal insufficiency

We propose plasmapheresis should be considered a viable bridge to surgery in refractory AIT when conventional strategies fail.

Abstract citation ID: lvag096.1665

EP1494 - ECE_1473 - Thyrotoxic Hypokalemic Periodic paralysis and new-onset autoimmune diabetes: a rare, combined presentation

Osman Abdalrazag[1], Zambu Kyaw[2] and Zayd Merza[1]
[1]*Diabetes & Endocrinology Centre, Barnsley Hospital Nhs Foundation Trust, Barnsley, United Kingdom;* [2]*Barnsley Hospital Nhs Foundation Trust, Barnsley, United Kingdom*

Introduction: Thyrotoxic Hypokalemic Periodic paralysis (THPP) is a rare but potentially life-threatening complication of thyrotoxicosis, mostly associated with Graves' disease. It presents as episodic muscle weakness brought on by triggers like carbohydrate intake, exercise or stress. Insulin causes shifting of potassium intracellularly increasing the risk of hypokalaemia and complicating management in patients with coexisting autoimmune diabetes.

Case report: A 41-year-old Caucasian male presented with acute lower limbs weakness progressing over a day without sensory symptoms. Examination revealed no objective weakness or clinical features of hyperthyroidism. Investigations demonstrated mild hypokalaemia of 3.4 mmol/L, TSH < 0.01, a raised Free FT4 of 49.3 pmol/L, and FT3 of 18.9 pmol/L. TSH receptor antibodies were positive, supporting a diagnosis of Graves' disease, and treatment with carbimazole and propranolol was commenced, alongside oral potassium replacement, resulting in complete recovery of the weakness.

One month later, he re-presented with bilateral lower limb heaviness following a high-carbohydrate meal. Neurological examination showed normal power, tone, reflexes, and sensation. Blood tests showed recurrent hypokalemia of 2.9 mmol/L, FT4 33 pmol/L, ECG showed no significant abnormalities. Based on the clinical presentation and biochemical findings, a diagnosis of THPP was established. Intravenous potassium replacement resulted in rapid resolution of symptoms. A random glucose measured 16 mmol/L with an HbA1C of 53 mmol/mol, indicating previously undiagnosed diabetes.

Positive anti-GAD antibodies >2000 u/mL with negative islet A2 and ZnT8 antibodies were consistent with newly diagnosed autoimmune diabetes. His C-peptide of 1413 pmol/L was raised with a glucose of 16.8 mmol/L.

Conclusions: This case highlights the importance of considering THPP in patients presenting with acute episodic weakness, even in the absence of objective neurological or thyrotoxic features. Recognition of triggers such as high-carbohydrate intake is important. The coexistence of Graves' disease, hypokalemic periodic paralysis, and newly diagnosed autoimmune diabetes underscores the need for comprehensive endocrine evaluation.

Abstract citation ID: lvag096.1666

EP1496 - ECE_3588 - Tocilizumab as second-line therapy in 67-year-old female with severe graves' orbitopathy and corticosteroid-induced cataract

Petros Papalexis[1], Vasiliki Siampanopoulou[2], Alexandros Lafioniatis[2], Georgia Tsirou[2], Varvava Chalmantzi[2], Despoina Tsopouzidou[2], Paschalia Bekiaridou[2] and Anna Angelousi[2]
[1]*First Department of Medicine, Unit of Endocrinology, Laiko General Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece;* [2]*Unit of Endocrinology, First Department of Internal Medicine, National and Kapodistrian University of Athens, Laiko General Hospital, Athens, Greece*

Background/Introduction: Graves' orbitopathy (GO) is the most common extrathyroidal manifestation of Graves' disease and can be sight-threatening in severe cases. While corticosteroids are the first-line treatment, their use may be limited by adverse effects or therapeutic resistance, necessitating second-line interventions.

Purpose: To present a clinical case of Graves' orbitopathy treated with the monoclonal antibody tocilizumab in a female patient who developed steroid-induced cataract.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Methods: A 67-year-old female with a history of Graves' disease since 2020 and persistently positive thyroid-stimulating immunoglobulin (TSI) antibodies presented with progressive bilateral exophthalmos and active GO (Clinical Activity Score [CAS] of 4/7). Despite antithyroid treatment with unimazole, her TSI levels remained elevated. She was also receiving selenium supplementation. The patient had previously undergone high-dose corticosteroid pulse therapy but developed steroid-induced cataracts, precluding further steroid use. Orbital MRI confirmed bilateral extraocular muscle enlargement and mild optic nerve compression.

Results: Tocilizumab was initiated at a dose of 500-520 mg intravenously every four weeks for four cycles. The treatment was well tolerated and led to a reduction in CAS from 4/7 to 3/7. Hertel exophthalmometry measurements decreased from 24 mm to 21 mm. Follow-up orbital MRI demonstrated partial regression of extraocular muscle enlargement. Although TSI antibody titers declined post-treatment, they remained persistently positive.

Conclusions: Tocilizumab, an IL-6 receptor antagonist, is emerging as an effective second-line agent in corticosteroid-resistant GO. In this case, it resulted in modest clinical improvement without adverse effects. The case underscores the challenges of managing refractory GO and the potential need for a multimodal treatment approach.

References

1. Bartalena L, Kahaly G J, Baldeschi L, et al. The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. *Eur J Endocrinol*. 2021;185(4):G43-G67. https://doi.org/10.1530/EJE-21-0479
2. Bartalena L, Tanda ML. Current concepts regarding Graves' orbitopathy. *J Intern Med*. 2022;292(5):692-716. https://dx.doi.org/10.1111/joim.13524
3. Gontarz-Nowak K, Szychlinska M, Matuszewski W, Stefanowicz-Rutkowska M, Bandurska-Stankiewicz E. Current Knowledge on Graves' Orbitopathy. *J Clin Med*. 2021;10:16. https://dx.doi.org/10.3390/jcm10010016

Abstract citation ID: lvag096.1667

EP1497 - ECE_2945 - Successful levothyroxine discontinuation in patients with a persistently normal TSH

David Fisher[1,2], Ori Adler[3], Tamar Freud[4], Howard Tandeter[4] and Merav Fraenkel[1,2]

[1]Endocrinology, Soroka, University Medical Center, Be'er Sheva, Israel; [2]Faculty of Health Sciences, Ben-Gurion University of the Negev, Be-er Sheva, Israel; [3]Internal Medicine B, Soroka, University Medical Center, Be'er Sheva, Israel; [4]Department of Family Medicine and Siaal Research Center for Family Medicine and Primary Care, Ben-Gurion University of the Negev, Be'er Sheva, Israel

Background: Levothyroxine is widely prescribed for subclinical and overt hypothyroidism yet in some patients the indication for lifelong therapy remains uncertain. This study assessed whether long-term levothyroxine therapy can be safely discontinued in patients with persistently normal thyroid function. Secondary objectives were to identify predictors of successful levothyroxine discontinuation.

Methods: This prospective cohort study included adults (≥18 years) treated with levothyroxine for ≥5 years who maintained a normal annual TSH for five consecutive years. Eligible patients were identified through a computerized search of electronic medical records of Clalit Health Services, Southern District. Exclusion criteria included prior thyroidectomy, radioactive iodine therapy, diagnosis of congenital hypothyroidism or women with childbearing potential.

After obtaining informed consent, demographic data and baseline clinical, biochemical (including anti-thyroid peroxidase (TPO) antibodies) and current levothyroxine dose were recorded. Levothyroxine was discontinued, and participants were followed for 24 weeks with thyroid function tests and clinical assessments for symptoms of hypothyroidism at 4, 10, 16, and 24 weeks.

Treatment was restarted if during follow-up one of the following occurred:

1. TSH >10 mIU/L and/or free T4 below the lower limit of normal
2. Symptoms of hypothyroidism developed

The primary outcome was resumption of levothyroxine. Hazard ratios (HRs) for levothyroxine reinitiation were calculated using Cox proportional hazards models.

Results: Eighty-three patients were enrolled (69 women, 83%), mean age 70.5 ± 9.1 years; 32 were anti-TPO seropositive, 45 were seronegative and in 6 patients antibody status was unavailable. As of January 2026, sixty-seven patients completed 24-weeks follow-up; 33 patients (49.3%) remained biochemically and clinically euthyroid. Thirty-four patients (50.7%) required levothyroxine resumption: 23 (34%) due to biochemical hypothyroidism and 11 (16.4%) due to clinical hypothyroidism (of these patients, 6 had subclinical hypothyroidism and 5 were biochemically euthyroid).

Mean time to levothyroxine resumption was 6.4 ± 4.8 weeks (median 4 weeks). Following multivariable analysis adjusted for age, sex, and duration of prior euthyroid status, only levothyroxine dose (μg/kg) at study entry independently predicted treatment resumption (HR 5.1, 95% CI 1.65-15.63; $P = .005$). No serious adverse events were observed.

Conclusions: Half of patients receiving long-term levothyroxine with biochemical control were able to discontinue therapy and remain euthyroid after 24 weeks. The need for treatment resumption occurred early in those who failed discontinuation and was predicted by a higher baseline levothyroxine dose at study entry. Supervised levothyroxine withdrawal is feasible and safe in selected patients and may reduce unnecessary long-term treatment.

Abstract citation ID: lvag096.1668

EP1498 - ECE_1989 - Graves' disease in patient with thyroid hormone resistance

Jan Drugda, Pavel Cee and Filip Gabalec

4th Department of Internal Medicine, University Hospital Hradec Králové, Hradec Králové, Czech Republic

Introduction: Thyroid hormone resistance (RTH) is a rare condition in which peripheral tissues fail to respond appropriately to thyroid hormones due to defects in thyroid hormone receptor

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

signaling, most commonly caused by mutations in the thyroid hormone receptor beta (THRB) gene. This condition leads to elevated circulating thyroid hormone levels (fT4/fT3) with normal or even increased thyroid-stimulating hormone (TSH). Clinical manifestations vary depending on the degree of resistance across different tissues. Graves' disease, on the other hand, is a much more common cause of elevated thyroid hormones caused by autoimmune activation of the TSH receptor. The coexistence of both conditions in a single patient is extremely rare and presents a significant therapeutic challenge.

Observation: We present a case of a 22-year-old woman without significant comorbidities. She was referred by our obstetrician after delivering a child with hyperthyroidism. Her testing showed elevated thyroid hormones, suppressed TSH, and elevated TSH receptor antibodies (TRAb). Ultrasound revealed a slightly enlarged, inhomogeneous thyroid with marked hypervascularisation. Graves' disease was diagnosed, and propylthiouracil treatment was started. Six months after labour, we switched to thiamazole as she stopped breastfeeding. The thyreostatic treatment was more or less successful during the first year, with fluctuating TSH and fT4 levels requiring several dose adjustments. Nevertheless, the patient remained practically asymptomatic since the beginning.

In parallel, her son was at first also treated with propylthiouracil. After the maternal TRAb clearance period, the treatment was discontinued. The thyroid hormones remained elevated, but the TSH normalized, and then became even mildly elevated. The boy underwent genetic testing, and the THRB mutation (c.1313G>A) was confirmed. The same mutation was later confirmed in our patient as well. That led us to a difficult decision: whether to continue the thyreostatic treatment. We decided to continue the current dose of 30 mg of thiamazole daily, because of the lack of symptoms and TSH suppression (we know that it used to be normal in the first trimester screening). We decided to adjust the dosing based on symptoms rather than laboratory findings.

Overview: This case report describes a rare coexistence of thyroid hormone resistance (RTH) due to a THRB mutation and Graves' disease in a young woman. The case highlights the diagnostic and therapeutic challenges of managing Graves' disease in the presence of RTH and highlights the importance of prioritizing clinical symptoms over biochemical parameters when guiding treatment.

Abstract citation ID: lvag096.1669

EP1499 - ECE_3014 - An atypical case of schmidt syndrome in a male without hyperpigmentation

Khadija Had, Hamza El Fekih[1], Wiem Saafi[2], Sawsen Nouira[1], Imen Halloul[2], Taieb Ach[2], Ghada Saad[2] and Yosra Hasni[1]
[1]Department of Endocrinology and Diabetology, Laboratory of Exercise Physiology and Pathophysiology (LR19ES09), Farhat Hached University Hospital, Sousse, Tunisia; [2]Department of Endocrinology and Diabetology, Farhat Hached University Hospital, Sousse, Tunisia

Introduction: Schmidt syndrome is rare autoimmune disease with an estimated prevalence ranging from 1.4 to 4.5 cases per 100 000 inhabitants. It may occur at any age but is uncommon in children and after the age of 60, and it predominantly affects middle-aged women.

Addison's disease is usually suspected in the presence of weight loss, hypotension, hypoglycemia, and cutaneous hyperpigmentation; however, hyperpigmentation may be absent, as illustrated in our patient.

Case report: A 35-year-old male presented with progressive asthenia worsening in the evening, anorexia, and weight loss of 6 kg over one month. Physical examination revealed blood pressure of 100/60 mm Hg, heart rate of 99 bpm, fasting blood glucose of 0.74 g/L. The patient exhibits no cutaneous hyperpigmentation and no melanotic macules of the oral mucosa. The diagnosis of primary adrenal insufficiency was confirmed by 8 a.m. serum cortisol level at 43 µg/L and ACTH levels raging from 30 to 35 pg/mL. The patient was treated with hydrocortisone leading to significant clinical improvement. Two months later, the patient presented with weight gain, asthenia, and constipation, with no goiter on physical examination. Thyroid function tests confirmed primary hypothyroidism with a TSH level of 48 mIU/L and positive anti-thyroid peroxidase antibodies at 59 IU/mL. Treatment with L-thyroxine was initiated, resulting in clinical and biological improvement. The patient was hospitalized multiple times for acute adrenal insufficiency, triggered by flu, with no skin hyperpigmentation observed after 5 years follow-up.

Discussion: Schmidt syndrome, defined by the association of Addison's disease with Hashimoto's thyroiditis, is known also as autoimmune polyglandular syndrome type 2. Addison's disease results from autoimmune destruction of the adrenal cortex resulting in an elevation of ACTH levels and its precursor, POMC, which stimulate melanocyte activity and cause melanoderma. However, hyperpigmentation may be absent in the very early stages of the disease, particularly when adrenal involvement is partial or when ACTH secretion is only moderately increased.

Additionally, genetic factors may contribute to the absence of hyperpigmentation, especially in individuals with very fair skin or reduced melanogenic responsiveness.

Abstract citation ID: lvag096.1670

EP1501 - ECE_2356 - MEN2A more indolent than expected: a report of two cases

Leandro Augusto Silva, Andreia Martins Fernandes, Ana Rita Elvas, Joana Couto, Raquel G. Martins, Teresa Martins, Jacinta Santos and Fernando Rodrigues
Endocrinology Department, Portuguese Institute of Oncology of Coimbra, Coimbra, Portugal

Introduction: Multiple endocrine neoplasia type 2A (MEN2A) is defined by medullary thyroid carcinoma (MTC) and/or C-cell hyperplasia, pheochromocytoma and primary hyperparathyroidism. 2015 American Thyroid Association (ATA) risk categories guide surveillance and timing of thyroidectomy; recommends, in ATA-MOD carriers, surveillance from age 5 and consideration of thyroidectomy mainly based on basal calcitonin levels; however, there is no consensus threshold for prophylactic surgery. Val804Met and Cys611Tyr variants, classified as ATA-MOD are associated with very high penetrance of MTC. We report two MEN2A asymptomatic carriers who remain disease-free under surveillance.

Case 1: Male, carrier of a pathogenic *RET* Cys611Tyr variant identified through family screening for MEN2A. At 73 years, biochemical

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

evaluation showed serum calcitonin <2 pg/mL (<14.3). Neck ultrasound detected two right-lobe thyroid nodules (7 and 8 mm, EU-TIRADS-4) and two right supraclavicular lymph nodes (11 and 15 mm); fine-needle cytology of the larger lymph node was negative for epithelial neoplastic cells and calcitonin in needle washout <2.0 pg/mL. Underwent active surveillance. At the last follow-up (age 82) he remained asymptomatic with normal examination; labs showed serum calcitonin 0.77 pg/mL and calcium, parathyroid hormone and plasma metanephrines within reference. Ultrasound demonstrated the previously nonspecific lymph nodes.

Case 2: Male, evaluated for a family history of MEN2A, at 72 years. Initial testing showed serum calcitonin 1.8 pg/mL, and three unsuspected micronodules in neck ultrasound. Familial variant Val804Met was identified. Prophylactic thyroidectomy was not pursued based on age, serum markers and ultrasound, surgical risk and patient preference. At the last assessment (age 81) he remained asymptomatic with an unremarkable examination; laboratory workup showed serum calcitonin 10.50 pg/mL and calcium, parathyroid hormone and plasma metanephrines within reference. Ultrasound demonstrated stable thyroid nodules (10 mm, EU-TIRADS-3).

Conclusions: Emerging data argue for re-appraisal of risk classification and management of 2015 ATA MTC guidelines, questioning the premise that prophylactic thyroidectomy is mandatory for all *RET* variant carriers. Active surveillance can be a safe strategy for selected carriers; however, robust data is needed to define optimal surveillance intervals, biomarkers and imaging triggers for intervention, maintaining a balance between safety and overtreatment.

Abstract citation ID: lvag096.1671

EP1503 - ECE_3981 - Why add contrast in thyroid ultrasound: what perfusion curves can tell us

Andreea Bena, Stefania Bunceanu and Stoian Dana
Endocrinology, Internal Medicine 2nd, Universitatea de Medicină și Farmacie Victor Babeș, Timișoara, Romania

Background: Contrast-enhanced ultrasound (CEUS) allows dynamic, real-time evaluation of thyroid nodule microvascularization. While qualitative enhancement patterns are commonly used, quantitative analysis of time–intensity curves (TIC) may offer objective perfusion biomarkers that improve lesion characterization.

Objective: To illustrate the potential role of TIC-derived CEUS parameters in differentiating benign from malignant solitary thyroid nodules, using example data aligned with trends reported in the literature.

Methods: CEUS examinations were performed in 78 solitary thyroid nodules from 49 patients, with standardized cine acquisition and global region-of-interest (ROI) analysis. Quantitative TIC metrics included time parameters—arrival time (AT), rise time (RT), time to peak (TTP), fall time (FT), and mean transit time (mTT)—as well as amplitude and combined parameters: peak intensity (PKI), area under the curve (AUC), wash-in AUC (WiAUC), wash-out AUC (WoAUC), ascending slope (AS), descending slope (DS), slope ratio (SR), and mean TIC (mTIC). Nodule classification (benign vs malignant) was based on standard reference assessment (cytology and/or histology with follow-up). Data are presented as illustrative examples for educational purposes.

Results: In this example dataset, malignant nodules demonstrated delayed enhancement kinetics and reduced perfusion magnitude compared with benign lesions. Median AT was longer in malignant nodules (13.2 s [IQR 11.7-15.0] vs 11.0 s [9.6-12.8], $P = .008$), along with a prolonged TTP (28.5 s [24.0-33.2] vs 24.1 s [20.8-27.9], $P = .012$). Peak enhancement was significantly lower in malignant nodules, reflected by reduced PKI values (19.0 [14.8-22.6] vs 27.4 [22.3-32.1], $P < .001$).

Perfusion burden indices followed a similar pattern, with lower WiAUC in malignant nodules (285 [230-345] vs 402 [330-480], $P < .001$), suggesting diminished microvascular perfusion. Slope-derived parameters showed additional discriminatory value: malignant nodules exhibited a lower AS (1.05 [0.82-1.33] vs 1.48 [1.12-1.86], $P = .004$) and a higher SR (1.21 [0.98-1.46] vs 0.93 [0.76-1.12], $P = .021$), indicating relatively faster wash-out in relation to wash-in.

Receiver operating characteristic analysis identified PKI as a strong single predictor of malignancy (AUC = 0.83), while a multiparametric model combining PKI, TTP, and WiAUC improved diagnostic performance (AUC = 0.88).

Conclusions: Quantitative TIC analysis in CEUS provides complementary information on thyroid nodule perfusion dynamics. Parameters reflecting enhancement timing and magnitude—particularly PKI, TTP, and AUC-derived indices—illustrate how multiparametric CEUS assessment may enhance thyroid nodule characterization beyond qualitative imaging alone.

Abstract citation ID: lvag096.1672

EP1504 - ECE_1653 - Thyroid nodule microwave ablation. First 100 cases in Romania

Emin Mammadov
Regina Maria Private Healthcare Network, Bucharest, Romania

Background: Microwave ablation (MWA) is a modern minimally-invasive technique using thermal ablation for outpatient treatment of benign and some malignant thyroid nodules, as well as parathyroid adenomas and metastatic lymph nodes. We report our experience with first 100 cases of MWA for thyroid nodules in Romania.

Methods: Retrospective analysis of the first 100 thyroid nodule MWA procedures performed in Romania. All MWA procedures were performed using cooled antenna 16G or 17G with a microwave generator manufactured by ECO Microwave. We followed our patients for at least 1 year after the procedure.

Results: Of 100 MWA procedures, 46 were performed for solitary non-functioning nodules, 30 for multinodular goitre, 24 for AFTN (autonomously functioning thyroid nodules) or toxic multinodular goitre.

The mean volume of nodules was 15.76cc (SD = 22.29) before ablation. Average ablation time was 6.7 minutes, average power used was 24.8 W.

The mean volume reduction rate (VRR) was 46% at 1-month, 61.4% at 3-month, 70.1% at 6-month and 79.4% at 12-month follow-up.

The VRR of at least 90% was seen in 4 patients at 3 months, 9 patients at 6 months and 17 patients at 12 months. Only 2 nodules had VRR less than 50% (mean 47.9%) at 12-month follow-up.

Minor complications included some bruising and post-procedural pain or local discomfort, controlled with non-

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

steroidal anti-inflammatory drugs. One patient with AFTN had transient post-procedural thyrotoxicosis, two patients developed transient dysphonia, no other significant complications.

Most patients who experienced compressive symptoms before ablation, had significant improvement at 1 month post ablation. All patients with AFTNs had their thyroid function normalized at 1 month, except for the aforementioned patient who developed transient thyrotoxicosis.

Conclusions: Thyroid nodule MWA is a safe and efficient treatment option for thyroid nodules, reducing volume and controlling thyroid function in case of AFTN or toxic multinodular goitre.

Abstract citation ID: lvag096.1673

EP1507 - ECE_3270 - Rare case of Graves' disease with concomitant thyroid cancer and TED developed after RAI

Anna Somogyi[1], István Molnár[1], Bernadett Ujhelyi[2], Erika Szántó[3], Endre V. Nagy[1], Eszter Berta[1] and Miklós Bodor[1]

[1]Department of Medicine, Division of Endocrinology, University of Debrecen, Debrecen, Hungary; [2]Department of Ophthalmology, University of Debrecen, Debrecen, Hungary; [3]Department of Oncoradiology, University of Debrecen, Debrecen, Hungary

Introduction: Although Graves' disease (GD) is associated with an increased risk of thyroid malignancy, the concomitant occurrence of thyroid eye disease (TED) and thyroid cancer is rare. In our case, thyroidectomy was performed for GD, and differentiated thyroid carcinoma was diagnosed incidentally. Following radioiodine ablation, the patient developed new-onset TED. The pathogenesis of TED is not yet fully clarified however, literature data suggest that hypothyroidism preceding radioiodine therapy as well as the use of recombinant human TSH (rhTSH) as an alternative method may influence disease activity. This effect is thought to be mediated by activation of signalling pathways via TSH receptors expressed on orbital fibroblasts.

Case Presentation: A 44-year-old female patient with smoking history presented to the emergency department in February 2024 with sinus tachycardia, dysphagia and weight loss. Laboratory investigations revealed suppressed TSH, elevated TSH receptor antibodies (TRAb), and normal thyroid peroxidase antibody levels. Ultrasound examination demonstrated findings consistent with thyroiditis. Based on these results, Graves' disease was diagnosed, and thiamazole therapy was initiated.

Due to compression symptoms, total thyroidectomy was performed in August 2024, followed by hormone replacement with levothyroxine 100 µg daily. Histopathological examination revealed diffuse goiter and bilateral papillary microcarcinomas (one in each lobe). Consequently, after a 4-week levothyroxine withdrawal, the patient received 3700 MBq radioiodine ablation in December 2024. Follow-up examinations showed no residual thyroid or tumor tissue.

In early 2025, the patient developed diplopia accompanied by discomfort and tearing of the right eye. Ophthalmological assessment and ^{99m}Tc-DTPA (diethylenetriaminepentaacetic acid) SPECT/CT demonstrated bilateral, right-dominant, moderately active TED. Laboratory tests confirmed euthyroidism with elevated TRAb levels and normal thyroglobulin concentrations. Over the subsequent months the patient underwent a 12-week course of intravenous methylprednisolone therapy followed by retrobulbar irradiation, resulting in only transient improvement. Diplopia recurred one month after completion of steroid therapy.

Conclusions: The development of TED after total thyroidectomy may have been significantly influenced by hypothyroidism prior to radioiodine therapy and by the patient's ongoing smoking. It remains unclear whether the use of recombinant human TSH or prophylactic steroid administration would have resulted in a more favorable outcome. Further management options include rituximab or teprotumumab therapy as well as orbital surgery.

Abstract citation ID: lvag096.1674

EP1508 - ECE_3693 - Riedel's thyroiditis associated with retroperitoneal fibrosis: a case presentation

Georgios Kostopoulos[1], Evangelia Makri[1], Georgios Tikos[1], Evangelia Katsiki[2], Dimitrios Deligeorgakis[3], Elpida Skouvaklidou[3], Christina Adamichou[3] and Zoe Efstathiadou[1]

[1]Endocrinology, Hippokration General Hospital, Thessaloniki, Greece; [2]Thessaloniki, Greece; [3]4th Department of Internal Medicine, Hippokration General Hospital, Thessaloniki, Greece

Background: Riedel thyroiditis (RT) is a rare, chronic fibro-inflammatory disorder of the thyroid, with challenging diagnosis and management. Although its exact aetiology is unknown, emerging evidence suggests RT is part of the spectrum of IgG4-related disease. Its coexistence with retroperitoneal fibrosis is uncommon but clinically significant, potentially reflecting multisystem involvement that requires prompt recognition.

Case Presentation: A 34-year-old male with autoimmune hypothyroidism on levothyroxine presented with a painless, progressively enlarging anterior neck mass and low-grade fever. His symptoms started 8 months before and initial evaluation suggested subacute thyroiditis; however, the patient lacked typical hormonal and ultrasonographic features and no improvement was noted upon glucocorticoid therapy.

On examination, he had a hard goiter with mild compressive symptoms. He was euthyroid on levothyroxine with elevated CRP and ESR. Ultrasound showed a diffusely enlarged, hypoechoic, hypovascular thyroid. RT was suspected. Fine-needle aspiration was nondiagnostic; core needle biopsy revealed fibrous tissue and inflammatory cells without thyroid follicles, raising suspicion for RT, while IgG4 immunohistochemistry was negative. Plasma IgG4 levels were also found within limits.

Cross-sectional imaging was ordered to assess for extrathyroidal fibrosis, but, at that time, the patient did not proceed due to personal reasons During follow-up, he developed acute lower abdominal pain radiating to the right testicular region. Imaging revealed a large right-sided retroperitoneal fibro-inflammatory mass encasing the distal abdominal aorta, inferior vena cava, iliac vessels, and right ureter, causing hydronephrosis and right renal cortical thinning—findings consistent with retroperitoneal fibrosis, likely IgG4-related. Following rheumatology assessment, the patient received high-dose intravenous methylprednisolone followed by rituximab and underwent right ureteral stent placement without complete resolution of hydronephrosis.Thyroid mass has partially regressed.

Conclusions: This case illustrates the rare coexistence of RT and retroperitoneal fibrosis, supporting a systemic

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

fibroinflammatory pathophysiology even in the absence of IgG4 positivity. Early recognition and multidisciplinary management by endocrinologists and rheumatologists are crucial to guide appropriate therapy.

Abstract citation ID: lvag096.1675

EP1510 - ECE_1566 - Relation of irisin to insulin sensitivity in overweight/obese hypothyroid patients

Marwa Salah
Faculty of medicine, Alexandria University, Internal Medicine, Endocrine, Alexandria, Egypt

Background/Aim: Thyroid hormones and irisin, an exercise-induced adipo-myokine, modulate thermogenesis and energy metabolism. Given conflicting data on irisin in obesity and hypothyroidism, we evaluated the effects of adiposity and hypothyroidism on irisin levels and their relationships with insulin resistance.

Patients & Methods: In this cross-sectional study, ninety individuals were classified as follows: Group I: newly diagnosed hypothyroid overweight/obese ($n = 30$), Group II: treated hypothyroid overweight/obese ($n = 20$), Group III: euthyroid overweight/obese ($n = 20$), and Group IV: euthyroid lean controls ($n = 20$). Anthropometrics, thyroid function, glycemic, lipid profiles, and serum irisin levels were assessed. Group comparisons, correlations, and logistic regression were evaluated.

Results: Irisin levels were lower in obese groups (I-III) compared to controls ($H = 35.169$, $\mathbf{P < .001}$), with no difference between newly diagnosed and treated hypothyroid obese patients. In the total cohort, irisin correlated positively with FT3 ($\mathbf{P < .001}$) and FT4 ($\mathbf{P = .006}$), and negatively with TSH ($\mathbf{P = .007}$). Irisin correlated inversely with BMI, waist circumference, and waist-to-hip ratio (all $\mathbf{P < .001}$). In subgroup analyses, irisin correlated negatively with HOMA-IR in treated hypothyroid obese individuals ($P = .021$) and euthyroid obese individuals ($\mathbf{P = .026}$). In multivariable regression, **lower irisin was independently associated with obesity (OR 0.970, 95% CI 0.952-0.988, $\mathbf{P = .001}$)**

Conclusions: Circulating irisin is downregulated in obesity and linked to insulin resistance, while its relationship with hypothyroidism is less consistent. Irisin may serve as a metabolic, rather than thyroid-specific, biomarker, potentially useful for identifying obesity-related insulin resistance.

Keywords irisin, hypothyroidism, obesity, insulin resistance, HOMA-IR, thyroid hormones

Abstract citation ID: lvag096.1676

EP1511 - ECE_1966 - Factors associated with the control of primary hypothyroidism in Northeastern Colombia

Maria Roa-Parra[1], Rubel Lafaurie-Noriega[1], Miguel Ochoa-Vera[1], María Luna-González[1], Juan Sarmiento-Ramón[1,2] and Edwin Wandurraga-Sánchez[2]
[1]*Universidad Autónoma de Bucaramanga—UNAB, Bucaramanga, Colombia;* [2]*Bucaramanga, Colombia*

Introduction: Primary hypothyroidism is the most common thyroid disease worldwide, with estimated prevalences of 3.8%-4.6%. Treatment consists of hormone replacement therapy, primarily with levothyroxine; however, 35%-60% of patients do not achieve adequate control. Several factors can influence TSH control; however, few studies have comprehensively evaluated these factors at the national level.

Objective: To identify factors associated with the control of primary hypothyroidism in a sample of Colombian adult patients.

Methods: Cross-sectional study including adult patients with primary hypothyroidism treated at an endocrinology referral center for more than 3 months. Variables included sociodemographic, paraclinical (serum TSH), clinical, and levothyroxine adherence, assessed using the 8-item Morisky–Green scale. The following tests were used for bivariate analysis: Fisher's exact test, the Mann–Whitney U test, and Pearson's chi-squared test. Prevalence ratios (PRs) were estimated using generalized linear models and Poisson models. This study was approved by the Ethics Committee of the Autonomous University of Bucaramanga.

Results: Of 318 patients evaluated (median age 60 years [IQR 46-73]; 82.08% women), 59.43% achieved hypothyroidism control (TSH 0.4-4.0 mU/L). The median levothyroxine dose was 1.20 mcg/kg/day (IQR 0.86-1.53), primarily using Eutirox (48.43%) or generics (46.23%). Men exhibited significantly higher TSH levels than women (4.0 vs 2.79 mIU/L; $P = .028$).

Factors associated with poorer control of hypothyroidism included: male sex (PR 0.73; 95% CI 0.54-0.98, $P = .039$), government-subsidized health insurance (PR 0.71; 95% CI 0.51-0.98, $P = .036$), overweight (PR 0.81; 95% CI 0.66-0.99, $P = .043$), and high-dose levothyroxine defined as >1.9 mcg/kg/day (PR 0.47; 95% CI 0.27-0.79, $P = .005$). Factors associated with better control of hypothyroidism were: levothyroxine brand with a PR 1.47 for Eutirox (95% CI 1.20-1.80, $P < .001$) and a PR 1.86 for Synthroid (95% CI 1.45-2.40, $P < .001$) in comparison with generic brands; and medication adherence with PR 2.16 for moderate (95% CI 1.30-3.58, $P = .003$) and PR 3.82 for high adherence (95% CI 2.43-6.02, $P < .001$) in comparison with low adherence.

Conclusions: The diversity in sociodemographic, clinical, and therapeutic factors associated with the control of primary hypothyroidism highlights the importance of a comprehensive approach focused on education, adherence, and appropriate prescribing.

Abstract citation ID: lvag096.1677

EP1514 - ECE_3561 - HLA class I and II allele distribution between Graves' disease patients in an Albanian population

Dorina Ylli[1], Megi Lekbello[2], Erkena Shyti[3], Violeta Hoxha[2], Donika Kasemi[3], Marjeta Kermaj[2], Zamira Ylli[2] and Genc Sulcebe[3]
[1]*Endocrinology, Internal Disease, University of Medicine Tirana, Tirana, Albania;* [2]*University of Medicine Tirana, Tirana, Albania;* [3]*Research Center of Biotechnology and Genetics, Tirana, Albania*

Background: Graves' disease (GD) is an autoimmune thyroid disorder with a strong genetic background, in which the human leukocyte antigen (HLA) region plays a central role in disease susceptibility. HLA associations with GD show marked population-specific variability, and no comprehensive HLA association studies have been reported for the Albanian population for GD.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Methods: We performed a case–control study in an Albanian population including 223 adult subjects who underwent HLA genotyping. Sixteen patients were diagnosed with Graves' disease, and 207 subjects served as controls. High-resolution HLA typing was available for class I (HLA-A, B, C) and class II (HLA-DRB1, HLA-DQB1) loci. Allele frequencies were compared between GD patients and controls using Fisher's exact test. Odds ratios (OR) with 95% confidence intervals were calculated.

Results: Significant differences in HLA class II allele distribution were observed between Graves' disease patients and controls. HLA-DRB1*16:01 was more frequent in GD patients compared with controls ($P = .01$), and HLA-DQB1*05:02 also showed increased frequency in GD patients ($P = .02$). However, after correction for multiple testing, these associations did not remain statistically significant, although the direction and magnitude of the effects were preserved. No significant differences were observed for HLA-A or HLA-C allele distributions.

Conclusions: In this Albanian cohort, Graves' disease was associated with differences in HLA class II allele distribution, particularly involving DRB116:01 and DQB105:02. These associations did not withstand correction for multiple testing, likely reflecting limited statistical power due to the small number of Graves' disease cases. Nevertheless, the observed trends are biologically plausible and consistent with the role of HLA class II mediated immune mechanisms in GD. Larger studies are required to confirm these findings and to better define population specific genetic susceptibility patterns.

Abstract citation ID: lvag096.1678

EP1515 - ECE_3953 - Thyroid tissue stiffness as a marker of disease evolution in subacute thyroiditis

Andreea Bena, Stefania Bunceanu, Roxana Pui, Monica Simina Mihuta and Stoian Dana
Endocrinology, Internal Medicine 2nd, Universitatea de Medicină și Farmacie Victor Babeș, Timișoara, Romania

Background: Subacute thyroiditis (SAT) is a self-limiting inflammatory thyroid disease with variable clinical and imaging manifestations. Conventional ultrasound typically reveals hypoechoic, heterogeneous areas, while ultrasound elastography allows quantitative assessment of thyroid tissue stiffness, potentially reflecting inflammatory activity and disease evolution.

Methods: We prospectively followed 35 patients diagnosed with subacute thyroiditis, monitored longitudinally using conventional ultrasound and elastography. Fifteen patients had a positive history of SARS-CoV-2 infection, while 20 were COVID-19 negative. All patients underwent baseline clinical, biochemical, and ultrasound evaluation, followed by elastographic assessment at 1, 3, and 6 months. Thyroid vascularity was classified according to the Schultz scale. Elasticity index values were recorded as median and interquartile range (IQR).

Results: At baseline, all patients presented with clinical or subclinical hyperthyroidism at various stages. Conventional ultrasound showed a heterogeneous thyroid parenchyma with hypoechoic areas in all cases except four, which displayed a normal ultrasound appearance. According to the Schultz classification, 9 patients (25.7%) were classified as grade 1 vascularity, 18 patients (51.4%) as grade 2, and the remaining 8 patients (22.9%) as grade 3. Thyroid nodules were identified in 7 patients.

Approximately 45% of patients ($n = 16$) required corticosteroid therapy during the disease course. No statistically significant differences were observed between patients who required corticosteroids and those who did not, in terms of elastographic parameters ($P = .23$).

At initial evaluation, the median thyroid elasticity index was 128 kPa (IQR: 112-146). A progressive decrease in tissue stiffness was observed over time, with significant improvement at 1 and 3 months. At 6 months, normalization of elastographic values occurred in 34 out of 35 patients; one patient experienced disease recurrence with persistently elevated stiffness values.

At the 1-month follow-up, a moderate, statistically significant positive correlation was observed between thyroid-stimulating hormone (TSH) levels and the elasticity index (Spearman's rho = 0.42, $P = .01$). A stronger correlation was found between the elasticity index and C-reactive protein levels (rho = 0.48, $P < .001$), suggesting a close relationship between tissue stiffness and inflammatory activity.

Conclusions: Thyroid elastography reflects dynamic changes in tissue stiffness during the evolution of subacute thyroiditis and correlates with biochemical and inflammatory markers. Elastographic assessment may represent a valuable non-invasive tool for monitoring disease activity and recovery in patients with SAT.

Abstract citation ID: lvag096.1679

EP1520 - ECE_1651 - First 830 thyroid core-needle biopsies (CNB) in Romania. Patient satisfaction questionnaires and complications analysis

Emin Mammadov[1], Dana Terzea[2] and Mihai Ciprian Stoicea[1]
[1]Regina Maria Private Healthcare Network, Bucharest, Romania; [2]CI Parhon National Institute of Endocrinology, Bucharest, Romania

Background: Core-needle biopsy (CNB) is a valuable option to investigate a thyroid nodule, offering possibility of histological rather than cytological evaluation. However, it is still seen as a sophisticated and potentially dangerous investigation. We report our data regarding results, complications and patient satisfaction with CNB.

Methods: Retrospective analysis of the first 830 thyroid nodule CNBs performed in Romania. All CNBs were performed using 18G semi-automatic biopsy instruments. We used the Korean Thyroid Association reporting system (KTA-CNB) for histology reports.

Results: Of 830 CNBs, there were only 6 non-diagnostic results (0.7%).

Among nodules which previously underwent FNA (fine-needle aspiration), CNB offered a conclusive result (either benign or malignant, KTA II, V and VI categories) in 69% of Bethesda 1, 75% of Bethesda 3, 53% of Bethesda 4 nodules. There were no non-diagnostic results in these nodules.

We performed on average 2.1 passes per lesion. There were no major complications (none of complications required hospitalisation), some minor adverse events were limited to bruising, perithyroidal hematoma (1.6%), anxiety and panic attacks (1.1%) and pain during or after procedure (1.2%). Five patients (0.6%) developed transitory hoarseness which resolved spontaneously in 20-90 minutes.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

150 patients completed a questionnaire at the end of procedure. Based on their responses, the anxiety level decreased from 5.1 (out of 10) to 0.92, pain level at the time of introduction of local anaesthesia was 2.3 (out of 10), during sampling was 0.93 and decreased to 0.57 after finishing procedure.

82% of patients declared CNB to be better or much better than they were expecting. 72% of patients who previously underwent FNA, also declared CNB to be better or much better.

All patients declared they would recommend or strongly recommend CNB to someone who got recommendation for thyroid biopsy.

Conclusions: The CNB is a safe and reliable diagnostic procedure for thyroid nodules. It offers very low chance of non-diagnostic results, as well as clarification of diagnosis in case of non-diagnostic or inconclusive FNA.

CNB is a procedure which improves patient experience by reducing the number of procedures needed to make a clinical decision.

CNB is well-tolerated and recommended by the patients who underwent this procedure.

Abstract citation ID: lvag096.1680

EP1521 - ECE_3386 - Allelic frequency and distribution of TSHR gene variants in pediatric and adult thyroid tumors

Olivia Cillikova[1], Karolina Dobiasovska[1], Vlasta Kuklikova[1], Barbora Bulanova[1], Katerina Vyhnalova[1], Marie Rodová[1], Eliska Vaclavikova[1], Jitka Carkova[1], Petr Lastuvka[2], Rami Katra[3], Petr Vlcek[4], Daniela Kodetova[5], Petr Bavor[6], Martin Chovanec[7], Jana Drozenova[8], Jaromir Astl[9], Jiří Soukup[10], Josef Vcelak[1] and Bela Bendlova[1]

[1]Department of Molecular Endocrinology, Institute of Endocrinology, Prague, Czech Republic; [2]1st Faculty of Medicine, Department of Otorhinolaryngology and Head and Neck Surgery, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [3]2nd Faculty of Medicine, Department of Ear, Nose, and Throat, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [4]2nd Faculty of Medicine, Department of Nuclear Medicine and Endocrinology, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [5]2nd Faculty of Medicine, Department of Pathology and Molecular Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic; [6]2nd Faculty of Medicine, Department of Surgery, Charles University in Prague and Motol University Hospital, Prague; [7]3rd Faculty of Medicine, Department of Otorhinolaryngology, Charles University in Prague and University Hospital Kralovske Vinohrady, Prague, Czech Republic; [8]3rd Faculty of Medicine, Department of Pathology, Charles University in Prague and University Hospital Kralovske Vinohrady, Prague, Czech Republic; [9]3rd Faculty of Medicine, Department of Otorhinolaryngology and Maxillofacial Surgery, Military University Hospital, Prague, Czech Republic; [10]Prague, Czech Republic

Background: *TSHR* gene variants have been identified in a range of thyroid tumors, yet their prevalence, clinical significance, and relevance for molecular testing remain unclear. This study aimed to assess the prevalence and allelic frequency of *TSHR* variants in a large cohort of benign, low-risk neoplasms, and malignant thyroid tumors and to examine their association with histopathology and patient age.

Methods: A total of 1141 fresh-frozen thyroid tumor samples (589 malignant carcinomas, 78 low-risk neoplasms, and 442 benign tumors) from 204 pediatric (<18 years) and 937 adult patients were analyzed. DNA was extracted and analyzed for *TSHR* exon 10 variants (NM_000369.5) using next-generation sequencing (Illumina MiSeq). Library preparation was performed using the Nextera XT and SeqWell ExpressPlexTM 2.0 kits. Variants were classified according to their predicted functional impact.

Results: A total of 13 *TSHR* variants were detected in 42 thyroid tumors from 41 patients (35 females, 6 males). Histology of *TSHR*-positive tumors included 33 (78.6%) benign tumors, 3 (7.1%) papillary thyroid carcinomas (PTCs), 3 (7.1%) follicular thyroid carcinomas (FTCs), and 3 (7.1%) low-risk neoplasms. Among these patients, 14 (34.1%) were pediatric (<18 years) and 27 (65.9%) were adults. The most frequent variants were M453T (10 tumors: 6 benign, 1 low-risk neoplasms, 1 PTC, 2 FTC), F631L (5 tumors: 4 benign, 1 FTC), and D633Y (5 benign tumors), with D633Y observed exclusively in pediatric patients. Only five variants (M453T, Q489*, L512R, I541V, F631L) were detected in low-risk neoplasms or malignant tumors, the I541V and the Q489* were each detected once, alongside known causal variants. M453T and F631L showed a higher allelic frequency (>40%) in malignant tumors (3 FTC and 1 PTC) than in benign tumors. Several additional variants (S425I, I486F, I568T, D619G, I630L, T632I, and D633H) were detected exclusively in benign tumors.

Conclusions: *TSHR* variants were detected across benign, low-risk neoplasms, and malignant thyroid tumors in both pediatric and adult patients. Most were associated with benign lesions, while some occurred in low-risk neoplasms and malignant tumors, occasionally alongside known driver alterations and at higher allelic frequencies. These findings underscore the potential importance of allelic frequency in interpreting *TSHR* variants, and further studies are needed to clarify their biological and clinical significance.

Supported by the Ministry of Health of the Czech Republic in cooperation with the Czech Health Research Council under project NU21-01-00448 and MH CZ RVO 00023761.

Abstract citation ID: lvag096.1681

EP1522 - ECE_1091 - Sublingual ectopic thyroid: two cases including malignant transformation

Mirona Dinca[1], Dana Tilici[1], Daniela Ioana Iulia Greere[1], Ruxandra Costinescu[1], Beatrice Grecu[1], Adina-Ioana Onofrei[1], Arnautu Ana Maria[2], Claudia Alexandra Nacea[1] and Diana Paun[1]

[1]The University Emergency Hospital Bucharest, Bucharest, Romania; [2]Endocrinology, University Emergency Hospital Bucharest, Bucharest, Romania

Background: Ectopic thyroid tissue is a rare congenital anomaly caused by abnormal migration of the thyroid gland during embryogenesis. The lingual region represents the most frequent location, while malignant transformation of ectopic thyroid tissue is exceptionally rare. Clinical presentation is often nonspecific, leading to diagnostic delay, especially in patients with congenital hypothyroidism and poor treatment adherence.

Cases: We present two cases of sublingual ectopic thyroid tissue with distinct clinical manifestations. The first case is a 24-year-old woman with congenital hypothyroidism who discontinued levothyroxine therapy for more than 10 years. She was

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

admitted for abdominal and chest pain associated with pyrosis. Laboratory evaluation revealed severe hypothyroidism (TSH >100 μIU/mL). Cervical ultrasound showed absence of thyroid tissue in the anterior neck. Technetium-99m pertechnetate scintigraphy followed by SPECT/CT demonstrated radiotracer uptake at the sublingual level, confirming ectopic thyroid tissue. Levothyroxine replacement therapy was reintroduced, with significant clinical and biochemical improvement, and surgical management was postponed.

The second case involves a 54-year-old male smoker with a history of congenital hypothyroidism and long-term treatment discontinuation, admitted for hematemesis, dysphonia, and progressive dysphagia. Biochemical evaluation showed severe hypothyroidism (TSH >48 μIU/mL, low FT4 and FT3). Upper gastrointestinal endoscopy revealed a large, intensely vascularized tumor at the base of the tongue. Cervical ultrasound did not reveal eutopic thyroid tissue, while scintigraphy and SPECT/CT confirmed the diagnosis of sublingual ectopic thyroid. After preoperative embolization of the feeding arteries, surgical excision was performed. Histopathological examination revealed poorly differentiated papillary thyroid carcinoma arising in ectopic thyroid tissue. Levothyroxine dose was increased, and the patient was referred for radioiodine therapy.

Conclusions: These cases illustrate the wide clinical spectrum of sublingual ectopic thyroid tissue and highlight the exceptional risk of malignant transformation. Awareness of this entity and appropriate use of functional imaging are essential for accurate diagnosis and management. Long-term follow-up is crucial in patients with congenital hypothyroidism, particularly in those with poor treatment adherence.

Abstract citation ID: lvag096.1682

EP1523 - ECE_2140 - Refractory hypothyroidism after radioactive iodine therapy for Graves' disease: the combined effect of TSH receptor–blocking antibodies and impaired levothyroxine absorption

Birgul Kirel[1,2], Merve Akkaş[3], Zeren Barış[4], Özben Işıklar[5], Evin Kocaturk[5], Murat Yılmaz[1], Zeynep Karkın[1] and Göknur Yorulmaz[6]

[1]Pediatrics, Pediatric Endocrinology, Eskişehir Osmangazi University Faculty of Medicine, Eskişehir, Türkiye; [2]Pediatric Endocrinology, Eskisehir Osmangazi University Hospital, Eskisehir, Türkiye; [3]Pediatric Endocrinology, Eskişehir Osmangazi University Faculty of Medicine, Eskisehir, Türkiye; [4]Pediatrics, Pediatric Gastroenterology, Eskişehir Osmangazi University Faculty of Medicine, Eskişehir, Türkiye; [5]Medical Biochemistry, Eskişehir Osmangazi University Faculty of Medicine, Eskişehir, Türkiye; [6]Internal Medicine, Endocrinology, Eskişehir Osmangazi University Faculty of Medicine, Eskişehir, Türkiye

Introduction: Refractory hypothyroidism is a rare and challenging condition in which biochemical and/or clinical improvement cannot be achieved despite standard levothyroxine (LT4) therapy. Here, we present a patient who developed hypothyroidism following radioactive iodine (RAI) therapy for Graves' disease and failed to respond despite very high doses of oral thyroid hormone replacement.

Case Presentation: A 16-year-old female patient diagnosed with Graves' disease failed to achieve remission after approximately one year of antithyroid drug therapy and subsequently received RAI treatment. After the development of hypothyroidism, LT4 therapy was initiated and the dose was gradually and carefully increased over a period of approximately 10 months up to 6 μg/kg/day; however, no biochemical response was obtained. The patient was positive for TSH receptor–blocking antibodies, while tests for celiac disease and stool examinations for malabsorption were negative. The thyroxine absorption test also showed no response. Liothyronine (T3) at a dose of 50 μg/day was added for one month, but no improvement was observed.The patient had no history of additional medication use, and poor compliance as well as analytical laboratory errors were excluded. Upper gastrointestinal endoscopy revealed chronic gastritis and *H. pylori* infection. Despite appropriate *H. pylori* eradication therapy, the patient remained unresponsive to oral treatment. Therefore, intravenous LT4 was administered for four days at a dose of 100 μg/day. Following this treatment, free T4 levels increased from 0.61 ng/dL to 0.95 ng/dL and TSH levels decreased from 95 μIU/mL to 69 μIU/mL.To enhance gastric absorption, vitamin C supplementation, a lactose-free diet, and oral liquid LT4 at a dose of 200 μg/day were reintroduced. With this treatment approach, euthyroidism was achieved.

Conclusions: In conclusion, both TSH receptor–blocking antibodies and impaired LT4 absorption due to chronic gastritis and *H. pylori* infection were identified in this patient with autoimmune thyroid disease. This case highlights the diagnostic difficulties and therapeutic options in the management of refractory hypothyroidism.

Keywords refractory hypothyroidism, levothyroxine malabsorption, TSH receptor–blocking antibodies, thyroxine absorption test, liquid levothyroxine

Abstract citation ID: lvag096.1683

EP1524 - ECE_2432 - Severe hyperkalemia in a hypothyroid patient presenting to the emergency department: a case of Autoimmune Polyendocrine Syndrome type 2

Nikoloz Tepnadze[1], Tamaz Mgaloblishvili[1], Nino Gvajaia[1], Salome Kaldani[2], Mariam Bardadze[2], Ana Khvedelidze[2], Tamar Didbaridze[3] and Karen Grigoryan[4]

[1]Endocrinology, Tbilisi State Medical University, Tbilisi, Georgia; [2]Tbilisi State Medical University, Tbilisi, Georgia; [3]Department of Microbiology, The First University Clinic of Tbilisi State Medical University, Tbilisi, Georgia; [4]Endocrinology, Tbilisi State Medical University, Tbilisi State Medical University The First University Clinic, Tbilisi, Georgia

Background: Schmidt syndrome, also known as Autoimmune Polyendocrine Syndrome type 2, is a rare condition characterized by the coexistence of autoimmune hypothyroidism and primary adrenal insufficiency. This case highlights the diagnostic challenges and clinical features of Schmidt syndrome in a patient with existing thyroiditis.

Case Presentation: A 32-year-old woman with a known history of Hashimoto's thyroiditis, treated with 150 μg of L-thyroxine, presented to the emergency department with severe fatigue and weakness. She had stopped her thyroid medication 6 months prior due to persistent nausea. On presentation, laboratory tests showed severe hyperkalemia (7 mmol/L) and elevated creatinine (200 μmol/L), with no genitourinary symptoms. Despite initial treatment for hyperkalemia, her potassium levels fluctuated.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Clinically, the patient was conscious and hemodynamically stable (HR-90/min, BP-115/90 mmHg) with generalized hyperpigmentation noted on physical examination.

Her medical history was significant for an emergency admission four months earlier due to shock, severe weakness, and unexplained hyperpigmentation. Blood cortisol levels were sampled, and hydrocortisone (100 mg) was administered empirically prior to results. Glucocorticoid therapy was subsequently continued**.** Her TSH was markedly elevated (95 mIU/L), and ACTH levels were also found to be elevated, cortisol level was significantly low, given the recurrent hyperkalemia, characteristic pigmentation, and autoimmune background, primary adrenal insufficiency was strongly suspected indicating primary adrenal insufficiency. Further testing revealed elevated renin levels and low aldosterone, supporting the diagnosis of concomitant Addison's disease. Given the recurrent hyperkalemia, characteristic pigmentation, and autoimmune background, primary adrenal insufficiency was strongly suspected.

Investigations: Hormonal evaluation demonstrated profoundly decreased serum cortisol (0.553 µg/dL) with markedly elevated ACTH (1925 pg/mL), confirming primary adrenal insufficiency. Aldosterone was decreased with elevated renin (134 µIU/mL), consistent with mineralocorticoid deficiency. Additional findings included hyponatremia (Na^+ 125 mmol/L), severe hypothyroidism with elevated TSH (95.25 mIU/L) and decreased free T4 (0.378 ng/dL), elevated anti-thyroid peroxidase antibodies (343 IU/mL), and elevated 21-hydroxylase antibodies (131 U/mL), confirming autoimmune etiology.

Conclusions: Schmidt syndrome should be considered in patients with autoimmune hypothyroidism who present with unexplained fatigue, hyperkalemia, and hyperpigmentation. Hypothyroidism alone does not cause hyperkalemia; therefore, severe electrolyte disturbances should prompt evaluation for Addison's disease. Early recognition of Schmidt syndrome with corticosteroid therapy and lifelong adrenal–thyroid monitoring is essential to prevent adrenal crises and misdiagnosis.

Keywords Autoimmune Polyendocrine Syndrome type II (APS Type 2), Hashimoto's thyroiditis, hyperkaleimia, addison syndrome

Abstract citation ID: lvag096.1684

EP1526 - ECE_1696 - The potential autoimmune thyroid effect of daratumumab treatment

Hana Matijaca[1], Klara Brčić[1], Fran Petričević[1,2], Ana Matijaca[3,4], Petar Gaćina[1,5] and Zvjezdana Genzić[1]
[1]*Department of Haematology, University Clinical Hospital Sisters of Mercy, Zagreb, Croatia;* [2]*Department of Haematology, Sisters of Charity Hospital, Zagreb, Croatia;* [3]*Department of Endocrinology, Diabetes, Diseases of metabolism and Clinical Pharmacology, Clinical Hospital Dubrava, Zagreb, Croatia;* [4]*Endocrinology and Diabetes, Clinical Hospital Dubrava, Zagreb, Croatia;* [5]*Faculty of Stomatology, University of Zagreb, Zagreb, Croatia*

Background: The human anti-CD38 monoclonal antibody daratumumab is currently licensed for the treatment of the plasma cell malignancy, multiple myeloma (MM). Beside targeting and eliminating malignant plasma cells, it also affects various immune cells, leading to complex immunomodulation, ultimately boosting the immune response against the cancer. However, the immune response can induce autoimmune reaction affecting the thyroid gland.

Aim: To determine if the cohort of the MM patients treated with daratumumab-containing regimens had differences in thyroid laboratory tests (TSH, FT4, anti-TPO) compared to patients treated without daratumumab.

Methods: A single-center retrospective observational analysis at Sisters of Mercy University Clinical Hospital (Zagreb, Croatia) was conducted in 43 MM patients with available thyroid laboratory data (TSH, fT4 and anti-TPO). The patients were categorized into two groups based on treatment exposure (group A daratumumab-containing therapy, $n = 19$; group B no daratumumab therapy, $n = 24$). The patients with previously known thyroid dysfunction were excluded.

Results: Group A received daratumumab-containing regimens: DRD ($n = 12$, 63.2%), Dara-VMP ($n = 3$, 15.8%), Dara-VCD ($n = 2$, 10.5%), Dara-VRD ($n = 2$, 10.5%). In group B VRD was used in 16 patients (66.67%), all other regimens (KRD, MPT, RD, IRD, VRD-lite, KD, VCD, VD) occurred in 1 patient (each 4.17%). The two groups were broadly comparable in age (Mean ± SD: 72.05 ± 6.05 vs 69.29 ± 7.78 years) and sex distribution (males $n = 12$, 63.2%; $n = 15$, 62.5% in group A and B, respectively). Median [IQR] time of treatment exposure was 10 [44] months in group A and 3.5 [25.5] months in group B. Most patients had TSH within the normal range (0.79-4.79 mIU/L). Median TSH was higher in group A (2.55[2.01] mIU/L) than in group B (1.51[1.31] mIU/L). ln (TSH) between-group difference was borderline ($P = .049$). FT4 did not differ between groups ($P = .501$). Median anti-TPO was higher in group A (42.9[11] kIU/L) than in group B (16.55[33.75] kIU/L); anti-TPO values differed between groups ($P = .001$). All values were below ULN (85.8 kIU/L).

Conclusions: Anti-TPO was higher in the daratumumab group and TSH showed borderline difference with higher values in daratumumab group, although values remained within the reference range. FT4 was similar between groups. This could suggest a potential subclinical autoimmune effect of daratumumab treatment. Limitations include retrospective design, small sample size, variable timing of thyroid testing, and potential confounding by other anti-myeloma therapies. Larger prospective studies with serial thyroid testing are needed to confirm these findings.

Abstract citation ID: lvag096.1685

EP1527 - ECE_2459 - Atypical Graves' orbitopathy with elevated serum IgG4: a report of two cases

Evangelia Makri, Georgios Kostopoulos and Foteini Adamidou
Endocrinology, Hippokration General Hospital of Thessaloniki, Thessaloniki, Greece

Background: Graves' orbitopathy (GO) presents with heterogenous clinical, serological, and radiological features. Occasional atypical presentations may overlap with IgG4-related ophthalmic disease (IgG4-ROD). Shared characteristics may create significant diagnostic uncertainty and therapeutic challenges.

Case Presentations: We describe two patients with atypical Graves' orbitopathy raising the suspicion of IgG4-ROD.

Case 1: A 53-year-old female presented with right upper eyelid discomfort and edema while euthyroid. Initial thyroid-stimulating immunoglobulins (TSI) and thyroid

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

autoantibodies were negative. Orbital MRI demonstrated normal extraocular muscles with an ill-defined T2 hyperintense enhancing lesion of the right lacrimal gland, suggestive of dacryoadenitis. Lacrimal gland biopsy revealed sparse IgG-positive plasma cells and few IgG4-positive cells, with an IgG4/IgG ratio <2%, excluding IgG4-related dacryoadenitis. Despite multiple courses of intravenous methylprednisolone, the patient developed progressive unilateral exophthalmos, eyelid edema, lid lag, and gaze-evoked pain. One year later, TSI became positive, and hyperthyroidism developed. Repeat imaging showed extraocular muscle edema, dacryoadenitis, mild apical crowding, and bilateral proptosis. Additional immunosuppression with mycophenolate mofetil led to marked clinical improvement, although eyelid edema persisted in the context of ongoing smoking.

Case 2: A 70-year-old was referred by the Neurology service for evaluation of diplopia at lateral gaze without soft tissue inflammation. Hyperthyroidism with elevated serum TSI and IgG4 levels was found. Orbital MRI demonstrated bilateral enlargement and enhancement of the superior and inferior rectus muscles predominantly, with increased orbital fat. The patient was treated with intravenous methylprednisolone pulses and intraorbital corticosteroid injections, resulting in complete resolution of diplopia despite persistent radiological abnormalities. No systemic involvement was documented.

Conclusions: These cases illustrate that uncommon presentations of GO may raise the suspicion of IgG4-ROD. The distinction in the absence of early thyroid autoimmunity is difficult, and tissue biopsy is necessary. In case of elevated serum IgG4 and GO, follow-up for systemic disease is prudent.

Abstract citation ID: lvag096.1686

EP1530 - ECE_3398 - BRAF mutation and tumor growth kinetics during active surveillance of papillary thyroid microcarcinoma

Ki-Hyun Baek
Seoul, South Korea

Background: We investigated tumor-volume doubling time (TVDT) during active surveillance of papillary thyroid microcarcinoma (PTMC) and reviewed clinical factors including BRAF mutation associated with tumor progression.

Methods: Patients with papillary thyroid microcarcinoma (PTMC) who deferred surgery for more than one year after diagnosis between 2014 and 2021 and were followed until 2023 were enrolled. Inclusion criteria were papillary thyroid carcinoma confirmed by fine-needle aspiration cytology (Bethesda categories V-VI), maximal tumor diameter ≤1 cm, and available BRAF mutation testing.

Results: A total of 85 patients were included. The median age was 49 years, and 63 patients (74%) were female. The positivity rate for BRAF mutation was 51% in the study cohort, and 16 patients (19%) showed rapid-growing disease, defined by a TVDT of less than five years. The median follow-up duration was 4.4 years, and 23 patients (27%) underwent surgery after a median of 3.2 years. When TVDT groups were analyzed using logistic regression, sonographic features with microcalcification were associated with tumor growth in binary regression (odds ratio for the group combining slowly and rapid-growing disease was 2.80 [95% CI 1.09-7.22], $P = .033$), and BRAF mutation was associated with rapid-growing disease in multinomial regression (odds ratio for rapid-growing disease was 4.58 [95% CI 1.11-18.94], $P = .036$).

Conclusions: BRAF mutation is presumed to be associated with tumor progression and may help predict growth of PTMC. Genetic testing including BRAF testing may help distinguishing rapid-growing thyroid cancer.

Abstract citation ID: lvag096.1687

EP1531 - ECE_3420 - Thyroid lymphoma case series: sonographic "pseudothyroiditis" and the role of core biopsy

Nuphar Vinegrad[1,2] and Uri Yoel[1,2]
[1]*Endocrinology, Soroka, University Medical Center, Be'er Sheva, Israel;* [2]*Ben-Gurion University of the Negev, Beer Sheva, Israel*

Introduction: Thyroid lymphoma is an exceptionally rare malignancy, representing <5% of thyroid cancers and ~2.5% of all lymphomas. It typically presents as a rapidly enlarging neck mass, often masquerading as benign goiter or aggressive carcinoma. Recent 2025 population-based data from the Tokyo Cancer Registry and the SEER database indicate that while histology-specific management significantly improves survival, diagnostic delays remain common. We present five cases highlighting the unique sonographic appearance of thyroid lymphoma and the critical role of core-needle biopsy (CNB) in avoiding unnecessary surgery.

Case Series: Five patients (median age 55, range 21-85; 3M/2F) presented with rapidly growing goiters (1-5 months duration) and compressive symptoms. Point-of-care ultrasound (POCUS) consistently revealed a distinctive "pseudothyroiditis" pattern: a markedly enlarged, heterogeneous, hypoechoic thyroid without distinct nodules, often mimicking thyroiditis despite discordant laboratory markers.

- **Patient 1 (50M):** Known Hashimoto's; initial FNA showed reactive lymphocytes. Open biopsy confirmed Diffuse Large B-cell Lymphoma (DLBCL). Treated with R-CHOP and thyroidectomy; achieved complete remission (CR).
- **Patient 2 (67F):** Poorly controlled hypothyroidism; Misdiagnosed as sub-acute thyroiditis. Ultrasound-guided CNB confirmed DLBCL. Achieved CR with R-CHOP alone.
- **Patient 3 (55M):** Large goiter and cervical lymphadenopathy. FNA was inconclusive (medullary vs lymphoproliferative). Open biopsy confirmed Low-grade Follicular Lymphoma. Achieved CR with Anti-CD20 + Bendamustine.
- **Patient 4 (21M):** Thyroid appeared normal except for islands of "thyroiditis-like" tissue and lymphadenopathy. FNA was Bethesda III; CNB diagnosed Stage IV Hodgkin Lymphoma. Successfully treated with ABVD.
- **Patient 5 (85F):** Elderly patient with aggressive B-cell lymphoma confirmed via Tru-cut (CNB). Rapidly initiated R-CHOP therapy.

Discussion: These cases emphasize that thyroid lymphoma frequently presents with a "pseudothyroiditis" sonographic appearance and a rapidly growing goiter, which, when paired with an inconclusive FNA, often leads to diagnostic delay or radical surgery. Our series aligns with recent literature suggesting that while age ≥70 and DLBCL histology are predictors of poorer

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

outcomes, early diagnosis via CNB facilitates rapid initiation of chemo-immunotherapy. This shift toward CNB (Cases 2, 4, 5) allowed for definitive diagnosis without the morbidity of diagnostic thyroidectomy.

Conclusions: Thyroid lymphoma should be suspected in any rapidly enlarging goiter exhibiting a "thyroiditis-like" sonographic pattern, especially when FNA is non-diagnostic. Core biopsy serves as a vital, minimally invasive tool for definitive classification, enabling excellent prognostic outcomes through modern multimodal therapy.

Abstract citation ID: lvag096.1688

EP1532 - ECE_1005 - Comparison of efficacy of Liothyronine (T3) 50 mcg + Levothyroxine (T4) combination therapy Vs T3 25 mcg + T4 therapy vs T4 therapy alone on body weight in patients with hypothyroidism followed for 6 months

Vishal Gupta and Vaishali Teli
Diabetes and Endocrinology, VG-ADVANTAGE Diabetes Thyroid & Endocrine Center, Mumbai, India

Aim & Objectives: Compare the efficacy of Liothyronine (T3) 50 mcg/day + Levothyroxine (T4) combination therapy Versus T3 25 mcg/d+T4 combination therapy Versus T4 therapy alone on clinical parameters (weight-kg [W], BMI-kg/m^2, systolic BP mm of Hg {SBP}/Diastolic BP {DBP}, Lipid Profile-mg/dl (TC, LDL, TG, HDL), highly sensitive C-reactive protein-mg/L (hs-CRP) & Thyrotropin stimulating hormone-mIU/L (TSH) evaluated every 2-3 months over 6 months period.

Methodology: Between Mar' 24-May '24, 414 patients receiving 50 mcg T3, 25 mcg T3 & T4 for autoimmune hypothyroidism were analysed retrospectively. They were divided into 3 groups & propensity score matched.

Group 1: (G1) 50 pt's received T3{50 mcg} + T4 therapy,
Group 2: (G2) 189 pt's received only T4 Therapy &
Group 3: (G3) 175 pt's received T3 {25 mcg} + T4 therapy.

Data Analysis: Baseline characteristics of G1 vs G2 vs G3 groups were analysed using descriptive statistics. Categorical variables were described by frequencies and %, and continuous variables by using {mean ± SD}. Paired t test & unpaired t test was used to compare groups. P value <.05 was considered significant (S).

Results: Baseline (B) characteristics: G1 ($n = 50$), G2 ($n = 189$), and G3 ($n = 175$) were well-matched: TSH [G1 (4.86 ± 3.66) vs G2 (5.96 ± 10.33) vs G3 (8.00 ± 19.47) μIU/mL, $P = .261$] except for Weight [G1 (87.61 ± 19.13) vs G2 (69.99 ± 13.82) vs G3 (74.89 ± 17.27) kg, $P < .001$], DBP [G1 (85.22 ± 9.03) vs G2 (77.72 ± 9.60) vs G3 (81.70 ± 10.88) mmHg, $P < .001$].

Average Age: Age [G1 (39.94 ± 9.45) vs G2 (43.01 ± 10.52) vs G3 (40.33 ± 11.69) years]

G1 (B to 6 months): S reduction W, BMI, TSH, TC; LDL-C.
G2 (B to 6 months): S reduction in SBP, TSH, TC, LDL-C, TG.
G3 (B to 6 months): S reduction in W, BMI, TSH, TC, LDL-C.

Differences between G1 & G2 & G3 at 6 months: TSH [G1 (3.59 ± 3.59) vs G2 (4.47 ± 10.51) vs G3 (5.98 ± 19.74), $P = .479$]. S reduction seen in hsCRP [G1 (2.01 ± 4.37) vs G2 (0.12 ± 2.75) vs G3 (−0.06 ± 2.22); $P < .001$], W [G1 (2.63 ± 4.78) vs G2 (0.58 ± 6.00) vs G3 (1.13 ± 2.95); $P = .026$] favouring G1.

Conclusions: T3 (50 mcg)/T4 combination therapy significantly reduced body weight & hsCRP in comparison to only T4 therapy & T3 (25 mcg)/T4 combination therapy, while having no negative impact on BP.

Abstract citation ID: lvag096.1689

EP1533 - ECE_2812 - Graves' orbitopathy remission after autologous stem cell transplantation in a patient with multiple myeloma

Veronika Špačková, Jakub Radocha, Pavel Cee and Filip Gabalec
IV Department of Internal Medicine, University Hospital Hradec Králové, Hradec Králové, Czech Republic

Introduction: Endocrine orbitopathy is the most common extrathyroidal manifestation of Graves' disease, characterized by an autoimmune attack on retro-orbital tissues. It significantly impairs quality of life. In severe cases can even be sight-threatening, so proper and timely therapy is crucial. Treatment primarily targets immune system suppression or modulation through different drugs and strategies.

Observation: We present the case of a 68-year-old patient with common comorbidities such as arterial hypertension and dyslipidaemia, but most importantly, with a history of multiple myeloma. She was presented to our department with Graves' disease complicated by orbitopathy. The patient exhibited typical manifestations of thyrotoxicosis alongside classic orbital involvement, including proptosis, swollen eyelids, and redness of the eyes. Given the severity and activity of the orbitopathy, treatment had to be initiated. We started thyrostatic treatment, followed by intravenous glucocorticoid pulses. At the same time, she was diagnosed with a relapse of multiple myeloma. In parallel to our treatment, she underwent chemotherapy consisting of bortezomib, lenalidomide and dexamethasone followed by an autologous haematopoietic stem cell transplant with melphalan conditioning. Throughout corticotherapy and chemotherapy, the patient showed a slight improvement in orbital symptoms. However, soon after stem cell transplant, the patient was completely relieved of symptoms and the orbitopathy seemed to be clinically inactive. The patient also achieved an ongoing complete remission of multiple myeloma. She tolerated the combined immunosuppressive therapy without major infectious or other complications.

Conclusions: This case shows the immunological reset achieved through high-dose corticotherapy, chemotherapy, and stem cell rescue. These addressed both active hematologic malignancy and autoimmune thyroid disease with Graves orbitopathy. This rare coincidence was beneficial in the management of thyroid eye disease. This highlights the importance of multidisciplinary coordination. In this case, the collaboration between the endocrinology, haematology, and ophthalmology teams was essential for success.

Abstract citation ID: lvag096.1690

EP1534 - ECE_2132 - Papillary thyroid carcinoma—a rare case of vanishing tumor after fine-needle aspiration cytology

Mariana Agapito Fonseca[1], Teresa Alegria Neto[1], Catarina Isabel Lopes[1], Miguel António Duarte[1], Marta Vaz Lopes[1,2], Mariana De Griné Severino[1,2], Ana Gomes[1,2], Ana Paula Barbosa[1,2] and Ema Lacerda Nobre[1,2]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]ULS Santa Maria, Endocrinology, Diabetes and Metabolism Department, Lisbon, Portugal; [2]Lisbon, Portugal

Background: Fine-needle aspiration cytology (FNAC) is an effective diagnostic tool in thyroid nodular disease, contributing to differentiation between benign and malignant lesions. Procedural complications are rare. However, the trauma caused by puncture may result in morphological changes in the nodules, expressed in variable forms, from infarction to completely replacing it (vanishing tumors). This happens in 1%-2% of papillary thyroid carcinomas (PTC) submitted to FNAC, with resultant difficulty in the interpretation of histopathologic material.

Case Report: A 47-year-old woman presented in primary care with unspecific cervical discomfort. She had no evidence of thyroid dysfunction, compressive symptoms, personal history of head and neck radiation or family history of thyroid cancer. Thyroid ultrasound showed a 30 mm isoechoic nodule with regular margins on the left lobe (EUTIRADS-3) and a 9 mm solid, markedly hypoechoic, non-oval and irregular nodule on the right lobe (EUTIRADS-5), without suspicious lymph nodes. She was referred to Endocrinology and FNAC was performed. The left lobe EUTIRADS-3 nodule was benign and the right lobe EUTIRADS-5 nodule was consistent with PTC. The multidisciplinary team decided for total thyroidectomy. The procedure had no complications. Gross pathology showed the known benign nodule on the left lobe. On the right lobe, there was only a 5 mm dark-brown nodule, without any viable PTC tissue. Immunohistochemistry was not performed. Facing the absence of carcinoma tissue, the cytology specimen was reviewed by an independent pathologist, who confirmed the preoperative diagnosis of PTC. Given the definitive confirmation of PTC on cytology and the absence of residual malignant cells in histology, a diagnosis of vanishing PTC was made, most likely due to infarction induced by FNAC.

Conclusions: This case illustrates that recognition of vanishing thyroid tumors, along with reassessment of the FNAC specimen, is pivotal for a correct diagnosis. The biggest challenge now lies on the follow-up of this patient, since there are no guidelines on further management of vanishing thyroid tumors. Since it was a microcarcinoma and patient was submitted to total thyroidectomy, prognosis seems to be highly favorable.

Abstract citation ID: lvag096.1691

EP1535 - ECE_2977 - Thyroid eye disease and myasthenia-myositis-myocarditis overlap syndrome: a cluster of rare immune-related adverse events secondary to pembrolizumab

Maria del Mar Garcia Gonzalez, Vanessa Triviño Yannuzzi, Isabel Huguet, Luyi Zeng, Laura Rambla Aguilar, Natalia Salvador Peiro, Marta Leon del Campo, Mikaela Zubillaga, Maria Llavero Valero, Olalla Meizoso-Pita, Alberto García Piorno, Elena Carrillo Lopez, Iciar Martin Timon, Inmaculada Moreno-Ruiz and Cristina Sevillano-Collantes
Endocrinology, Hospital Universitario Infanta Leonor, Madrid, Spain

A 72-year-old male was diagnosed in June 2024 with Stage IV(pT2N3M0) well-differentiated squamous cell carcinoma of the penis, treated with total penectomy and urethrostomy. Adjuvant chemotherapy combined with Pembrolizumab was initiated (1st cycle:07/2024, 2nd cycle:08/2024). Subsequently, maintenance of Pembrolizumab was started in 12/2024 after dermal metastases were observed in the scrotum. He was admitted on 01/31/2025 due to right eyelid ptosis, without dyspnea, dysphonia, diplopia, or motor deficits. Neurological examination revealed right eye ptosis, normal oculomotor movements, no sensory or motor alterations. Initially, a myasthenic syndrome in the context of immunotherapy was suspected due to the symptoms and positive anti-AChR antibodies (5.49 nmol/L).

During the etiological study, the following were observed: TSH: 107.28 µU/mL (0.35-5.5); free-T4: <0.20 ng/dl (0.77-1.76); Anti-TPO antibodies: 1289 UI/mL (<60); TSH receptor antibodies: <0.80 U/L(<1.75); and Anti-thyroglobulin antibodies: 113.30 UI/mL (<1.30). Previous studies were reviewed: TSH:0.01 µU/mL and free-T4: 2.93 ng/dl in 10/2024; thyroid function had been normal in 03/2024 and 08/2024. The assessment is consistent with chronic autoimmune thyroiditis/Hashimoto's thyroiditis precipitated by immunotherapy, with an initial phase of thyrotoxicosis followed by overt hypothyroidism. Treatment with levothyroxine was started reaching a total dose of 112 mcg.

Given the presence of eyelid ptosis and thyroid dysfunction, an orbital MRI was requested due to suspicion of thyroid eye disease. Results showed: signs of bilateral proptosis with increased fat space in the intra and extra-axial compartments, without focal or diffuse thickening of the orbital musculature and no abnormalities in the optic nerves. Thyroid eye disease was confirmed in the context of autoimmune hypothyroidism precipitated by immunotherapy. The patient showed progressive improvement and stability with eyelid asymmetry but no signs of fatigability, leading to discharge on 02/17/2025.

He was readmitted on 03/14/2025 due to motor deficits in the bulbar, cervical, and proximal limb territories, with clinical signs of fatigability. Given the positive anti-AChR results, generalized Myasthenia Gravis(MGFA IVb) was suspected, and Prednisone 1 mg/kg/day was initiated. Laboratory tests revealed elevated troponins (1336 pg/mL, normal<60), elevated CPK (1306 U/L), and hypertransaminasemia (ALT 70 mg/dl, normal <49; AST 115 mg/dl, normal <37), consistent with myocarditis, myositis, and Myasthenia Gravis overlap syndrome secondary to immunotherapy.

While these conditions are rarely reported individually, this is the first case report describing the concomitant occurrence of thyroid eye disease in the context of Hashimoto's thyroiditis and the overlap syndrome of myocarditis, myositis, and Myasthenia Gravis secondary to immune checkpoint inhibitors, to the best of our knowledge.

Abstract citation ID: lvag096.1692

EP1537 - ECE_3736 - Challenges in levothyroxine absorption in a patient with hashimoto's thyroiditis after bariatric surgery: a case report

Liana Jashi[1], Tamar Shervashidze[2], Tamar Peshkova[3], Lela Beridze[3], Koba Kamashidze[4], Rusudan Kvanchakhadze[5], Ana Abashidze[6] and Meri Beridze[7]
[1]Endocrinology, Avicenna—Batumi Medical University, Solomedi, Batumi, Georgia; [2]Avicenna—Batumi Medical University, T'bilisi, Georgia; [3]Batumi Shota Rustaveli State University, Batumi, Georgia;

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[4]University of Georgia, T'bilisi, Georgia; [5]David Agmashenebeli University of Georgia, T'bilisi, Georgia; [6]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia; [7]Caucasus University, T'bilisi, Georgia

Background: Achieving stable euthyroidism in patients with Hashimoto's thyroiditis may be challenging despite regular levothyroxine therapy. Gastrointestinal factors, dietary habits, and prior bariatric surgery can significantly affect levothyroxine absorption.

Case Presentation: A 36-year-old female bank employee presented with fatigue, generalized weakness, mild weight gain (≈2 kg over one year), cold intolerance, and morning facial edema. She had a 6-year history of Hashimoto's thyroiditis treated with levothyroxine 50 µg/day. Family history was positive for autoimmune hypothyroidism. Four years earlier, she had undergone sleeve gastrectomy for obesity. She was a non-smoker and did not consume alcohol.

Physical examination revealed a BMI of 27.5 kg/m^2, blood pressure 118/75 mmHg, and heart rate 62 bpm. Facial puffiness, dry skin, and emotional lability were noted. The patient reported regular morning consumption of fiber-rich food (bran prepared with milk).

Laboratory evaluation showed mildly elevated TSH (4.8 mIU/L), FT4 at the lower limit of normal, and markedly increased anti-TPO antibodies (190 IU/mL). Inflammatory markers, vitamin D, ferritin, and vitamin B12 levels were within normal ranges. Thyroid ultrasound demonstrated hypoechoic focal areas and hypovascularization.

Despite several levothyroxine dose adjustments, TSH levels fluctuated between 0.15 and 5.8 mIU/L. The main clinical concerns were progressive weight gain and deterioration of well-being.

Management and Outcome: Levothyroxine dose was increased by 12.5 µg, and the timing of administration was changed to bedtime, at least three hours after the last meal. After six weeks, TSH decreased to 2.9 mIU/L, and the patient reported improved energy levels and overall well-being.

Conclusions: In patients with a history of bariatric surgery and specific dietary habits, the efficacy of levothyroxine may depend not only on the dose but also on the timing of administration. An individualized therapeutic approach is essential to achieve stable euthyroidism.

Abstract citation ID: lvag096.1693

EP1540 - ECE_1061 - SPECT/CT textural features in differentiated thyroid cancer recurrence prognosis after radioiodine treatment

Sema Alieva[1], Alexey Trukhin[1], Tatyana Belotserkovskaya[1], Mikhail Maltsev[2], Almaz Manaev[2], Sergey Serzhenko[1], Konstantin Slashchuk[1] and Marie Reinberg[1]
[1]Moscow, Russia; [2]National Research Nuclear Institute "MEPhI", Moscow, Russia

Background: modern medical image analysis methods today include radiomics approaches, but implementation in practice across is still complicated. Promising field for textural features application is single-photon emission computed tomography combined with computed tomography (SPECT/CT). In this study we developed a diagnostic model for assessing differentiated thyroid cancer (DTC) recurrence based on SPECT/CT findings after radioiodine therapy (RIT), using texture features.

Materials and Methods: analysed group of patients includes 53 patients with DTC from 18 to 92 years: 24 with complete biochemical and structural remission after RIT; 29 with structural or biochemical recurrence after one or more courses of RIT and/or radioiodine refractoriness. First step in textural features extraction was manual expert lesion localization was performed with volume-of-interest (VOI) mask creation $3\times3\times3$-$11\times11\times11$ voxels centered on the maximum count voxel. Gray-level co-occurrence matrix, gray-level run-length matrix and gray-level size zone matrix matrices derived from created SPECT/CT all created masks. Count in voxels normalised to 128 and 256 scales.

Results: Best logistic regression model for metastatic lesions recurrence $\log\frac{p}{1-p} = 1.609x_1 - 0.730x_2 + 1.037x_3 + 1.553x_4 + 0.671x_5 - 0.855$ demonstrates AUC of 0.92 (0.78-1.00), where x_1—DiscretisedIntensitySkewness_11_128, x_2—NormalisedZoneSize NonUniformity_9_128, x_3—IntensityHistogramMeanAbsolute Deviation_5_128, x_4—DiscretisedIntensitySkewness_11_256, x_5—IntensityHistogramMeanAbsoluteDeviation_5_256. Numbers 5, 9, 11 are stand for mask size, 128 and are stand for normalization scale. Model for residual thyroid tissue reccurance (close tissue localization), due to cross textural contamination, shows low prediciton effectivness AUC 0.63 (0.53-0.69).

Conclusions: SPECT/CT textural features demonstrate high prognostic power for metastatic lesions recurrence and may be used for additional risk stratification. The effect of textural contamination limit application of method in residual thyroid tissue. Textural feature analysis has high potential for DTC radioiodine therapy personalization and should be compared to absorbed dose methods.

Abstract citation ID: lvag096.1694

EP1541 - ECE_1614 - Radiofrequency ablation as a minimally invasive treatment for recurrent papillary thyroid carcinoma: a four-case experience

Maria Chrysoula Tatarida Palla[1], Aspasia Drosou[1], Georgia Samakidou[1], Olga Tsantarlioti[1], Nikoletta Mirtsou[1], Eleni Kotsi[1], Sotiroula Adamidou[1], Fani Chaikali[1], Demosthenes Mazarakis[1], Achilleas Meskos[1], Pyrros Gkousis[2], Anna Drakopoulou[1], Victoria Kaltzidou[1], Eirini Veniou[1] and Myrsini Gkeli[2]
[1]Endocrinology, Metaxa Cancer Hospital Piraeus, Athens, Greece; [2]Radiology, General Hospital "Agios Savvas", Athens, Greece

Papillary thyroid carcinoma (PTC) accounts for approximately 80%-85% of all thyroid cancers, with cervical lymph node metastases (CLNM) occurring in 40%-90% of patients. Although surgery and radioactive iodine (RAI) therapy remain the first-line treatments for recurrent PTC and nodal metastases, many patients become unsuitable for further surgery due to multiple prior operations, challenging lymph node locations, or poor clinical condition. Ultrasound-guided radiofrequency ablation (US-RFA) has emerged as a minimally invasive alternative, offering effective local control with fewer complications compared with reoperation.

We present four patients with recurrent PTC who had previously undergone multiple surgeries with lymph node dissections and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

received more than one course of RAI therapy. All subsequently developed cervical lymph node metastases deemed unresectable because of their location or high surgical risk. Each patient was treated with US-RFA, and clinical, biochemical, and imaging outcomes were evaluated, including lymph node volume reduction and serum thyroglobulin (Tg) levels during follow-up. All four patients demonstrated substantial remission following RFA. Lymph node volume reduction rates reached approximately 74% at the first follow-up and progressed to as high as 95% at 6-12 months after treatment. Serum Tg levels decreased in all patients during follow-up, reflecting a favorable biochemical response.

Although surgery and RAI remain the standard first-line therapies for recurrent PTC, many patients are not candidates for further surgical intervention. RFA represents a promising minimally invasive alternative that provides effective local control and biochemical improvement. However, further research is needed to define optimal patient selection and long-term outcomes.

Abstract citation ID: lvag096.1695

EP1542 - ECE_2367 - Impact of thyroid autoantibodies on the prognosis of differentiated thyroid cancer: a retrospective analysis

Sinem Başak Tan Öksüz, Hilal Güngör, Murat Erdogan, Sevim Güllü, Rıfat Emral, Özgür Demir, Asena Gökçay Canpolat and Mustafa Sahin
Department of Endocrinology and Metabolism, Ankara University School of Medicine, Ankara, Türkiye

Objective: Thyroid autoantibodies (TAAs) are detected in approximately one-quarter of patients with differentiated thyroid cancer (DTC). Although persistent or rising anti-thyroglobulin (anti-Tg) is accepted as an indicator of recurrence, whether TAAs and thyroid autoimmunity detected at diagnosis affect thyroid cancer behavior remains controversial. This study aimed to investigate whether TAA positivity detected at diagnosis influences DTC recurrence and survival.

Methods: Clinical and pathological data of 275 patients followed for DTC at the Department of Endocrinology and Metabolism, Ankara University Faculty of Medicine between 2005 and 2020 were retrospectively evaluated. Patients were grouped according to anti-Tg and anti-thyroid peroxidase (anti-TPO) antibody status at diagnosis. Anti-Tg and anti-TPO levels were measured by electrochemiluminescence immunoassay in all patients.

Results: Of the 275 patients included, the median age was 43 years (17-79), and 77.1% were female. The mean follow-up duration was 8.9 ± 5.6 years, with recurrence observed in 5.5%, distant metastasis in 2.5%, and DTC-related death in 2.2% of patients. Lymphocytic thyroiditis was present in 35.6% of patients. TAA-positive patients had significantly lower age at diagnosis ($P = .047$), higher preoperative TSH levels ($P = .038$), and markedly higher frequency of lymphocytic thyroiditis ($P < .001$). Stimulated thyroglobulin levels were significantly lower in the TAA-positive group ($P < .001$). However, no significant differences were found between the two groups regarding tumor size, histopathological features, lymph node metastasis, disease stage, risk groups, or recurrence rates ($P > .05$). Multivariate analysis identified lymph node metastasis (OR:2.12, $P = .002$), advanced stage disease (Stage IV OR:10.23, $P < .001$), and high-risk group (OR:4.28, $P < .001$) as independent predictors of recurrence.

Conclusions: TAA positivity alone does not predict DTC recurrence. Recurrence risk assessment should be based on objective factors such as lymph node metastasis, disease stage, and risk stratification. Preoperative TAA positivity may be misleading by causing lower thyroglobulin measurements in the postoperative period.

Abstract citation ID: lvag096.1696

EP1544 - ECE_2767 - Immunohistochemical features of multiple parathyroid gland disease in sporadic primary hyperparathyroidism and MEN-1 syndrome

Hanum Bagirova, Rustam Salimkhanov, Tatiana Kokorina, Anna Eremkina and Natalia Mokrysheva
Endocrinology Research Centre, Moscow, Russia

Background: Multiglandular parathyroid disease (MGD) occurs in both sporadic primary hyperparathyroidism (PHPT) and multiple endocrine neoplasia type 1 (MEN-1) syndrome. These conditions can exhibit overlapping clinical and morphological features, complicating their differentiation, especially when genetic testing is unavailable or inconclusive. Immunohistochemical (IHC) analysis may offer valuable additional insights into the patterns of parathyroid involvement.

Aim: To compare the IHC profiles of MGD in sporadic PHPT (MEN-) and MEN-1-associated disease (MEN+), with a particular focus on menin expression.

Materials and Methods: A cohort of 47 patients with MGD was analyzed, including 20 with sporadic PHPT (MEN−) and 27 with MEN-1 syndrome (MEN+). IHC was performed on all tumor samples received from the patients using a panel of 8 markers: PTH, Ki-67, chromogranin A, synaptophysin, parafibromin, menin, CaSR, and VDR. Staining intensity, cellular distribution, and interglandular variability were compared between groups.

Results: Distinct IHC patterns were observed between the MEN+ and MEN- groups. Loss of nuclear menin expression was the most prominent finding, detected in 97% (85/88) of MEN+ samples. In contrast, preserved nuclear menin expression was seen in the majority of MEN- cases (67%, 30/45), establishing it as the most reliable discriminator between the groups.

Synaptophysin expression was positive in 31% of MEN− samples vs 28% of MEN+. However, MEN-1-associated lesions exhibited more uniform synaptophysin expression across multiple glands within individual patient, whereas sporadic cases showed greater interglandular variability.

The Ki-67 was generally low in both groups, with more homogeneous expression in MEN+ lesions and greater variability in MEN− cases. Chromogranin A expression was preserved in both cohorts, tending toward more diffuse staining in MEN+ and more focal positivity in MEN− lesions. Parafibromin expression was largely retained, although MEN+ lesions more frequently displayed heterogeneous nuclear staining. Expression of CaSR and VDR showed greater heterogeneity or reduction in MEN+ lesions.

Conclusions: MEN-1-associated MGD is marked by near-universal loss of menin expression and high IHC concordance

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

across glands. In contrast, sporadic MGD typically shows retained menin expression and more pronounced interglandular heterogeneity. Assessment of menin expression may serve as a useful adjunctive tool for the morphological differentiation between MEN-1 and sporadic MGD.

Abstract citation ID: lvag096.1697

EP1545 - ECE_1248 - Severe post–radioactive iodine thyroiditis causing thyroid storm and rapid-onset hypothyroidism in a young man with Graves' disease: a biphasic and iatrogenically amplified course

Aung Kaung Sett Hein[1], Rawia Adoma[2], Nini Nagyha Binti Nordin[2,3] and Oraizi Jafery[2]
[1]University Hospital North Durham, Durham, United Kingdom; [2]Bedford Hospital, Bedford, United Kingdom; [3]Medical Department, Bedford Hospital, Bedfordshire, United Kingdom

Radioiodine (RAI-131) is a standard treatment for Graves' hyperthyroidism, with hypothyroidism usually developing gradually over 8-16 weeks.[1] Following RAI, a minority of patients (1%-5%) can develop radiation-induced thyroiditis,[2] leading to a transient surge in thyroid hormone levels. Thyroid storm after RAI is rare, and the rapid progression to severe hypothyroidism is even more uncommon. Careful clinical assessment and close biochemical monitoring are essential for accurate diagnosis and management.

A 23-year-old man with Graves' disease who previously developed neutropenia on carbimazole has been maintained on propylthiouracil (PTU). Following RAI in May 2025, he developed destructive thyroiditis with extreme thyrotoxicosis (Free T4 >100 pmol/L) and clinical thyroid storm, requiring high-dose PTU and steroid therapy. Six weeks later, while still on PTU 100 mg three times daily, he transitioned rapidly into marked hypothyroidism (Free T4 1.5 pmol/L, TSH 63 mIU/L) with profound fatigue and cold intolerance. Stopping PTU led to gradual biochemical improvement. This case highlights an uncommon sequence of severe post-RAI thyrotoxicosis followed by abrupt, profound hypothyroidism, with persistent PTU use likely intensifying the transition. Following radioactive iodine (RAI) therapy, it is important that antithyroid medications are appropriately withdrawn and in cases of patients continuing on PTU, TFTs should be checked every 2-4 weeks to detect rapid changes.[3]

References

1. Horton K. Can we predict time to develop hypothyroidism after hyperthyroidism treatment? *J Nucl Med*. 2024;65(Suppl 2):242467.
2. Tay WL, Lee LMY, Tong AKT, Chng CL. Severe radiation thyroiditis after radioactive iodine for treatment of Graves' disease. *Singapore Med J*. 2021;62(9):486-491. https://doi.org/10.11622/smedj.2020039
3. National Institute for Health and Care Excellence. Thyroid Disease: Assessment and Management. NICE Guideline NG145. London: NICE; 2019 November. Last reviewed October 03, 2025. https://www.nice.org.uk/guidance/ng145

Abstract citation ID: lvag096.1698

EP1546 - ECE_1720 - Clinical remission of pretibial myxedema in a female patient with thyroid eye disease after tocilizumab treatment

Georgios Boutzios and Anastasia Nikolopoulou
Department of Pathophysiology, National and Kapodistrian University of Athens, Outpatient Clinic of Autoimmune Endocrinopathies, Athens, Greece

Introduction: Pretibial myxedema is an infrequent extrathyroidal manifestation of Graves' disease, mostly occurring in the presence of orbitopathy, with its prevalence at 0,15 per 10 000 persons with Graves' orbitopathy (GO). Similarly to the pathophysiology of GO, pretibial myxedema lesions result from fibroblast-derived glycosaminoglycans accumulation in the dermis after immune stimulation of fibroblasts from circulating cytokines and thyroid stimulating immunoglobulins (TSI). Its current management consists of topically administered corticosteroids, with variable response rates.

Case presentation: A 52-year-old woman presented with eyelid edema, redness of the conjunctiva and pretibial myxedema. She was diagnosed with Hashimoto thyroiditis in 2004 and there was a disease transformation to Graves' disease with GO in 2021. She had previously received two cycles of intravenous corticosteroids and a total thyroidectomy, achieving clinical remission after the second cycle of intravenous corticosteroids. On clinical examination, she had inactive GO as defined by a 7-point Clinical Activity Score (CAS) of 2/7, while she exhibited proptosis (20 mm in the right and 21 mm in the left eye, measured by Hertel exophthalmometer), inconstant diplopia, bilateral lagophthalmos and dry eye, suggesting moderate-to-severe disease. Dermopathy lesions located in the pretibial area of lower extremities and were nodular, painful, firm in palpation, erythematous, with non-pitting edema. She was clinically and biochemically euthyroid, with positive anti-thyroid peroxidase antibodies and high TSI levels. On orbital MRI, enlargement of all extraocular muscles with pathological intravenous contrast enhancement, indicative of active inflammation, was revealed. Given all the above, treatment with tocilizumab at a dose of 8 mg/kg every four weeks for four cycles was initiated. A complete resolution of the lesions was observed in the 5 weeks post- treatment. Reduction in CAS to 1/7 and diminution TSI levels could indicate a disease- modifying effect. Proptosis and lagophthalmos showed no improvement, while no side effects were reported and the patient remained euthyroid. In her follow—up visit, six months after tocilizumab last dose, GO remained inactive, with no pretibial myxedema recurrence and stable TSI levels.

Conclusions: This case highlights tocilizumab's efficacy for the management of inflammation in the context of steroid-resistant GO with concurrent pretibial myxedema as shown by a clinical and biochemical response.

Abstract citation ID: lvag096.1699

EP1547 - ECE_3276 - Efficacy and safety of intrathyroidal dexamethasone injections in severe subacute thyroiditis—a single center cohort study

Magdalena Stasiak[1], Magdalena Rosińska[1], Bartłomiej Stasiak[2], Renata Michalak[1] and Arkadiusz Zygmunt[1]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Department of Endocrinology and Metabolic Diseases, Polish Mother's Memorial Hospital—Research Institute, Łódź, Poland; [2]Lodz University of Technology, Łódź, Poland

Clinically severe or recurrent subacute thyroiditis frequently requires high cumulative doses of systemic steroids. Such therapy is associated with high risk of steroid-related complications.

The aim of the study was to assess efficacy and safety od intrathyroidal dexamethasone and lidocaine injections (DLI) in comparison to standard oral steroid therapy.

Methods: A total number of 60 patients were included in the study, among whom 30 were treated with DLI (study group, SG) and 30 were treated with standard protocol of oral prednisone therapy (control group, CG).

In all SG patients, a dose of 4 mg of dexamethasone with 1 mL of 2% lidocaine, was injected into each affected thyroid lobe. On the basis of the obtained clinical and biochemical results, doses were repeated every 2-5 days, as required. Before and after injections, as well as after therapy completion, the following parameters were measured: pain severity, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), thyroid stimulating hormone (TSH), free thyroxine (FT4) and free triiodothyronine (FT3). The total steroid dose required for complete remission and the therapy duration was considered primary endpoint of the study. Additionally, the frequency of recurrence and of persistent hypothyroidism in SG and CG were compared.

Results: Excellent rapid and long-term response was observed in all SG patients, with no side effects except for injection-related discomfort. After the first injection, in all SG patients pain decrease from 4-8 to 2-5 points in the numerical rating scale—NRS, as well as improvement in ESR, CRP, and thyroid parameters were observed. The mean number of doses required for total recovery were 6.83 ± 2.88, median 7, with a mean dose of dexamethasone for a total recovery 49.7 mg. The longest therapy period was 43 days, mean 26.4 days. In CG, the mean therapy period was 118.9 days and a mean dose of oral prednisone was 1702.17 mg, which is equal to 255.23 mg of dexamethasone ($P < .0001$). Three cases of recurrence (10%) were observed in both of SG and CG. Persistent hypothyroidism occurred in three patients (10%) in SG and in five patients (16.6%) in CG.

Conclusions: The efficacy and safety of DLI in SAT therapy were excellent and the method was demonstrated to be significantly more beneficial than standard oral steroid therapy, which is especially important for patients with high risk of steroid-related complications.

Abstract citation ID: lvag096.1700

EP1552 - ECE_1224 - Marked thymic hyperplasia and widespread lymphadenopathy in a patient with thyroid storm due to Graves' disease

Htet Htet Aung[1,2], Neelam Khalid[1] and Rahat Tauni[1]
[1]Endocrine and Diabetes, West Hertfordshire Teaching Hospitals NHS Trust, Watford, United Kingdom; [2]Endocrine and Diabetes, West Hertfordshire NHSTrust, Watford, United Kingdom

We present the case of a 21-year-old woman who presented with symptoms of tonsillitis and tachycardia. She had a strong family history of thyrotoxicosis and hypothyroidism in first-degree relatives. Biochemical investigations revealed severe thyrotoxicosis, and carbimazole was commenced. Thyroid eye disease and strongly positive TSH receptor antibodies confirmed **Graves' disease**. Ten months later, she presented with **tonsillar abscess** complicated by *Staphylococcus epidermidis* bacteraemia, requiring emergency incision and drainage, followed by antibiotics. Despite progressive escalation of carbimazole to 60 mg daily, thyrotoxicosis worsened, and FT4 rose by more than 60% in three months. Due to concerns of non-compliance and features consistent with thyroid storm, she was admitted for emergency **total thyroidectomy.** Preoperative optimisation included intravenous prednisolone, propranolol, propylthiouracil and Lugol's iodine. Preoperative CT chest & neck demonstrated a diffuse goitre without retrosternal extension but revealed **marked thymic enlargement and mediastinal lymphadenopathy**. She underwent successful total thyroidectomy, and histology showed mild lymphocytic thyroiditis with focal non-necrotising granulomatous inflammation, possibly sarcoidosis. A CT chest, abdomen and pelvis was performed on the recommendations of thyroid multidisciplinary team (MDT) demonstrated marginal residual thymic enlargement without lymphadenopathy. MRI chest later revealed marked regression of the thymic enlargement compared with prior imaging, supporting the diagnosis of **thymic hyperplasia associated with Graves' disease**. No radiological features of sarcoidosis were identified on either imaging. Patient remains well on Levothyroxine replacement and is under endocrine follow-up.

Thymic hyperplasia associated with Graves' disease is a rare entity but is under-recognised as chest imaging is not routinely performed unless retrosternally extended goitre is suspected. As imaging becomes more accessible, clinicians should remain cognisant of this rare association of Graves' disease. In our case, thymic hyperplasia seems to be marked with presence of lymphadenopathy which is even rarer. We postulate that it may have been contributed to by the preceding tonsillar infection. Thymic enlargement typically resolves following definitive treatment and resolution of thyrotoxicosis. Clinicians should consider the differential diagnosis of thymic hyperplasia in patients with Graves' disease if chest or neck imaging is performed; however, it is critical to avoid unnecessary intervention/s due to benign and reversible nature of the disease. MDT approach involving radiologists, surgeons, pathologists and endocrinologists is necessary in decision making.

Abstract citation ID: lvag096.1701

EP1555 - ECE_1633 - Balancing efficacy and safety in antithyroid therapy: a case of carbimazole-induced agranulocytosis

Thaalitha Naidu Suranthiran Naidu, Masliza Hanuni Mohd Ali and Wan Mohd Hafez Wan Hamzah
Medical Department Hospital Kemaman, Ministry of Health, Terengganu, Malaysia

Antithyroid drug–induced agranulocytosis represents a rare yet potentially catastrophic idiosyncratic reaction. It most frequently manifests within the first three months of therapy and is potentiated by higher cumulative drug exposure or underlying genetic susceptibility. We report a case of early-onset carbimazole-induced agranulocytosis complicating the management of severe Graves' disease.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

A 32-year-old man with a one-year history of progressive thyrotoxic symptoms, including chronic diarrhoea, palpitations, heat intolerance, and postural tremors, was diagnosed to have Graves' disease complicated by thyroid eye disease at a private centre. Initial thyroid biochemistry demonstrated extreme thyrotoxicosis (free T4 >154.8 pmol/L, T3 >30.8 pmol/L, TSH 0.01 mIU/L), prompting initiation of methimazole 20 mg twice daily with verapamil. Within 4 days, he re-presented to our district hospital with febrile illness, profound lethargy, gastrointestinal disturbance, and escalating palpitations. Clinical assessment revealed marked agitation, bilateral fine tremors, a diffuse non-tender goitre, exophthalmos, temperature 37.5 °C, atrial fibrillation (heart rate 140-170 bpm) with rapid ventricular response. Biochemical indices confirmed persistent severe thyrotoxicosis (T4 of >100 pmol/L with suppressed TSH levels) and concomitant mild mixed hepatocellular–cholestatic transaminitis (ALT 78 U/L, ALP 198 U/L).

He was managed emergently for thyroid storm with high-dose propylthiouracil, non-selective beta-adrenergic blockade, Lugol's iodine, and intravenous hydrocortisone, resulting in substantial clinical stabilisation. The patient was discharged with carbimazole 30 mg daily and propranolol. However, eight days later, he was readmitted with high-grade fever (38 °C) and palpitations despite confirmed treatment adherence. Haematological evaluation revealed profound agranulocytosis (TWC 4×10^9/L, absolute neutrophil count 0.09×10^9/L, Hb 14 g/dL, platelet count 256×10^9/L), consistent with antithyroid drug–induced agranulocytosis. Carbimazole was immediately withdrawn, and he was commenced on broad-spectrum intravenous antimicrobials, granulocyte colony-stimulating factor, Lugol's iodine, with beta-blockade. Inflammatory markers were elevated (CRP 45 mg/L), blood cultures remained sterile, and serial full blood counts demonstrated prompt marrow recovery in 3 days (TWC 10.77×10^9/L, ANC 2.52×10^9/L).

He was subsequently discharged with oral ciprofloxacin, cholestyramine, Lugol's iodine, and propranolol. Close outpatient surveillance and repeat thyroid function testing were planned.

This case underscores the formidable risk of rapid, potentially fatal hematological toxicity with antithyroid therapy, even at standard doses. Clinicians must maintain a heightened index of suspicion for agranulocytosis in any patient presenting with fever, malaise, or constitutional symptoms during the early phase of antithyroid therapy, and alternative therapeutic strategies for thyrotoxicosis should be promptly considered in the setting of drug intolerance.

Abstract citation ID: lvag096.1702

EP1556 - ECE_2129 - Can resistance to I-131 in differentiated thyroid cancer regress after treatment with tyrosine kinase inhibitors?

Vakaris Kaminskas[1], Aiste Stonyte[1] and Raimonda Klimaite[2]
[1]*Lithuanian University of Health Sciences, Kaunas, Lithuania;* [2]*Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania*

Introduction: Between 5%-15% of patients with differentiated thyroid cancer (DTC) and 50% of patients with metastatic DTC are resistant to radioactive iodine (RAIR). Patients with RAIR-DTC metastatic disease have the poorest prognosis—their 10-year survival is below 10%. Although tyrosine kinase inhibitors (TKIs) provide effective treatment options for RAIR-DTC, most patients remain incurable, and disease progression occurs over time.

Clinical Case: A 68-year-old man underwent thyroidectomy at LUHS Kaunas Clinics in 2013; confirmed follicular thyroid carcinoma (pT3NxMx). Radioactive iodine treatment was administered.

In autumn 2018, the patient developed gluteal pain; MRI showed S2-S5 metastases. S2-S3 laminectomy confirmed follicular thyroid carcinoma, followed by 30 Gy palliative radiotherapy. In winter 2019, the third I-131 course showed minimal uptake, and CT revealed a large destructive S2-S3 lesion. A right renal lesion detected in May 2019 was resected, confirmed as papillary renal cell carcinoma type I.

In late 2021, a newly detected pathological lymph node near the right kidney was treated with stereotactic radiotherapy. By May 2022, disease progressed with thyroid lodge changes, lung metastases, possible liver metastasis, enlarged paracaval lymph nodes, and sacral involvement; biopsies confirmed Hürthle cell thyroid carcinoma. Lenvatinib, started in June 2022, induced initial regression of lung metastases and the lymph node metastases.

By spring 2025, no new metastases were seen, but fluid accumulation developed. Lenvatinib withdrawal due to nephrotic syndrome led to tumor progression, with increased thyroid mass, pain, and rising thyroglobulin (306 → 1000 µg/L).

A fourth I-131 course was given to assess restored sensitivity, but post-therapy scintigraphy again demonstrated no significant uptake. Concurrent CT revealed persistent disease. The findings indicate a lack of restored RAI sensitivity, confirming ongoing RAI-refractory disease.

Conclusions: This case illustrates a patient with metastatic, RAIR-DTC who initially showed structural response to lenvatinib but did not regain significant iodine avidity. Lenvatinib withdrawal due to nephrotoxicity led to rapid tumor progression, highlighting the temporary nature of systemic control and confirming the patient's continued RAI-refractory status. This case underscores the limited potential for restoring I-131 sensitivity in advanced DTC.

Abstract citation ID: lvag096.1703

EP1560 - ECE_1619 - Mild-to-moderate basal hypercalcitoninemia with different histology findings after thyroidectomy: a single-centre case study

Zoran Gluvic[1,2], Vladimir Samardzic[1], Milena Lackovic[1], Marija Sinik[1], Bojan Joksimovic[1], Milos Marinkovic[1], Ilinka Popovic[1], Lidija Kojic[1], Sonja Zafirovic[3], Milan Obradovic[3] and Esma R. Isenovic[3]
[1]*Department of Endocrinology, Faculty of Medicine, Zemun Clinical Hospital, University of Belgrade, Belgrade, Serbia;* [2]*Endocrinology, Zemun Clinical Hospital, Belgrade, Serbia;* [3]*Laboratory for Radiobiology and Molecular Genetics, Institute of Nuclear science "Vinca", National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia*

Mild-to-moderate increases in basal calcitonin (bCT) levels pose diagnostic challenges. To enhance accuracy in diagnosing medullary thyroid carcinoma (MTC), the calcium stimulation test (CST) is employed. Currently, age and gender-specific stimulated calcitonin (sCT) *cut-off* levels are used, underscoring the complexity of interpretation in clinical practice.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

We present a case study of 5 patients aged 42-74 years (4 females and one male) with a mild-to-moderate increase in bCT levels, ranging from 13 to 165 pg/mL, detected during thyroid nodular disease workup. Except for the patient who presented with the highest bCT level (165 pg/mL), all other patients were referred for a CST. The sCT values were: 168, 568, >2000, and >2000 pg/mL. The entire group of patients experienced total thyroidectomy, resulting in diverse postoperative histological findings. The first two patients were diagnosed with follicular adenoma, and Thyroid Follicular Nodular Disease (TFND) coexisted with C-cell hyperplasia (CCH). Patients exhibiting enhanced sCT levels (>2000 pg/mL) were diagnosed with papillary thyroid microcarcinoma (mPTC), and medullary thyroid carcinoma (MTC) coexisted with mPTC. A parathyroid adenoma was histologically verified in a patient with a bCT level of 165 pg/mL who was not tested with CST.

Mild-to-moderate basal hypercalcitoninemia warrants comprehensive evaluation, with the CST as the gold standard. The observed sCT responses align with follicular and C-cell malignancies. When sCT response appears evident but clinically insignificant, benign causes must be ruled out. Failure to demonstrate increased sCT response during CST necessitates investigation for neuroendocrine tumors.

Keywords basal hypercalcitoninemia, calcium stimulation test, stimulated calcitonin, thyroidectomy

Abstract citation ID: lvag096.1704

EP1562 - ECE_1745 - Probiotics and antioxidants as a synergistic immunomodulatory therapy in autoimmune thyroiditis

Federica Riccobene[1,2] and Luciana Carmen Nitoi[3,4]
[1]*Faculty of Medicine and Pharmacy, "Dunărea de Jos" University, Galati, Romania;* [2]*Facoltà di Medicina "Dunarea De Jos", Enna, Italy;* [3]*Medical Clinical Department, "Dunarea de Jos" University, Galati, Romania;* [4]*"St. Apostol Andrei" Clinic Emergency Hospital, Galati, Romania*

Background: Autoimmune thyroiditis represents a group of chronic inflammatory disorders characterized by aberrant immune activation and loss of self-tolerance, leading to progressive thyroid inflammation and destruction. The most common forms, Hashimoto's thyroiditis (HT) and Graves' disease (GD), involve both genetic and environmental factors, including the intestinal microbiota. Through the gut–thyroid axis, the microbiota regulates thyroid function and dysbiosis may promote autoimmunity. Probiotics can restore microbial balance and modulate the Th17/Treg lymphocyte ratio, while antioxidants such as vitamin C and selenium may enhance these immunomodulatory effects by reducing oxidative stress.

Objectives: To evaluate the efficacy of probiotics combined with the antioxidants vitamin C or selenium as adjunctive therapy in autoimmune thyroiditis, assessing their effects on immunological and endocrine parameters.

Design: A cross-sectional and prospective study was conducted in 48 patients treated with *OMNi-BiOTiC® Stress Repair*, containing nine human-derived bacterial strains of *Lactobacillus* and *Bifidobacterium*. The study sample included 30 patients with HT (62.5%), managed with levothyroxine and 18 with GD (37.5%) under treatment with thiamazole. According to disease type and adjunctive supplementation with probiotics combined with either vitamin C or selenium, patients were stratified into four subgroups.

Methods: Serum concentrations of thyroid-stimulating hormone (TSH), free thyroxine (FT4), anti-thyroid peroxidase antibodies (anti-TPO), anti-thyroglobulin antibodies (anti-TG) and anti-thyrotropin receptor antibodies (TRAb) were measured at baseline and after six months of treatment. Statistical analysis was performed using SPSS 18.0, with a 95% significance level.

Results: After six months of treatment, both HT subgroups demonstrated a reduction in mean TSH levels accompanied by an increase in FT4 concentrations. Anti-TG titres decreased significantly, while changes in anti-TPO titres were modest. At baseline, all GD patients had TSH concentrations below the reference range; after six months, approximately 90% of participants in both treatment groups achieved normalization, a change that was statistically significant. Additionally, TRAb values decreased significantly at six months, particularly in the group receiving probiotics and vitamin C.

Conclusions: Probiotics, particularly combined with vitamin C, demonstrated potential immunomodulatory effects in autoimmune thyroiditis, especially among patients with GD.

Keywords probiotics, Hashimoto, Graves, gut-thyroid axis, immunomodulation

Abstract citation ID: lvag096.1705

EP1563 - ECE_1863 - Should subclinical hypothyroidism always be treated with thyroid hormone?

Barbara Bordacs, Krisztina Kupai and Zsuzsanna Valkusz
Department of Endocrinology, University of Szeged, Internal Medicine, Szeged, Hungary

Introduction: Hypothyroidism is a common disease, especially among women, with a prevalence of around 20%. The treatment of mild and subclinical hypothyroidism is controversial. Initiating pharmacotherapy has a long-term impact on patients's lives, so choosing the right indication is a challenge for clinicians. Selenium is necessary for the synthesis of thyroid hormones, and myo-inositol signaling pathways have a positive effect on the course of many autoimmune and endocrine diseases. The immunomodulatory effect of vitamin D3 has been known for a long time. In our study, we aimed to provide our patients with primary care in the form of dietary supplements in order to prolong or possibly avoid the introduction pharmacotherapy.

Patients and Methods: Our single-center study included 60 newly diagnosed hypothyroid patients (age: 48.7 ± 14.9 years, mean $\pm$ SD) who had not previously received thyroid hormone replacement therapy. For 6 months, we administered a dietary supplement containing 83 µg of selenium and 600 mg of myo-inositol daily, together with 2000 IU of vitamin D3. From the laboratory values, TSH levels were determined at baseline and at least 6 months after treatment. The two values were statistically compared using a T-test.

Results: The therapy used in the study significantly reduced the TSH levels after at least 6 months (6.28 ± 3.4 vs 4.3 ± 2.9; $P < .001$).

Summary: Our results show a significant improvement in thyroid function with the use of a combined agent. By stimulating endogenous hormone synthesis, the initiation of pharmacotherapy could be avoided.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1706

EP1564 - ECE_2302 - Metabolic health and obesity phenotypes and thyroid autoimmunity in euthyroid individuals

Hye Jeong Kim
Seoul, South Korea

Background: Thyroid autoimmunity is a complex condition in which genetic and environmental factors interact to trigger an autoimmune response against the thyroid. This study aimed to investigate the association between metabolic health and obesity phenotypes and thyroid autoimmunity in euthyroid individuals.

Methods: We included participants aged ≥20 years from the National Health and Nutrition Examination Survey (2001-2002, 2007-2008, 2009-2010, and 2011-2012) with thyroid autoantibody results and normal thyroid function. Participants were categorized into four groups based on their metabolic health and obesity phenotypes: metabolically healthy non-obese (MHNO), metabolically unhealthy non-obese (MUNO), metabolically healthy obese (MHO), and metabolically unhealthy obese (MUO). Thyroid autoimmunity was defined as anti-thyroid peroxidase antibody positive and/or anti-thyroglobulin antibody positive. Weighted multiple logistic regression models estimated odds ratios (ORs) for thyroid autoimmunity, adjusting for confounders.

Results: The prevalence of MHNO, MUNO, MHO, and MUO phenotypes was 26.8%, 41.1%, 4.8%, and 27.3%, respectively. The prevalence of thyroid autoimmunity differed by groups (8.8% in MHNO, 12.9% in MUNO, 10.8% in MHO, and 10.2% in MUO; $P = .02$). The MUNO group had a significantly higher risk of thyroid autoimmunity compared with the MHNO group, even after adjusting for confounding variables, including sex, age, race/ethnicity, and smoking [adjusted OR 1.45; 95% confidence interval (CI), 1.06-1.99; $P = .02$]. In the subgroup analyses, the MUNO group had a significantly higher risk of thyroid autoimmunity compared with the MHNO group, particularly among younger individuals under 60 years (adjusted OR 1.73; 95% CI, 1.22-2.47; $P < .01$) and non-Hispanic White individuals (adjusted OR 1.66; 95% CI, 1.12-2.46; $P = .01$).

Conclusions: In euthyroid individuals, the MUNO phenotype was associated with an increased risk of thyroid autoimmunity. Further studies are needed to clarify causality and underlying mechanisms.

Abstract citation ID: lvag096.1707

EP1565 - ECE_2326 - Management of severe Graves' disease in a patient with antithyroid drug intolerance

Nino Tedoradze
Endocrinology, Caucasus Medical Center, Tbilisi, Georgia

Background: Antithyroid drugs (ATDs) are the first-line treatment for Graves' disease; however, their use may be limited by adverse effects such as allergic reactions and hepatotoxicity. In these situations, definitive therapy with radioactive iodine or surgery becomes necessary. Achieving euthyroidism before thyroidectomy is essential to minimize perioperative risk. When ATDs are contraindicated, potassium iodide represents an effective alternative for short-term preoperative management.

Case Presentation: We report the case of a 26-year-old woman with a 3-year history of Graves' disease who developed severe thyrotoxicosis after discontinuation of antithyroid therapy. Reintroduction of methimazole resulted in an allergic reaction, prompting a switch to propylthiouracil (PTU) combined with prednisone and a beta-blocker. During PTU therapy, the patient developed a second allergic reaction characterized by skin rash, edema, and pruritus, accompanied by elevated liver transaminases (hypertransaminasemia). Consequently, PTU was discontinued.

On admission, the patient presented with marked weakness, dyspnea, tachycardia, emotional lability, weight loss, arterial hypertension, tremor, and exophthalmos. Laboratory evaluation revealed severe thyrotoxicosis (TSH 0.008 mIU/L, FT4 53 pmol/L, FT3 >20 pg/mL), elevated TSH receptor antibodies (30.87 IU/L), increased liver enzymes, and elevated IgE levels. Thyroid ultrasound demonstrated a diffuse goiter with a total thyroid volume of 72 cm^3.

Management and Outcome: Given intolerance to both methimazole and PTU, definitive treatment options were considered. In view of the large goiter size, severe hyperthyroidism, and presence of Graves' orbitopathy, total thyroidectomy was selected. Preoperative preparation was achieved with potassium iodide drops administered for 14 days, resulting in successful attainment of a euthyroid state. The patient subsequently underwent an uncomplicated total thyroidectomy.

Conclusions: This case illustrates the complexity of managing Graves' disease in patients with allergic reactions and intolerance to antithyroid medications. When both methimazole and PTU are contraindicated, potassium iodide can serve as an effective short-term therapy to achieve euthyroidism prior to surgery. Total thyroidectomy is a safe and definitive treatment option in patients with severe hyperthyroidism, large goiter, and Graves' orbitopathy.

Abstract citation ID: lvag096.1708

EP1568 - ECE_2013 - A multifocal differentiated high grade thyroid carcinoma in a young female patient with Hashimoto thyroiditis

Georgios Boutzios[1], Anastasia Nikolopoulou[1], Christos Doudakmanis[2] and Gerasimos Tsouroufl is[2]
[1]*Department of Pathophysiology, National and Kapodistrian University of Athens, Outpatient Clinic of Autoimmune Endocrinopathies, Athens, Greece;* [2]*Second Department of Propaedeutic Surgery, Medical School, National and Kapodistrian University of Athens, Athens, Greece*

Introduction: Differentiated high grade thyroid carcinoma (DHGTC) is a new classification of thyroid cancer introduced in 2022 by WHO. It is an aggressive type of tumor that retains a well-differentiated architecture and cytology but is characterized by invasive properties, increased mitotic counts and tumor necrosis. Its prevalence is low, representing <3% of all thyroid cancers, it is mostly seen in older individuals and it has a female preponderance.

Case presentation: We present a 34-year-old Caucasian female, smoker, with a disease-free medical history, with a suspicious thyroid nodule on the upper pole of the left thyroid lobe, in a routine neck ultrasonography. The nodule was 12 mm in

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

diameter, hypoechoic with irregular margins and calcifications. Biochemically, she was euthyroid with positive thyroglobulin antibodies and negative calcitonin levels. The patient underwent a FNAB and the lesion was characterized as suspicious for malignancy (Bethesda Category VI).

The patient underwent a total thyroidectomy with central neck compartment dissection. Pathological examination of a specimen of the upper pole of the left thyroid lobe showed evidence of papillary thyroid carcinoma of the follicular type with papillary and mainly follicular pattern, while revealing isolated clusters of solid neoplastic cells infiltrating the thyroid capsule, mild mitotic activity, focal necrosis and important inflammatory infiltration in the cancer focus. Moreover, in a tissue specimen of the lower pole of the right thyroid lobe, a microscopic focus of encapsulated papillary thyroid carcinoma of the follicular type without capsule extension was addressed. The rest of the thyroid parenchyma revealed chronic lymphocytic thyroiditis. None of the seventeen exerted lymph nodes were invaded by neoplastic cells leading to the diagnosis of multifocal differentiated high-grade thyroid carcinoma with papillary follicular and solid growth pattern, pathological stage mT1b, N0, with focal capsule invasion. After thyroid surgery, the patient was treated with Radioactive Iodine.

Conclusions: DHGTC is associated with aggressive clinicopathological features and poor clinical outcome, similar to poorly differentiated thyroid cancer. Early diagnosis seems to be crucial for the patient's outcome.

Abstract citation ID: lvag096.1709

EP1569 - ECE_2328 - A rare complication of untreated thyrotoxicosis: thyrotoxic periodic paralysis

Banu Ocak[1], Hakan Ömer Karataş[2], Hülya Karadağ[3] and Murat Tuğcu[3]

[1]*Department of Internal Medicine, Marmara University Faculty of Medicine, İstanbul, Türkiye;* [2]*Department of Internal Medicine, Van Gürpınar State Hospital, Van, Türkiye;* [3]*Department of Internal Medicine, Division of Nephrology, Marmara University Faculty of Medicine, İstanbul, Türkiye*

Background: Thyrotoxic hypokalemic periodic paralysis (THPP) is a rare but potentially life-threatening complication of thyrotoxicosis, characterized by episodic hypokalemia and acute flaccid muscle weakness. The underlying pathophysiology involves increased Na^+/K^+-ATPase activity in the hyperthyroid state, leading to an intracellular shift of potassium rather than true potassium depletion. Genetic susceptibility, including mutations affecting skeletal muscle inward-rectifying potassium (Kir) channels, has also been implicated. THPP predominantly affects young adult males and is commonly precipitated by strenuous physical activity, emotional stress or high-carbohydrate intake. In this context, the present case aims to draw attention to thyrotoxic hypokalemic periodic paralysis as an important endocrine cause of acute paralysis.

Methods: Case presentation

Case Presentation: A 27-year-old male presented to the emergency department with sudden-onset, symmetrical weakness of both lower extremities. Neurological examination revealed bilateral proximal muscle weakness graded 3/5, while sensory and cranial nerve examinations were normal. Vitals showed sinus tachycardia with 112 beats/min and blood pressure of 135/70 mmHg. Laboratory testing revealed significant hypokalemia (2.6 mmol/L) and electrocardiography revealed repolarization abnormalities consistent with hypokalemia. Oral and intravenous potassium replacement was initiated under cardiac monitoring.

Further history revealed recurrent self-limited episodes of muscle weakness over the preceding year, previously evaluated in neurology and physical medicine clinics. Neuroimaging and electromyography had been unremarkable. Renal function was normal and there was no evidence of gastrointestinal or renal potassium loss, medication use, or reduced oral intake. The patient reported intermittent palpitations and an unintentional weight loss of approximately 10% over the past year.

Although the patient denied a known thyroid disorder at presentation, review of prior medical records revealed abnormal thyroid function tests obtained one year earlier, with incomplete follow-up due to relocation. Repeat testing revealed thyrotoxicosis consistent with autoimmune thyroid disease (TSH <0.003 mIU/L; free T3: 7.55 ng/L; free T4: 2.76 ng/dL; anti-thyroid peroxidase antibody: 594 IU/mL; TSH receptor antibody: 20 IU/L). Thyroid ultrasonography showed increased vascularity and pseudonodular changes.

Based on clinical and biochemical findings, THPP due to Graves' disease was diagnosed. Complete clinical recovery occurred within hours after potassium replacement, methimazole and propranolol therapy was initiated. The patient has remained asymptomatic during follow-up.

Conclusions: THPP is an uncommon manifestation of thyrotoxicosis and may present as the initial clinical feature, particularly in young men. This case highlights the importance of careful assessment of hyperthyroid symptoms in the emergency setting. Early recognition of the underlying endocrine disorder can facilitate appropriate management and help prevent recurrent paralytic episodes.

Abstract citation ID: lvag096.1710

EP1570 - ECE_3856 - Amiodarone-induced thyrotoxicosis associated with papillary thyroid cancer: diagnosis and treatment difficulties

Melania Balas, Ioana Golu, Plotuna Iulia-Ştefania, Daniela-Georgiana Amzar, Oriana Pelineagra, Oana Popa, Ana-Silvia Corlan and Mihaela Maria Vlad

2nd Internal Medicine, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

Case presentation: A 57-year-old patient was diagnosed with atrial fibrillation in 2022, treated with amiodarone for 2 years (no thyroid ultrasound was performed, thyroid function was normal during monitoring). In November 2023 he was referred to Endocrinology Department with weight loss, palpitations (recurrent atrial fibrillation), sweating and insomnia. The laboratory evaluation confirmed amiodarone-induced thyrotoxicosis (AIT) with suppressed TSH, increased serum FT4, normal FT3, negative antithyroid and TSH-receptor antibodies, negative inflammatory markers.

Thyroid ultrasound revealed normal volume, moderately hypoechoic parenchyma, decreased vascularization. In both lobes, in the posterior region, solid nodules were described, 8.7/9.4/

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

10 mm on the left, respectively 9.2/12.2/11.5 mm on the left, with similar features: marked hypoechoic, "taler than wide" shape, irregular borders, absent intranodular vascularity, microcalcifications, absent halo (TIRADS 5). Thyroid scintigraphy Tc^{99m} showed very low uptake in the thyroid tissue.

Shear-wave elastography found mean IE of 51.5 Kpa of the right nodule, respectively 36 kPa of the left nodule. Contrast-Enhanced Ultrasound (CEUS) showed lower enhancement compared to surrounding tissue. Antithyroid drugs were administered with favorable response.

As the patient was under anticoagulant treatment, fine-needle aspiration biopsy (FNAB) was postponed. FNAB performed in both nodules was reported as suspicious for malignancy (Bethesda category V).

After euthyroidism was achieved, total thyroidectomy was performed in December 2024, confirming the diagnosis of multifocal papillary thyroid carcinoma (PTC), with conventional and Warthin-like features (pT1bN1M0). ^{131}I ablation with 3.7 GBq was performed, with no abnormal uptake at total body scan. During follow-up, stimulated serum thyroglobulin levels were below 0.04 ng/mL, with negative antithyroglobulin antibodies. Under treatment with levothyroxine, TSH values are maintained slightly suppressed, with normal serum thyroid hormones.

Discussion: Although rare, cases of papillary thyroid cancer associated with AIT (mainly type 2), has been reported. The main issue is to distinguish AIT types and to treat thyroid dysfunction accordingly, as PTC can coexist, leading to diagnosis pitfalls.

Managing PTC in an AIT patient can be challenging, due to the high iodine content of amiodarone, its long half-life, factors that may hinder radioactive iodine treatment.

Abstract citation ID: lvag096.1711

EP1572 - ECE_1014 - Transient hyperthyroid Graves' disease following subacute thyroiditis: a case report

Yotsapon Thewjitcharoen[1], Veekij Veerasomboonsin[2], Soontaree Nakasatien[1] and Thep Himathongkam[1]
[1]*THEPTARIN Diabetes, Thyroid and Endocrine Center, Vimut-Theptarin Hospital, Bangkok, Thailand;* [2]*Radiology, Vimut-Theptarin Hospital, Bangkok, Thailand*

Background: There have been reports on subacute thyroiditis, Graves' disease and Hashimoto's thyroiditis following COVID-19 infection. Appearance of overt autoimmune thyroid disease (AITD) following subacute thyroiditis is very rare. It is also uncommon for subacute thyroiditis to progress to either Graves' disease or Hashimoto's thyroiditis. In previous case reports, most patients had negative baseline thyroid antibodies, so that the autoimmune process was postulated to have been triggered by the release of antigenic material from the inflamed thyroid gland. Herein, we report an interesting case of hyperthyroid Graves' disease following post COVID-19 infection subacute thyroiditis.

Clinical case: A 40-year-old woman presented with palpitation and 4-kilogram weight loss within 1 month following tenderness in her neck. No family history of AITD was reported. One month earlier, she experienced thyroid tenderness after flu-like symptoms. The patient was not tested for COVID-19 at that time. She was treated with oral prednisolone 20 mg/day with presumptive diagnosis of subacute thyroiditis. Her symptoms rapidly improved within 24 hours and oral prednisolone was tapered-off within 2 weeks. However, she developed hyperthyroid symptoms one month later. Physical examination revealed a heart rate of 120 beats/minute and a normal size, non-tender thyroid gland without evidence of orbitopathy. TFT showed serum TSH <0.01 μIU/mL (normal value 0.27-4.20 μIU/mL), FT4 2.8 ng/dL (normal value 0.9-1.7 ng/dL), total T3 218 ng/dL (normal value 60-177 ng/dL), negative anti-Tg but positive anti-TPO titers. Thyroid ultrasonography showed slightly enlarged heterogeneous thyroid gland with mild hypervascularity. Serum TSH receptor antibody (TRAb) was positive at 4.9 IU/L (normal value <1.7 IU/L). Oral methimazole 15 mg per day was given and then tapered to 5 mg per day. At 7 months later, the patient discontinued methimazole by herself from weight gain and feelings of tiredness. Repeated serum TRab turned to negative result with normal TFT. At 2 years later, the patient was still in remission.

Conclusions: The development of Graves' disease after the resolution of subacute thyroiditis is an uncommon condition but had been reported occasionally in previous studies. This case emphasized the need for careful follow-up during steroid treatment and long-term surveillance for thyroid dysfunction.

Abstract citation ID: lvag096.1712

EP1573 - ECE_2630 - Thyroid-stimulating immunoglobulin in Graves' disease: association with biochemical disease severity and real-world monitoring practices

Win Lei Yin[1], Blaise Emery[1], Therese Michael[2], Angharad Shore[2] and Thinzar Min[1]
[1]*Department of Endocrinology, Swansea Bay University Health Board, Swansea, United Kingdom;* [2]*Laboratory Medicine, Swansea Bay University Health Board, Swansea, United Kingdom*

Background: Thyroid autoantibodies are recommended as first-line investigations in the differential diagnosis of hyperthyroidism. Thyroid-stimulating immunoglobulin (TSI) is increasingly used to support the diagnosis of Graves' disease and has potential value in predicting treatment response. This study aimed to: (1) evaluate whether TSI level at diagnosis correlates with the biochemical severity of Graves' disease, and (2) assess the extent to which TSI is routinely measured during the treatment course.

Methods: We conducted a retrospective observational study of patients diagnosed with Graves' disease who had a positive TSI between January 2023 and December 2024 within Swansea Bay University Health Board. Demographic data, TSI results at or around diagnosis, thyroid function tests at baseline and at 12-month follow-up, and the number of repeat TSI measurements were collected.

Results: A total of 130 patients (mean age 48 ± 19 years; 79% Female) were included. All patients were treated with carbimazole at variable doses. Baseline biochemical measurements showed: median Free T4 FT4:37.8 pmol/L; median Free T3 15.1 pmol/L and median TSI: median 4.20 IU/L. TSI levels at diagnosis correlated positively with biochemical severity: TSI vs FT4: $r = 0.55$, $P < .001$ and TSI vs FT3: $r = 0.49$, $P < .001$ ($n = 129$). At 12 months, 93 (71%) patients remained on antithyroid medication 30 (23%) remained thyrotoxicosis (12 had low TSH, and 18 had suppressed TSH). 19 (14%) patients achieved biochemical euthyroidism and were off antithyroid therapy at

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

the 12-month assessment. Only 10 of 130 patients underwent repeat TSI testing during treatment.

Conclusions: Higher TSI levels at diagnosis are moderately correlated with biochemical severity in Graves' disease. Despite its recognised diagnostic and prognostic value, repeat TSI measurement was infrequently performed in routine practice. The low proportion of patients achieving treatment-free euthyroidism at 12 months highlights the need for improved tools to guide treatment duration. More consistent longitudinal use of TSI may enhance clinical decision-making and support personalised management strategies in Graves' disease.

Abstract citation ID: lvag096.1713

EP1574 - ECE_2545 - Nonspecific increase of thyroglobulin in a patient with papillary thyroid carcinoma

Agnieszka Suligowska and Aldona Kowalska
Skarzysko-Kamienna, Poland

Case Presentation: A 36-year-old woman with a history of multinodular goiter was referred for further evaluation after a suspicious focal lesion was identified on ultrasound.

On 11 June 2011, she underwent total thyroidectomy with prophylactic central compartment lymph node dissection. Histopathological examination confirmed a papillary thyroid carcinoma of the right thyroid lobe measuring 9 mm in greatest diameter, classified as pT1a. One metastatic lymph node was identified in the central compartment, with a metastatic focus measuring 2 mm (pN1a). On 20 July 2012, she received ablative treatment with 2700 MBq of radioactive iodine (^{131}I). Post-therapy whole-body scintigraphy showed no abnormal iodine uptake outside the thyroid bed. During the initial follow-up period, the patient demonstrated an excellent response to treatment. She was maintained on levothyroxine therapy aimed at TSH suppression and remained clinically stable for several years.

During long-term follow-up, a gradual increase in serum Tg levels was observed. Basal Tg rose to 0.9 ng/mL, and stimulated Tg reached 3.0 ng/mL. Repeated ultrasound examinations of the thyroid bed and cervical lymph nodes revealed no suspicious lesions or lymphadenopathy. In view of the biochemical evidence suggestive of persistent or recurrent disease, the patient was qualified for whole-body scintigraphy.

The whole-body scintigraphy revealed an unexpected focus of increased radioiodine uptake located in the left pelvic region. Subsequent SPECT/CT imaging precisely localized the uptake to a lesion within the left ovary.

Further evaluation with pelvic magnetic resonance imaging (MRI) demonstrated a well-defined 16 × 11 mm lesion in the left ovary with thin septations, while the right ovary contained a 13 × 9 mm lesion with imaging characteristics consistent with a fibroma.

The patient was referred for gynecological surgery, and bilateral ovarian lesions were surgically excised. Histopathological examination confirmed the diagnosis of mature cystic teratomas, with thyroid tissue present in the left ovarian lesion. Following surgical removal of the ovarian tumors, serum Tg levels returned to undetectable values, confirming that the elevated Tg levels were not due to recurrent thyroid carcinoma but rather to ectopic thyroid tissue within the ovarian teratoma.

Conclusions: We report a rare case of nonspecific Tg elevation in a patient with papillary thyroid carcinoma, caused by struma ovarii within an ovarian teratoma. This case underscores the importance of considering extrathyroidal sources of Tg when evaluating rising Tg levels in the absence of locoregional or distant recurrence. Accurate recognition can prevent unnecessary interventions and ensure appropriate management.

Abstract citation ID: lvag096.1714

EP1581 - ECE_1050 - Unmasking pembrolizumab-induced hypothyroidism in a complex multimorbid renal tumour patient: a case report

Shadman Rahman, Muhammad Dalili, Sumaiya Kamal, Sameer Sighakoli and Kh Imranul Alam
Endocrine and Diabetes, Medway NHS Foundation Trust, Gillingham, United Kingdom

Background: Immune checkpoint inhibitors (ICIs), such as pembrolizumab, are increasingly employed in the treatment of advanced malignancies, including renal cell carcinoma. Thyroid dysfunction is a well-recognised immune-related adverse event (irAE) associated with ICIs, typically manifesting as transient thyrotoxicosis followed by hypothyroidism.[1] This case report highlights the development of overt hypothyroidism in a patient with previously normal thyroid function following pembrolizumab therapy.

Case Presentation: A 70-year-old male with multiple comorbidities—including ischemic heart disease, heart failure with reduced ejection fraction, chronic obstructive pulmonary disease (COPD), hypertension, atrial fibrillation, psoriasis, and a history of prostate cancer treated with robotic prostatectomy—was admitted with chest sepsis requiring inotropic support. Incidentally, two renal masses were identified on CT imaging, demonstrating heterogeneous enhancement, regional lymphadenopathy, and a suspected tumour thrombus extending into the renal vein and inferior vena cava. The patient subsequently underwent robotic right nephrectomy with excision of the tumour thrombus.

Postoperatively, pembrolizumab therapy was initiated. Baseline thyroid function tests were within normal limits (TSH: 0.45 mIU/L). However, within weeks of treatment initiation, the patient developed overt hypothyroidism, characterised by a markedly elevated TSH of 49.60 mIU/L and a low free T4 level of less than 3.2 pmol/L. Oral levothyroxine therapy was commenced, and the patient is currently under close monitoring with regular thyroid function tests and outpatient thyroid ultrasound evaluation.

Conclusions: Pembrolizumab-induced thyroid dysfunction is a common irAE, with hypothyroidism reported in up to 10% of patients.[2] The underlying pathophysiology may involve destructive thyroiditis or autoimmune mechanisms, even in individuals without prior thyroid disease. This case underscores the critical importance of routine thyroid function monitoring during ICI therapy. Early recognition and management of endocrine irAEs are essential to ensure the safe continuation of immunotherapy and optimise patient outcomes.[3]

References

1. Iwama S, et al. Recent advances in clinical endocrinology and metabolism. *Best Pract Res Clin Endocrinol Metab*. 2022;36(1):101667.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

2. Pollack MH, et al. Safety of immune checkpoint inhibitors: implications for cancer immunotherapy. *Cancer Immunol Res*. 2018;6(2):146-154.
3. Barroso-Sousa R, et al. Incidence of immune-related adverse events and association with survival in patients treated with immune checkpoint inhibitors: a systematic review and meta-analysis. *JAMA Oncol*. 2018;4(12):1780-1788.

Abstract citation ID: lvag096.1715

EP1582 - ECE_3531 - Graves' disease after long-term levothyroxine-treated hypothyroidism

Lia Katcharava[1,2] and Salome Kalandadze[1]
[1]*New Hospitals, Tbilisi, Georgia;* [2]*Endocrinology, New Hospitals, Tbilisi, Georgia*

Background: Biochemical thyrotoxicosis in patients receiving levothyroxine is often attributed to over-replacement. However, persistence of suppressed thyrotropin (TSH) with elevated free thyroxine (FT4) and free triiodothyronine (FT3) after dose reduction and complete withdrawal should trigger prompt evaluation for a new hyperthyroid disorder. Rarely, patients previously treated for hypothyroidism may subsequently develop Graves' disease ("conversion"), creating a diagnostic pitfall.

Case presentation: A female patient diagnosed with primary hypothyroidism in 2020 remained clinically stable and biochemically euthyroid on levothyroxine 75 μg/day with regular monitoring. In December 2024, she developed symptoms suggestive of thyrotoxicosis; thyroid function tests demonstrated suppressed TSH with elevated FT4/FT3. Iatrogenic thyrotoxicosis was suspected and levothyroxine was reduced, then fully discontinued in January 2025. Despite cessation, repeated testing continued to show suppressed TSH with elevated FT4/FT3. The patient did not seek specialist care until April 2025, when she developed bilateral periorbital edema with mild proptosis, accompanied by palpitations, tremor, and diaphoresis. Thyroid ultrasound revealed no focal nodules. Anti-TPO and anti-TG antibodies were negative. TSH receptor antibodies (TRAb) were strongly positive (11 IU/L; assay reference <1.22 IU/L), confirming Graves' disease with early thyroid-associated orbitopathy.

Management and Follow-up: Methimazole therapy was initiated with symptomatic improvement and biochemical monitoring. Levothyroxine remained discontinued. Given ocular involvement, the patient was referred for ophthalmologic assessment and multidisciplinary management according to orbitopathy activity and severity.

Conclusions: Suppressed TSH in a patient receiving levothyroxine should not automatically be attributed to over-replacement. Persistence of thyrotoxicosis despite dose reduction and drug cessation—especially when orbital signs develop—should prompt immediate TRAb testing to confirm Graves' disease, avoid diagnostic delay, and ensure timely initiation of antithyroid therapy and coordinated ophthalmologic care.

Abstract citation ID: lvag096.1716

EP1583 - ECE_1839 - Exogenous T3 ingestion leading to T3 thyrotoxicosis

Ishara Ranathunga, Chandima Idampitiya and Fathima Pambinezhut
Endocrinology, North Cumbria University Hospitals Nhs Trust—Carlisle Library, Carlisle, United Kingdom

Background: T3 thyrotoxicosis due to exogenous triiodothyronine (T3) ingestion is a rare cause of hyperthyroidism, mimicking endogenous thyroid dysfunction. It results from intentional or accidental ingestion of T3 or T3 containing supplements leading to suppression of endogenous thyroxine production. Diagnosis can be challenging, requiring exclusion of endogenous causes and establishing exogenous ingestion. This case highlights the complexity of diagnosis of a patient with persistent T3 toxicosis who denied exogenous T3 use.

Case Report: A 45-year-old female was diagnosed to have thyrotoxicosis during investigations for persistent post-operative tachycardia following laparoscopic cholecystectomy in August, 2023. On further evaluation, she was noted to have typical thyrotoxic symptoms since March 2023. Examination revealed elevated blood pressure (160/105 mmHg), sinus tachycardia (heart rate 123 pbm), and a weight of 48 kg. She did not have a palpable goitre and any signs of thyroid eye disease. Investigations showed elevated T3 of >50 pmol/L with suppressed fT4 (fT4 2.7 pmol/L (11-22)), and TSH <0.02 mU/L (0.3-4.5). TRAb and TPO was negative, and biotin interference was excluded. Ultrasound showed a small thyroid and technetium uptake scan showed absence of thyroid uptake. Urine iodine was inconclusive. Normal pelvic ultrasound and pelvic MRI ruled out ectopic thyroid tissue. The imaging showed the presence of an undisclosed gastric band. Whole-body iodine scan showed increased uptake around the thyroid, but a repeat technetium scan confirmed absence of thyroid uptake. As the patient denied exogenous T3 use, she was initially treated with antithyroid medication and beta blockers. Subsequently due to absence of response, she was started on steroids and later on cholestyramine without any success. She was closely observed as an inpatient for exogenous use for 1 week without a confirmation. Despite denying exogenous T3/supplements use, persistently high T3 and discordant scans suggest undisclosed ingestion of T3 as the cause of her refractory thyrotoxicosis. Therefore, the above mentioned medications were discontinued.

Conclusions: This case emphasises the need to consider exogenous T3 ingestion in refractory thyrotoxicosis, particularly with discordant imaging. The failure of conventional antithyroid or steroid treatment highlights the importance of discontinuing ineffective therapies and pivoting to alternative treatment strategies, including counselling to encourage disclosure. Further exploration of the patient's lifestyle, dietary habits, and potential environmental exposures is essential to pinpoint the exogenous T3 source. This approach not only resolves the diagnostic enigma but also paves the way for tailored management, potentially preventing long-term complications and improving the patient's quality of life.

Abstract citation ID: lvag096.1717

EP1584 - ECE_2222 - Carbimazole-induced systemic lupus erythematosus complicating the management of Graves' disease: a rare but serious association

Hafiz Awais Javed, Haris Marath, Daisy Beard, Jayamalee Jayaweera, Arooj Zulfiqar and Amna Zeeshan
Endocrinology, West Suffolk Hospital, Bury St Edmunds, United Kingdom

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Background: Graves' disease and systemic lupus erythematosus (SLE) are autoimmune conditions that predominantly affect young women. While Graves' disease is organ-specific, SLE is a multisystem autoimmune disorder with diverse clinical manifestations. Drug-induced lupus erythematosus (DILE) is classically associated with medications such as hydralazine, procainamide, and isoniazid; however, antithyroid drugs are rarely implicated.

Case Presentation: We report the case of a 44-year-old female presented with new-onset atrial fibrillation resistant to standard rate-control therapy, pyrexia and classical features of thyrotoxicosis, including palpitations, unintentional weight loss, and fine tremors. Biochemical testing confirmed severe thyrotoxicosis (TSH < 0.02 mIU/L, fT4 69.6 pmol/L). A Burch–Wartofsky score of 55 was highly suggestive of thyroid storm. She was treated with intravenous beta-blockade and steroids, oral propylthiouracil, and Lugol's iodine, resulting in marked clinical improvement. She was discharged on carbimazole 10 mg twice daily with a tapering course of prednisolone.

Four weeks later, she was re-admitted with persistent fever and flu-like symptoms. She remained febrile with a persistently elevated C-reactive protein despite antiviral therapy and broad-spectrum antibiotics. Investigations for pyrexia of unknown origin, including blood and urine cultures and cross-sectional imaging, were unremarkable. Autoimmune testing showed positive ANA, Anti dsDNA, anti-Ro, and anti-histone antibodies, supporting a diagnosis of carbimazole-induced SLE.

Carbimazole was switched to propylthiouracil, and oral prednisolone 20 mg daily was initiated, resulting in rapid resolution of fever and arthralgia. Hydroxychloroquine was later introduced for ongoing disease control. Subsequent evaluation revealed significant proteinuria, and renal biopsy confirmed class III lupus nephritis, necessitating treatment with mycophenolate mofetil.

Discussion: This case demonstrates a rare but serious complication of carbimazole therapy. The coexistence of Graves' disease and drug-induced SLE presents diagnostic and therapeutic challenges, particularly when persistent systemic symptoms are misattributed to infection or relapse of thyrotoxicosis.

Conclusions: Clinicians should recognise carbimazole as potential trigger for drug induce lupus and maintains a high index of suspicion for autoimmune pathology in patients who develop unexplained systemic symptoms. Early recognition, prompt withdrawal of the offending drug, and appropriate immunosuppressive therapy can result in favourable outcomes.

Abstract citation ID: lvag096.1718

EP1586 - ECE_3112 - Ectopic papillary thyroid carcinoma of the lateral neck: an unusual presentation

Milena Brkic[1,2,3], Tade Popovic[1], Ljiljana Tadic Latinovic[4], Aleksandra Markovic[1] and Zoran Dakic[5]

[1]Medical Faculty, Banja Luka, Bosnia and Herzegovina; [2]School of Medicine, University of Banja Luka, Banja Luka; [3]Faculty of medicine University of Banja Luka, Banja Luka, Bosnia and Herzegovina; [4]Institute of Pathology, University Clinical Centre of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina; [5]Thoracic Surgery Department, University Clinical Centre of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina

Introduction: The presence of thyroid tissue outside its normal anatomical location, between the second and fifth tracheal rings, is defined as ectopic thyroid tissue. Approximately one to three percent of ectopic thyroid tissue is located in the lateral neck. Most cases are asymptomatic and considered benign.However, lateral neck ectopic thyroid tissue may also represent metastatic disease from an occult primary thyroid carcinoma, making accurate diagnosis challenging.

Case presentation: A 36-year-old male presented for microwave ablation of a large right-lobe thyroid nodule after five years of ultrasound surveillance. Progressive growth had been documented, and surgery was recommended, but the patient opted for minimally invasive treatment. Repeated fine-needle aspiration of the right-lobe nodule showed benign cytology, thyroid function tests were normal, and no cervical lymphadenopathy was detected. Clinical examination revealed a palpable right thyroid mass causing compressive symptoms and cosmetic concerns. Ultrasound demonstrated a parenchymatous-colloid nodule measuring $3.1 \times 4.1 \times 2.5$ cm in the right lobe, a 0.2 cm micronodule in the left lobe, and an enlarged left lateral cervical lymph node with microcalcifications, highly suspicious for malignancy.

During microwave ablation in November 2024, fine-needle aspiration of the suspicious lymph node suggested papillary carcinoma, possibly arising from ectopic thyroid tissue. In February 2025, right lobectomy with excision of lateral neck tissue and lymph node dissection was performed. Histopathology confirmed a benign right-lobe nodule and papillary carcinoma of conventional and follicular variants originating from ectopic thyroid tissue, with microscopic lymphatic invasion and no vascular invasion.Postoperative evaluation revealed elevated serum thyroglobulin levels of 123.6 ng/mL. Computed tomography identified enlarged lateral cervical lymph nodes. Completion thyroidectomy and removal of metastatic lymph nodes were performed. Histology demonstrated a 0.2 cm papillary microcarcinoma in the left thyroid lobe and metastases in three of eleven lymph nodes, while remaining thyroid tissue showed nodular colloid goiter. Follow-up computed tomography and whole-body scintigraphy were normal. The patient received radioactive iodine therapy I-131 150 mCi.

Conclusions: Ectopic thyroid carcinoma of the lateral neck is a rare but clinically important entity. Papillary microcarcinoma, despite its small size, may exhibit aggressive behavior and requires careful evaluation. Thermal ablation enabled early detection, appropriate surgical management, and adjuvant therapy, resulting in a favorable oncological outcome and long-term disease control. This case highlights the importance of multidisciplinary assessment, imaging, and histopathological correlation in complex thyroid disease presentations in clinical practice.

Keywords papillary microcarcinoma, thyroid nodule, ectopic thyroid tissue

Abstract citation ID: lvag096.1719

EP1588 - ECE_3284 - Thyroid hormone transporter defect (Allan-Herndon-Dudley syndrome)—a rare syndrome masquerading as dyskinetic cerebral palsy: a case report

Iryna Lastivka

Bukovinian State Medical University, Chernivtsi, Ukraine

Topicality: Allan-Herndon-Dudley syndrome (AHDS) (ORPHA:59) (synonym monocarboxylate transporter 8 (MCT8) deficiency) is a

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

syndrome caused by mutations in the *SLCI6A2* gene (Xq13.2), which encodes MCT8, which acts as a thyroid hormone (TH) transporter. Since MCT8 is crucial for the transport of TH across the blood-brain barrier and into neurons, its deficiency leads to intellectual disability and thyroid dysfunction. It occurs only in males. It's diagnosed by clinical signs, changes in serum TH levels, and DNA diagnostics.

Objective: To present a case of Thyroid Hormone Transporter Defect in a child.

Methods: TH assay by immunochemiluminescent method; whole-exome sequencing.

Clinical case: A 7-month-old boy from the 3rd pregnancy on the background of polyhydramnios, third delivery at 39 weeks. Birth weight 2500 g (−3σ), length—47 cm (−3σ). Intrauterine growth retardation, symmetrical variant. Complaints of convulsions, restlessness, crying. Children (females) from two previous pregnancies are healthy. At birth—hypotension, difficulties with feeding; at 2 month—tremor, restlessness, sleep-wake disorder; at the age of 2 months—tremor, restlessness, sleep-wake disorder; at the age of 6 months—spasticity with hyperreflexia, clonus and dystonic movements of the face, neck and distal extremities. At the age of 7 months—weight 6300 g (−2σ), length—62 cm (−3σ).

Phenotype: apathy, slow reaction, hypotrophy, open mouth, short upper lip, ear deformity, right eye converging slant, constant chin tremor. He does not hold head, does not sit, positive Moro reflex, increased muscle tone. Weakness of neck muscles, hypertonicity of limbs, retroflexion of head, microcephaly, poor motor coordination are detected. Laboratory: cholesterol—2.2 mmol/L; TH: TSH—5.0 μM IU/mL (normal: 0.3-4.0 μM IU/mL); T4—7.8 pmol/L (normal: 9.0-20.0 pmol/L). Thyroid ultrasound—without abnormalities. EEG: diffuse abnormalities with focal sharp waves in the parieto-occipital-temporal region; Brain MRI: bilateral dilatation of the ventricular system and delayed myelination. Whole-exome sequencing of the child and parents: a mutation c.330C>A, p.(Cys110*) was detected in the hemizygous variant in the *SLC16A2* gene (NM_006517.5) of maternal origin.

Conclusions: Allan-Herndon-Dudley syndrome or MCT8 transporter deficiency is a rare syndrome that should be considered in male infants with idiopathic hypotension and weakness. The diagnosis of SAHD is based on the determination of a complex of indicators (T3, T4 and TSH) of thyroid function. Cytogenetic diagnostic methods allow to verify the diagnosis at an early age.

Abstract citation ID: lvag096.1720

EP1589 - ECE_3574 - A rare hematologic emergency during treatment of hyperthyroidism: a clinical case

Nuno Faria, Rita Ribeiro, Patrícia Brito, Adriana de Sousa Lages, Maria Joana Santos, Olinda Marques and Catarina MacHado
Endocrinology department, Unidade Local de Saúde de Braga, Braga, Portugal

Background: Antithyroid drugs remain the first-line treatment for Graves' disease, with methimazole preferred for its efficacy and safety profile. Agranulocytosis is an extremely rare but potentially life-threatening adverse effect, occurring in <0,5% of patients. Early recognition is critical to avoid serious infectious complications and uncontrolled thyrotoxicosis.

Case Description: We describe a case of a previously healthy 39-year-old woman with newly diagnosed Graves' disease [TSH <0.008 μUI/mL, free T4 2.57 ng/dL (0.89-1.76), TRAb 1.79 UI/L (<0.55)], who was started on methimazole 15 mg/day. A previous history of other autoimmune diseases and smoking were excluded.

One month later, she presented to the emergency department with fever (39.7°C), odynophagia, and malaise. Examination revealed a tender goiter and bilateral tonsillar hypertrophy with asymmetric bulging. Laboratory testing showed severe leucopenia (1000/mm^3) with neutropenia (100/mm^3), elevated C-reactive protein (299.9 mg/L; <5.0), and a peritonsillar abscess on cervical CT. Thyroid function had partially improved [TSH 0,011uUI/mL; free T4 1,8 ng/dl; free T3 6,02 pg/mL (2,3-4,2)].

Methimazole was immediately discontinued, and broad-spectrum antibiotics and corticosteroids were initiated. Due to the risk of cross-reactivity, propylthiouracil was avoided. Given the risk of thyroid storm in the absence of antithyroid therapy and the need for definitive treatment, Lugol's solution (10 drops every 8 hours) and propranolol (40 mg twice daily) were introduced for thyrotoxicosis control before total thyroidectomy. Other causes of agranulocytosis were excluded, namely renal or hepatic impairment or viral infections. No microbiological agents were isolated in the collected blood samples.

After recovery of the neutrophil count and normalization of thyroid hormone levels (free T4 0,921 ng/dl; free T3 2,96 pg/mL), total thyroidectomy was performed without complications. Postoperatively, the patient developed transient hypoparathyroidism with mild hypocalcemia, which resolved with calcium carbonate and calcitriol. She was discharged on levothyroxine 88 ug/day and remains euthyroid.

Conclusions: This case underscores the rarity and severity of methimazole-induced agranulocytosis and the challenges in managing hyperthyroidism when this complication occurs. Early drug withdrawal, infection control, and prompt preoperative stabilization of thyrotoxicosis are crucial to prevent thyroid storm. Definitive surgery, once hematologic recovery is achieved, remains the safest curative option.

Abstract citation ID: lvag096.1721

EP1590 - ECE_1907 - Indole-3-carbinol as a potential protective agent—lipid peroxidation determination in porcine thyroid after Fenton reaction damage and application of molecular docking

Anna Skoczyńska[1], Michał B. Ponczek[2], Jan Stępniak[1] and Małgorzata Karbownik-Lewińska[1,3]
[1]*Department of Endocrinology and Metabolic Diseases, Medical University of Łódź, Łódź, Poland;* [2]*Department of General Biochemistry, University of Łódź, Łódź, Poland;* [3]*Polish Mother's Memorial Hospital—Research Institute, Łódź, Poland*

Objectives: Indole-3-carbinol is a known dietary supplement and naturally occurs in vegetables like broccoli, cabbage, cauliflower, kale, kohlrabi, mustard greens, belonging to the cruciferous family *(Brassicaceae)* and exhibiting medicinal activities. The thyroid is an endocrine gland, which is a good example of an organ, where intense redox reactions occur. The aims of this research are the evaluation of the influence of indole-3-carbinol wide range of concentrations on membrane lipid peroxidation

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

caused by Fenton reaction substrates ($FeSO_4$ and H_2O_2) in porcine thyroid homogenates and application of molecular docking with homology modelling in case of indole-3-carbinol possible interactions with known antioxidative enzymes, ie, superoxide dismutase (SOD) and glutathione peroxidase (GPx).

Methods: To determine lipid peroxidation products, ie, malondialdehyde+4-hydroxyalkenals (MDA+4-HDA), a spectrophotometric assay was used. The Fenton reaction substrates were used in the following concentrations: 1200, 600, 300, 150, 75, 37.5, 18.75, 9.375, 4.687, 2.343, 0.0 μM for $FeSO_4$ and 5.0 mM for H_2O_2. Indole-3-carbinol was used in the following concentrations: 20.0, 10.0, 5.0, 1.0, 0.5 and 0.0 mM. Additionally, *in silico* molecular docking to isoforms of antioxidative enzymes, such as SOD and GPx of human and pig was performed using SwissDock (https://www.swissdock.ch/) with AutoDock Vina algorithm. Porcine SOD and GPx homology models were generated in SwissModel based on human SOD and GPx isoforms as PDB templates.

Results: Indole-3-carbinol showed dual activity that depends on the concentration of iron ions and the indole derivative itself. This indole derivative showed antioxidant activity across its entire concentration range, particularly against $FeSO_4$ concentration equal to 18.75 μM. On the other hand, indole-3-carbinol enhanced stimulatory effect of $FeSO_4$ (1200-300 μM) on lipid peroxidation. The pro-oxidant activity of indole-3-carbinol was also observed at two highest its concentrations, when the antioxidant was used alone. Results of *in silico* molecular docking suggest that indole-3-carbinol does not interact with SOD and GPx at lower concentrations. At higher concentrations used in the *in vitro* homogenate experiments, nonspecific partial inhibition of SOD or GPX cannot be excluded, which may contribute to reduced endogenous ROS scavenging.

Conclusions: Dual nature of indole-3-carbinol relies on its anti- and pro-oxidant properties and is consistent with literature reports. Although our results do not clearly confirm any interaction between indole-3-carbinol and superoxide dismutase and glutathione peroxidase, non specific partial inhibition of these enzymes cannot be excluded, contributing to reduced endogenous ROS scavenging. Therefore, additional research is needed to determine the specific mechanism of action of indole-3-carbinol in thyroid cells.

Abstract citation ID: lvag096.1722

EP1591 - ECE_2886 - Assessment of BRAF V600E-mutated circulating tumour DNA in papillary thyroid microcarcinoma

Emilia Niedziela[1,2], Kinga Hińcza-Nowak[3], Justyna Miłek-Krupa[3], Iwona Palyga[1,2], Agnieszka Walczyk[1,2], Danuta Gąsior-Perczak[1,2], Janusz Kopczyński[4], Artur Kowalik[3,5] and Aldona Kowalska[1,2]

[1]Department of Endocrinology, Holy Cross Cancer Center, Kielce, Poland; [2]Collegium Medicum, Jan Kochanowski University, Kielce, Poland; [3]Department of Molecular Diagnostics, Holy Cross Cancer Center, Kielce, Poland; [4]Department of Tumor Pathology, Holy Cross Cancer Center, Kielce, Poland; [5]Division of Medical Biology, Jan Kochanowski University, Institute of Biology, Kielce, Poland

Background: Papillary thyroid microcarcinoma (PTMC) is a tumour ≤1 cm with a generally favourable prognosis. Management options include surgery, percutaneous ablation or active surveillance, based on clinical risk and patient preference. To date, the role of molecular assessment in the risk stratification and clinical decision-making of PTMC is limited due to insufficient evidence. Although the *BRAF* V600E mutation is detected in up to 70% of PTMC, previous studies have reported conflicting results on this mutation as a risk factor. Detection of *BRAF* V600E-mutated circulating tumour DNA (ctDNA), reflecting the release of mutated DNA from tumour cells and potentially indicating more aggressive tumour biology, may therefore be investigated as a potential marker of disease risk.

Aim: The aim of this study was to investigate the clinical utility of detection of *BRAF* V600E-mutated ctDNA in plasma as a minimally invasive adjunct to the primary diagnosis of PTMC.

Methods: This prospective, single-center study was conducted between 2021 and 2024. Patients with focal thyroid lesions who were scheduled for total thyroidectomy were enrolled. Blood samples of 10 mL were collected during the perioperative period and subsequently centrifuged. The plasma was frozen and biobanked. Plasma samples from patients with confirmed *BRAF* V600E-positive PTMC were tested for the presence of circulating nucleic acids. Positive samples were further tested for the *BRAF* V600E mutation using digital droplet PCR (ddPCR). The reference test was the detection of the *BRAF* V600E mutation in tumour tissue using real-time PCR. Patients diagnosed with other malignant tumours were excluded from the final analysis. The obtained results were correlated with clinical data.

Results: 19 plasma samples from patients with *BRAF* V600E-positive PTMC were included in the final analysis. All patients had stage I PTMC. Median time from blood sampling to surgery was 26 days (IQR: 9-35). The median size of a tumour was 7 mm (IQR: 5-8.5). No plasma samples were positive for *BRAF* V600E-mutated ctDNA.

Conclusions: The assessment of circulating tumour DNA does not seem to be a suitable test to supplement the diagnosis of PTMC, presumably due to low release of free DNA into circulation.

Abstract citation ID: lvag096.1723

EP1592 - ECE_1203 - Is statin use linked to thyroid cancer? What does NHANES show?

Christos Savvidis, Vasiliki Tsiama, Stella Proikaki, Konstantinos Belis, Efthymia Kallistrou, Dimitra Ragia, Dimitra Motsiou and Ioannis Ilias

Department of Endocrinology, Hippokration Hospital, Athens, Greece

Introduction: The use of statins and its relation to thyroid cancer have been under continuous research with somewhat conflicting findings; however, evidence also leans toward a potential protective effect rather than harm.

Aim: To assess statin use in relation to thyroid cancer using the NHANES data.

Methods: Data from NHANES 2013-2020 were analyzed (*n*: 35 706, 1:1 gender ratio). NHANES is a continuous, nationally representative program, which runs in the U.S.. The program monitors the health and nutritional status of the U.S. population through interviews, physical examinations, and laboratory tests. Statin use was recorded ($n = 3643$, all medications combined) as was thyroid cancer history (all histologies, $n = 59$). Statistical analysis

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

was done with logistic regression and the chi square test; associations between thyroid cancer history, age, gender and reported statin use were assessed.

Results: Thyroid cancer history was positively linked ($P < .05$) to age (weakly, Nagelkerke R2:0.065), female gender (OR: 1.311-3.201) and statin use (OR: 0.739-1.933), but for the latter, the confidence intervals of the OR were not significant.

Discussion: The number of thyroid cancer cases was small ($n = 59$); this may limit definitive epidemiologic conclusions. Many recent large-scale observational data suggest that statin use is not associated with an increased risk of thyroid cancer; studies even suggest that statin use may even confer a protective effect. The protective effect may be related to the known anti-proliferative and pro-apoptotic effects of statins on thyroid cancer cells, as well as their ability to modulate metabolic pathways linked to cancer risk. However, some studies have reported an increased risk, particularly in women: patient-specific factors, statin type, dosage, and duration of use might influence outcomes. Limitations of existing studies include their retrospective design, potential confounding, and reliance on administrative data for diagnoses; all these factors necessitate cautious interpretation.

Conclusions: This work is congruous with previous smaller studies that suggested a possible increased risk of thyroid cancer with statins' use. However, larger studies have reported negative associations, indicating that statin use may reduce thyroid cancer risk. This is corroborated by mechanistic studies, which have shown that statins exert anti-cancer properties on thyroid cells. Additional research is needed to conclusively establish this.

Abstract citation ID: lvag096.1724

EP1594 - ECE_3384 - Subject: anaplastic thyroid carcinoma: clinical presentation, diagnosis and management in a four-case series

Charikleia Paschalidi[1], Anna-Maria Papadopoulou[2], George Papastergiou[2], Marina Sassi[3], Akrivi Kostopoulou[3], Danai Georgakopoulou[1], Athina Markou[1], Athanasios Fountas[1] and Labrini Papanastasiou[1]

[1]Unit of Endocrinology and Diabetes, General Hospital of Athens "G. Gennimatas", Athens, Greece; [2]Otolaryngology, General Hospital of Athens "G. Gennimatas", Athens, Greece; [3]Pathology, General Hospital of Athens "G. Gennimatas", Athens, Greece

Introduction: Anaplastic thyroid carcinomas (ATC) is a rare tumor usually presented at an advanced stage and characterized by aggressive behavior and poor prognosis. Current best practices consist of radical surgery combined with postoperative radiotherapy and chemotherapy. For BRAF*V600E*-positive tumors, targeted BRAF inhibitors are available.

Objective: We report on a series of four cases of patients with ATC presented in our clinic between 2023-2025.

Case reports: 1st case

A 69-year-old male underwent total thyroidectomy due to a large thyroid nodule. Histology showed poorly differentiated thyroid carcinoma. He presented a month later with locally advanced disease, causing airway obstruction necessitating emergency tracheostomy. The CT scan showed pulmonary metastases (stage IVC). New histological examination revealed ATC positive for BRAF mutation. Treatment with dabrafenib-trametinib was initiated combined with ERBT and chemotherapy. Three months later, the patient developed rare metastases to the right pulmonary artery and left ventricle. He passed away three months after disease progression.

2nd case

A 90-year-old male presented to the outpatient department with a three-month history of coarseness and cough. Thyroid ultrasound revealed a 3-cm nodule with cytology positive for ATC. PET-FDG scan was negative for metastatic disease (stage IVB), and the patient underwent total thyroidectomy. Histology confirmed the diagnosis of ATC positive for BRAF mutation. The patient was treated with dabrafenib—trametinib and refused to undergo radiotherapy or chemotherapy. He passed away four months after the diagnosis.

3rd case

A 73-year-old female underwent total thyroidectomy due to a nodule with cytology positive for papillary carcinoma. During the surgery, a large thyroid nodule was discovered, extensively infiltrating the surrounding tissues. Histology showed ATC, while molecular profiling showed an HRAS mutation. A PET-FDG scan one month later revealed metastatic disease (stage IVC). Due to the absence of specific targeted therapy, she received standard radiotherapy and chemotherapy which was complicated by radiation-induced esophagitis.

4th case

A 73-year-old female with a history of advanced dementia presented to the emergency department with a progressively enlarging cervical mass. FNB confirmed the diagnosis of ATC. Imaging revealed an enlarged cervical mass and multiple pulmonary nodules (stage IVC). Given the patient's poor clinical condition and the advanced stage of disease, a palliative approach was decided. The patient died within a month.

Conclusions: The management of ATC remains challenging due to its rapid progression and limited response to conventional therapies. These cases underscore the need for early diagnosis, multidisciplinary approach, and molecular profiling to guide personalized therapy.

Abstract citation ID: lvag096.1725

EP1596 - ECE_3482 - Herpetic keratitis complicating thyroid eye disease: a report of two rare cases

Dionysios Vrachnis[1], Grigoris Effraimidis[1,2], Nektarios Adamopoulos[1], Athanasios Kasotas[1], Maria Galani[1], Eleni Georgiou[1], Ioannis Gkountios[1], Anastasia-Konstantina Sakali[1], Apostolia Pouliou[1], Stefanos Tamouridis[1], Maria Apostolopoulou[1,2] and Alexandra Bargiota[1,2]

[1]Department of Endocrinology and Metabolic Diseases, University General Hospital of Larissa, Larissa, Greece; [2]Faculty of Medicine, Department of Endocrinology and Metabolic Diseases, School of Health Sciences, University of Thessaly, University General Hospital of Larissa, Larissa, Greece

Introduction: Thyroid Eye Disease (TED) is an autoimmune inflammatory disease of the orbit that primarily affects the extraocular muscles, orbital adipose tissue, and surrounding soft tissues. Herpes simplex virus (HSV) keratitis may lead to exposure keratopathy with epithelial breakdown and corneal ulceration, potentially resulting in sight-threatening visual loss.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Case 1: A 71-year-old woman with a 35-year history of Graves' disease and post-thyroidectomy hypothyroidism presented with moderate-to-severe TED, with symptoms of two months' duration. One month prior to her visit to our clinic, she had been diagnosed with herpetic keratitis in the left eye. Slit-lamp examination revealed a central corneal scar with old fibrosis. For TED, intravenous glucocorticoid (IVGC) therapy was administered (cumulative dose of 4.5 g of methylprednisolone over 12 weeks), resulting in improvement of TED symptoms and she also received topical and therapy for herpetic keratitis, with concomitant clinical improvement.

Case 2: A 74-year-old man presented to our clinic with a recent diagnosis of Graves' disease and moderate-to-severe TED, with symptoms of three months' duration. Two months prior to his visit to our clinic, he had been diagnosed with herpetic keratitis in the right eye. IVGC therapy was administered (cumulative dose of 4.5 g of methylprednisolone over 12 weeks),leading to significant improvement of TED and he had topical therapy and oral acyclovir for his h keratitis, with associated improvement on slit-lamp examination.

Discussion: TED is a challenging condition to manage and may become more complex when herpetic keratitis coexists. Clinical manifestations of TED include tear film instability, proptosis with dry eye symptoms, eyelid retraction, restricted ocular motility, and impaired Bell's phenomenon, all of which contribute to ocular surface destabilization and corneal exposure. Patients with active TED are at increased risk of developing corneal infections, including herpetic or bacterial keratitis, and in severe cases, corneal ulceration with potential visual impairment. When initiating IVGC therapy, clinicians should be mindful of the risk of HSV reactivation. Regular slit-lamp examination is essential for evaluating disease activity and detecting corneal complications.

Abstract citation ID: lvag096.1726

EP1597 - ECE_1134 - Variable clinical manifestations of thyroid carcinoma associated with struma ovarii; role of serum thyroglobulin

Ho-Cheol Kang[1], Jeehee Yoon[1], Ji Yong Park[1], A Ram Hong[1], Young Sang Lyu[2], Jin Woo Jung[3] and Hee Kyung Kim[1]
[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Chonnam National University Medical School, Chonnam University Hwasun Hospital, Hawsun, South Korea; [2]Division of Endocrinology and Metabolism, Department of Internal Medicine, Chosun University School of Medicine, Gwangju, South Korea; [3]Division of Endocrinology and Metabolism, Department of Internal Medicine, Wonkwang University Scholl of Medicine, Iksan, South Korea

Introduction: Struma ovarii (SO) is a specialized form of ovarian teratoma in which more than 50% of the tumor is composed of thyroid tissue, and malignant transformation is extremely rare. Owing to its rarity and the fact that most cases are initially managed in gynecology, SO associated with thyroid carcinoma has been reported only sporadically in the form of individual case reports or small series. We report three cases of thyroid carcinoma associated with SO managed at a single tertiary referral center.

Patients: The first patient, a 51-year-old woman who underwent total thyroidectomy for papillary thyroid carcinoma (PTC) showed persistently elevated thyroglobulin (Tg) levels despite negative neck and chest imaging. PET-CT revealed an adnexal mass, and surgery confirmed SO; her Tg normalized and remission was maintained for three years.

The second patient, a 65-year-old woman, was diagnosed with PTC arising in SO after oophorectomy. Subsequent total thyroidectomy revealed occult papillary carcinoma in the thyroid. Her postoperative serum Tg decreased to 18.4 ng/mL and became undetectable following radioiodine ablation (RAI). she remained in remission for four years. The third patient, a 37-year-old woman, had SO with peritoneal strumosis but no malignant cells. Small enhancing pelvic lesions persisted postoperatively, and total thyroidectomy revealed multiple PTCs (5 mm and 2 mm). Her postoperative serum Tg was 13.3 ng/mL, and she was scheduled to receive RAI.

Conclusions: These cases demonstrate the heterogeneous clinical spectrum and diagnostic challenges of thyroid carcinoma coexisting SO. Unexplained serum Tg elevation after thyroidectomy warrants evaluation for ectopic thyroid tissue, including SO, and can aid in determining the need for RAI.

Abstract citation ID: lvag096.1727

EP1601 - ECE_1326 - Diagnostic challenges of TSH–FT4 discordance: a case of TSHoma with Graves' disease and a case of chronic TSH elevation with uncertain origin

Guan-Ho Chen and Chih-Yuan Wang
Division of Metabolism and Endocrinology, National Taiwan University Hospital, Taipei, Taiwan

Background: Discordant TSH and FT4 levels represent a major diagnostic challenge, particularly when pituitary lesions, evolving autoimmunity, or chronic TSH elevation coexist. We report two contrasting cases illustrating different mechanisms of pituitary–thyroid axis dysregulation.

Methods: Clinical, biochemical, autoimmune, imaging, and TRH stimulation data were reviewed longitudinally.

Results: Case 1 demonstrated persistently elevated or high-normal thyroid hormone concentrations accompanied by inappropriately non-suppressed TSH, consistent with a TSH-secreting microadenoma. Several years later, new-onset Graves' disease emerged, producing abrupt thyrotoxicosis while TSH remained unsuppressed. Case 2 exhibited more than a decade of markedly elevated TSH with only mild reductions in FT4, minimal symptoms, and a small pituitary lesion. An exaggerated TRH response supported primary thyroid dysfunction but did not fully exclude subtle pituitary dysregulation.

Conclusions: These cases highlight the complexity of interpreting TSH–FT4 discordance and the limitations of TRH stimulation in long-standing abnormalities. Integrating longitudinal biochemical trends, evolving autoimmunity, and pituitary imaging is essential for distinguishing primary from central mechanisms.

Abstract citation ID: lvag096.1728

EP1602 - ECE_2092 - Rapid malignant transformation of long-standing multinodular goiter into anaplastic thyroid carcinoma

Jezdancher Watti
Gyöngyösi Bugát Pál Hospital, Gyöngyös, Hungary

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Anaplastic thyroid carcinoma (ATC) is a rare, highly aggressive malignancy, frequently arising in elderly patients with pre-existing benign thyroid disease. It is characterized by rapid local progression, early distant metastases, and dismal prognosis. Early recognition of warning symptoms is critical.

A 78-year-old woman with a >30-year history of non-toxic multinodular goiter and multiple cardiovascular comorbidities presented with a 3-month history of progressive left-sided neck enlargement, dysphagia, hoarseness, dyspnea, and stridor, accompanied by weight loss. Physical examination revealed a firm, fixed cervical mass (~15 cm) with airway deviation. Laboratory tests showed euthyroidism and normocytic anemia.

Contrast-enhanced neck and chest CT demonstrated a markedly enlarged thyroid with a heterogeneous solid mass (68 × 76 mm axial, 96 mm craniocaudal) arising from the left lobe, displacing the trachea and laryngeal structures, with retrosternal extension. Multiple bilateral pulmonary nodules consistent with metastases and right-sided pulmonary embolism were identified. No overt tracheal lumen obstruction was present, but significant airway compromise was evident clinically.

Fine-needle aspiration cytology and ultrasound-guided core biopsy revealed high-grade undifferentiated carcinoma consistent with anaplastic thyroid carcinoma.

Immunohistochemistry demonstrated broad cytokeratin positivity (CK8/18) with negative TTF-1, PAX8, BRAF, pan-TRK, and HER2. PD-L1 expression was strikingly high (CPS 100; TPS 100%).

Given ECOG performance status 2, extensive locoregional disease, pulmonary metastases, and acute pulmonary embolism, curative treatment was not feasible. The patient received anticoagulation (LMWH) and palliative hypofractionated radiotherapy to the thyroid mass (5 × 4 Gy) for airway protection and symptom relief. A nasogastric feeding tube was placed to secure nutrition. Multidisciplinary tumor board recommended further oncologic evaluation for systemic therapy; molecular profiling was initiated.

This case highlights the catastrophic malignant transformation of long-standing multinodular goiter into ATC, presenting with rapidly progressive airway-threatening disease, distant pulmonary metastases, and thromboembolic complications. Red-flag symptoms—rapid neck mass growth, dysphagia, hoarseness, and stridor—in patients with benign thyroid disease mandate urgent evaluation. The exceptionally high PD-L1 expression underscores the potential role of immunotherapy in selected ATC patients. Despite modern multimodal approaches, ATC remains a devastating disease, emphasizing the need for early detection and personalized therapeutic strategies.

Abstract citation ID: lvag096.1729

EP1603 - ECE_3734 - Levothyroxine-induced agranulocytosis: an exceptional adverse effect in a patient with congenital heart disease

Zaynab Ezzahoum[1,2], Nassim Essabah Haraj[1,2], Malak Iggar[1,2], Siham El Aziz[1,2] and Asma Chadli[1,2]
[1]*Endocrinology, Diabetology, Metabolic Diseases and Nutrition Department, Ibn Rochd University Hospital, Casablanca, Morocco;* [2]*Clinical Neuroscience and Mental Health Laboratory, Faculty of Medicine and Pharmacy, Hassan II University-Casablanca, Casablanca, Morocco*

Introduction: Levothyroxine is widely used in the management of hypothyroidism. Its adverse effects are predominantly cardiovascular or metabolic. Hematologic complications, particularly neutropenia or agranulocytosis, are exceptionally reported. We present a case of central neutropenia potentially induced by levothyroxine, in the context of concomitant medication use, with a review of possible mechanisms.

Case Report: A 26-year-old patient with Tetralogy of Fallot, not indicated for surgical correction, followed for inflammatory anemia, was admitted for a prolonged febrile syndrome evolving over three months, without an evident infectious focus. Initially treated with ceftriaxone 2 g/day, laboratory tests revealed hypothyroidism, and levothyroxine at 12.5 µg/day was initiated. After 15 days, severe agranulocytosis was observed (absolute neutrophil count: 240/mm^3). Discontinuation of levothyroxine led to gradual improvement in hematologic parameters (ANC: 11 620/mm^3), suggesting a probable drug-related origin. The imputability of levothyroxine was retained (I3B2), although this effect is exceptionally described.

Conclusion: This case highlights the need to consider levothyroxine as a rare but possible cause of central agranulocytosis, particularly in combination with other medications. Rigorous hematologic monitoring may be warranted in the presence of infectious signs during thyroid hormone replacement therapy.

Abstract citation ID: lvag096.1730

EP1604 - ECE_1490 - Prevalence of hypothyroidism and its association with metabolic parameters in patients with metabolic syndrome: a retrospective cross-sectional study

Mariami Azirashvili and Lia Pertaia
Endocrinology Department, Consilium Medulla Multiprofile Clinic, Tbilisi, Georgia

Background: Metabolic syndrome is a complex cardiometabolic condition characterized by dyslipidemia, hypertension, and impaired glucose metabolism. Thyroid hormones play a key role in lipid and energy homeostasis, and thyroid dysfunction may exacerbate metabolic abnormalities. The coexistence of thyroid dysfunction and metabolic syndrome may therefore contribute to increased cardiometabolic risk; however, data on their association in routine clinical practice remain limited.

Aim: To determine the prevalence of overt and subclinical hypothyroidism in patients with metabolic syndrome and to compare selected metabolic parameters between euthyroid and hypothyroid individuals.

Methods: This retrospective cross-sectional observational study included 70 patients diagnosed with metabolic syndrome. Patient data were extracted from electronic medical records of the Multiprofile Clinic "Consilium Medulla" in Tbilisi, Georgia.

Metabolic syndrome was defined according to the NCEP ATP III criteria. Due to the unavailability of waist circumference measurements, metabolic syndrome was diagnosed in patients meeting at least three of the four available ATP III criteria.

Hypothyroidism was defined as a serum thyroid-stimulating hormone (TSH) level >3.8 mIU/L. Both overt and subclinical hypothyroidism were included; overt hypothyroidism was defined by elevated TSH with reduced free thyroxine (FT4), whereas subclinical hypothyroidism was defined by elevated TSH with normal FT4.

Metabolic parameters were compared between euthyroid and hypothyroid patients. Data distribution was assessed using the

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Shapiro–Wilk test; between-group comparisons were performed using the independent samples t-test or the Mann–Whitney U test, as appropriate. A *P*-value <.05 was considered statistically significant.

Results: The median age was 52 years (IQR 40-64), and 40 patients (57.1%) were male. Hypothyroidism was present in 31 patients (44.3%, 95% CI: 33.2-55.9), including 15 with subclinical hypothyroidism and 16 with overt hypothyroidism. Compared with euthyroid patients, those with hypothyroidism had significantly higher low-density lipoprotein (LDL) cholesterol levels ($P = .027$) and lower diastolic blood pressure ($P = .017$). No statistically significant differences were observed in other metabolic parameters (Table 1).

Conclusion: Hypothyroidism was common among patients with metabolic syndrome and was associated with higher LDL cholesterol levels and lower diastolic blood pressure. Routine assessment of thyroid function may help identify patients with an unfavorable cardiometabolic profile in this population.

Table 1 Comparison of metabolic parameters between euthyroid and hypothyroid patients.

Metabolic parameter	*P*-value
BMI	0.986[a]
Fasting glucose	0.221[a]
Triglycerides	0.321[a]
HDL cholesterol	0.471[a]
LDL cholesterol	**0.027**[b]
Systolic blood pressure	0.053[a]
Diastolic blood pressure	**0.017**[a]

[a]Mann–Whitney U test.
[b]Independent t-test.

Abstract citation ID: lvag096.1731

EP1605 - ECE_1086 - Performing hemithyroidectomy for nodular and unilateral multinodular euthyroid goiters

Farida Saidova[1], Oruc Shahsuvarov[1], Rasim Huseynov[1], Shahla Alakbarova[1], Aygun Mayilova[1], Nizami Muradov[2] and Natavan Aliyeva[3]
[1]Endocrine Surgery, Scientific Center of Surgery named M.A.Topchubashov, Baku, Azerbaijan; [2]Anesthesiology and Reanimatology, Scientific Center of Surgery named M.A.Topchubashov, Baku, Azerbaijan; [3]Radiology, Scientific Center of Surgery named M.A.Topchubashov, Baku, Azerbaijan

The aim of the study is to evaluate the results of hemithyroidectomy for nodular and unilateral multinodular euthyroid goiter.
Material and Methods: Total of 98 patients, aged 20-74 years with nodular (46) and unilateral multinodular euthyroid goiter (52) who had undergone hemithyroidectomy, were examined (women – 80.6%, men – 19.4%). Most of patients were women aged 41-50 years (30.6%). All patients underwent hemithyroidectomy (removal of the one lobe and isthmus). The majority (73.5%) of patients were follow-up within 4-5 years after surgery.

Results and Discussion: In patients with nodular and unilateral multinodular euthyroid goiter who underwent hemithyroidectomy, the following was observed low recurrence rates (4.3% and 11.5%, respectively). The incidence of postoperative hypothyroidism compensated by replacement therapy after hemithyroidectomy for NEG and MNEG is 19.6% and 21.2%, respectively. The quality of life was much better for patients after hemithyroidectomy, than for patients who underwent radical surgeries: 84.8% of patients with NEG and 78.8% of patiens with unilateral MNEG did not require burdensome hormone therapy. However, patients with hypothyroidism need a low level of postoperative replacement therapy. A comparison of levothyroxine levels taken by patients with NEG and MNEG after hemithyroidectomy revealed a non-significant ($P > .05$) difference between the groups, consistent to 36.1 ± 4.4 μg and 40.9 ± 5.1 μg, respectively. Risk factors for the development of recurrence of MNEG include the patient's young age, the duration of follow-up, the absence of replacement therapy, the presence of a hereditary genesis of the disease and lymphoid infiltration. Factors predisposing to the development of postoperative hypothyroidism include lymphoid infiltration of the glandular tissue, the duration of follow-up hereditary genesis of the disease.

Findings: Performing a hemithyroidectomy for NEG and unilateral MNEG is the optimal volume of surgery. However, the choice of this procedure for unilateral MNEG is a joint decision between the surgeon and the patient, made, taking into account risk factors for recurrence and postoperative hypothyroidism are determined individually for each patient.

Abstract citation ID: lvag096.1732

EP1606 - ECE_2617 - Thyroid storm at onset-an uncommon first presentation of Graves disease

Muhammad Dalili[1], Shadman Rahman[1], Sarah El-Toukhy[1], Hussam Khalifa[1], Jayalekshmi Leena[1], Jaspal Kallah[2], Thomas Yau[2] and Sameer Sighakoli[1]
[1]Diabetes and Endocrine, Medway Maritime Hospital, Gillingham, United Kingdom; [2]Medway Maritime Hospital, Gillingham, United Kingdom

Introduction: Graves' disease is an autoimmune disorder causing hyperthyroidism through antibodies that stimulate levothyroxine (T4) and triiodothyronine (T3) production.[1] It typically presents with palpitations, weight loss, tremors, and sweating.[2] While thyroid storm is a rare complication of Graves' disease, its occurrence as the first clinical manifestation is exceptionally uncommon.[3] Therefore, a detailed history, thorough examination and holistic approach are essential for diagnosis, management, and follow-up.[2]

Case: A 62-year-old woman with a background of hypertension, T2DM, COPD, OSA, and HF presented with acute-onset confusion, shortness of breath, chest and abdominal pain, and vomiting. Examination revealed GCS 14/15, hypoxia and signs of decompensated cardiac failure.

ABG on 4 L of oxygen demonstrated T1RF. Chest radiography showed features consistent with pulmonary oedema (Figure 1). Blood investigations revealed AKI-1 and an elevated BNP (Table 1). CT of the head and abdomen/pelvis were unremarkable.

The patient was transferred to the critical care unit in view of multi-system involvement. A thyroid function test demonstrated a hyperthyroid picture (Table 1). The Burch–Warsofsky Point Scale score was 80, highly suggestive of thyroid storm. Thyroid ultrasonography demonstrated features

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

of thyroiditis (Figure 2). ECHO showed preserved EF.

The patient was started on carbimazole, intravenous hydrocortisone, and beta-blocker. The patient's symptoms improved clinically, and repeat thyroid function tests on day 6 showed biochemical improvement, with positive TSH receptor antibodies (Table 2).

The patient continued to improve and was discharged after two weeks with a plan for repeat thyroid function testing in two weeks and follow-up in endocrinology and arrhythmia clinics.

Conclusion: This case illustrates the rare occurrence of thyroid storm as the initial presentation of Graves' disease and underscores the critical importance of timely diagnosis and appropriate management in the intensive care setting due to the high mortality rate of this endocrine emergency.

Figure 1

Figure 2

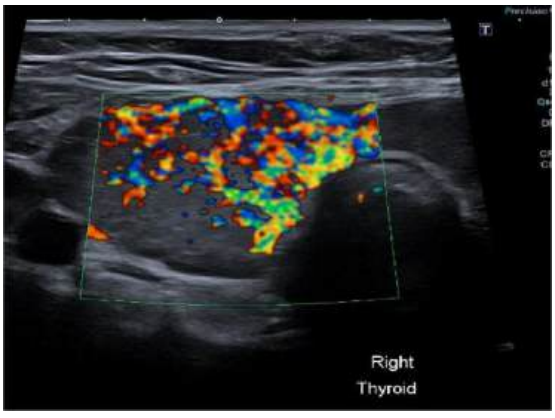


Table 1

Blood tests	11/8/25	6/8/25	Reference
TSH	<0.02	<0.02	0.3-4.8 mIU/L
Free T3	4.1	7.9	4.2-6.9 pmol/L
Free T4	12.4	52	7.7-20.6 pmol/L
TSH receptor antibody	385		0.0-0.9 IU/L
BNP	2692		0.0-99 pg/mL

References

1. Smith J, Doe A, Brown B. Graves' disease and its impact on thyroid hormone production. *J Clin Endocrinol Metab*. 2020;105(2):423-429. https://doi.org/10.1210/jc.2020-00123
2. Smith TJ, Hegedüsp L. Graves' disease. *N Engl J Med*. 2016;375(16):1552-1565. https://doi.org/10.1056/NEJMra1510030
3. Karriqi E, Padfield E. Lost in a thyroid storm—psychosis as a first presentation of Grave's disease. *BJPsych Open*. 2025;11(S1):S306. https://doi.org/10.1192/bjo.2025.10737

Abstract citation ID: lvag096.1733

EP1607 - ECE_2876 - The role of the free triiodotyronine to free thyroxine ratio in the differential diagnosis of thyrotoxicosis: a cross-sectional study

Saieehwaran Menon[1], Sy Liang Yong[1], Abdullah Shamshir Abd Mokti[2] and Vijiya Mala Valayatham[2]
[1]Hospital Tengku Ampuan Rahimah Klang, Klang, Malaysia; [2]Institut Endokrin, Hospital Putrajaya, Putrajaya, Malaysia

Thyrotoxicosis is a clinical state of excessive thyroid hormone action arising from diverse etiologies and accurate differentiation of these causes is essential for optimal management. Advanced diagnostic modalities, such as thyrotropin receptor antibody (TRAb) assay and ultrasonography are not often accessible in resource-limited settings, underscoring the need for cost-effective alternatives. Emerging evidence suggests that the free triiodothyronine to free thyroxine (FT3/FT4) ratio may serve as a potential biomarker for distinguishing the causes of thyrotoxicosis.

This study aimed to compare the FT3/FT4 ratio among patients with different etiologies of thyrotoxicosis and to correlate these findings with autoantibodies. A cross-sectional study was conducted among patients aged ≥18 years with newly diagnosed thyrotoxicosis recruited from Hospital Tengku Ampuan Rahimah, Hospital Banting, Klinik Kesihatan Pelabuhan Klang and Klinik Kesihatan Pandamaran. All participants underwent thyroid function testing (ie, FT3, FT4 and thyroid-stimulating hormone (TSH)) and autoantibody assays (ie, TRAb and anti-thyroid peroxidase antibody (anti-TPO)). Receiver operating characteristic (ROC) curve was performed to evaluate the discriminatory value of FT3/FT4 ratio in Graves' disease, Hashimoto's disease and thyroiditis. A total of 58 patients were recruited from February to December 2025. Of these, 58.6% were diagnosed with Graves' disease, 22.4% with thyroiditis, and 19.0% with Hashimoto's disease. FT3 levels in patients were significantly higher in Graves' disease (Median 16.8 pmol/L; Interquartile range (IQR) 10.9-25.7) compared with Hashimoto's disease (Median 10.6 pmol/L; IQR 6.9-15.2) and thyroiditis (Median 6.6 pmol/L; IQR = 5.2-9.6) ($P < .001$). A similar trend was observed for FT4 levels ($P < .001$). However, the FT3/FT4 ratio did not differ significantly between Graves' disease, Hashimoto's disease and thyroiditis ($P > .05$). ROC curve analysis revealed limited discriminatory ability of the FT3/FT4 ratio, with area under the curve (AUC) ranging from 0.503 to 0.720. Notably, its discriminatory ability improved when stratified by FT4 levels. At FT4 of 30-49 pmol/L, the FT3/FT4 ratio showed good discriminatory ability in distinguishing Hashimoto's disease from thyroiditis

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(AUC = 0.958, 95% CI = 0.837-1.000; $P = .019$), with 100% sensitivity and 83.3% specificity at a cutoff of 0.2884. In addition, the FT3/FT4 ratio showed no significant correlation with TRAb or anti-TPO.

In conclusion, while the overall discriminatory value of the FT3/FT4 ratio is limited, it may still provide adjunctive diagnostic insight in selected biochemical contexts, complementing established immunologic investigations.

Abstract citation ID: lvag096.1734

EP1609 - ECE_3740 - Unusual case of concomitant papillary thyroid cancer and malignant choroidal melanoma

Vitali Vashakidze, Tea Khurodze, Ana Pruidze, Basa Gegeshidze and Elisabed Pkhaladze
Tbilisi, Georgia

Introduction: Papillary thyroid carcinoma (PTC), the most common malignant thyroid neoplasm, accounts for approximately 1% of newly diagnosed malignancies and is predominantly found in females. Melanoma is the type of cancer that develops from melanin-producing cells, and in 3-4% can arise in the eyes. The PTC increases the risk of melanoma by 1.8-fold. Recent studies revealed that the coincidence of these two malignancies has various probable mechanisms and can be associated with BRAF and BRCA-1-associated protein (BAP1) gene mutations. Although the coexistence in the same patient is uncommon, the occurrence can have significant implications for the patient's clinical presentation, diagnostic evaluation, and treatment approach.

Case Presentation: A 65 years old caucasian female was diagnosed with thyroid papillary cancer. She was asymptomatic and was found to have right thyroid mass on routine neck ultrasound exam—classified as TIRADS V, euthyroid state, and negative antithyroid antibodies confirmed with lab. Tests. FNAC findings were consistent with papillary carcinoma, Bethesda class VI.

The patient's Past medical history was remarkable for arterial hypertension, prediabetes (treated with Ace inhibitor in combination with Thiazide diuretic, metformin 750 mg, and atorvastatin 20 mg), and left-sided nephrectomy due to nephrolithiasis with hydronephrosis in 2018. Her family history was significant with paternal bladder carcinoma and maternal diabetes mellitus. The patient's social history was negative for cigarette smoking or alcohol use.

The patient underwent thyroidectomy and left-sided lymphadenectomy. Pathologic report demonstrated papillary carcinoma without lymphovascular invasion. After thyroidectomy, 50-mCi I-131 was administered, and levothyroxine suppressive treatment was started.

Six months later, the whole-body scan didn't show any evidence of an abnormal radioiodine-avid lesion throughout the body. Regular checkups and scans every six months for the first two years excluded the recurrence of TPC. But for the past two months patient started complaining about seeing left-sided flashes of light, noticing floating objects (photopsia, metamorphopsia). She was referred for eye exam and imaging tests, clinical and imaging features were consistent with the diagnosis of left eye malignant choroidal melanoma. Soon after, left globe enucleation and implant replacement were performed.

At this time, the patient is in good health and under continuous medical supervision.

Conclusion: In this unique case report, we present a patient demonstrating papillary thyroid carcinoma and malignant choroidal melanoma. With some evidence in favor of associations between the two cancers, the case illustrates the importance of routine follow-up and active surveillance.

Abstract citation ID: lvag096.1735

EP1610 - ECE_2160 - Tōku Ara OraNGA* (TAONGA): development and testing of a thyrotoxicosis model of care co-designed with Indigenous whānau

Jade Tamatea[1,2], Taisha Abbott[1], Matire Harwood[1] and Marianne Elston[1,2]
[1]*University of Auckland | Waipapa Taumata Rau, Auckland, New Zealand;* [2]*Endocrinology Department, Te Whatu Ora Waikato/Health New Zealand, Hamilton, New Zealand*

Introduction: Unfair, unjust healthcare inequities are experienced by many Indigenous populations.[1] In Aotearoa/New Zealand, Indigenous healthcare inequities have long been documented, more recently including in thyrotoxicosis.[2] Healthcare design is an important determinant impacting inequities.

Objectives: Grounded in Indigenous (kaupapa Māori) methodology,[3] *Tōku Ara OraNGA* (TAONGA)* is an Indigenous-led four-staged mixed-methods project, setting out to work alongside *whānau* (Māori patients and families) to reimagine thyrotoxicosis services.

Methods: *Whakatakatū* (Stage 1 – Research foundation) established governance and responsibility relationships, and mapped available quantitative evidence of ethnic inequities in thyrotoxicosis in Aotearoa/New Zealand. *Kōrero mai, kōrero atu* (Stage 2 – Qualitative) added narrative of thyrotoxicosis care via thematic analysis within a kaupapa Māori paradigm of four focus groups with whānau and stakeholders. Grounded in reciprocity, Stage 3 – model of care co-design—shared earlier findings within three facilitated *wānanga* (workshops) to identify action areas (define/engage) and allow 'no-limit' solutions (test/finalise). Informed by both CONSIDER[4] and CONSORT[5] statements, a pilot of clinical care (Stage 4) delivered in partnership with a local Indigenous community health provider will test this model of care.

Results: Indigenous governance and responsibility relationships informed all four stages. A metaphoric river summarises the 'patient journey map' of quantifiable Māori thyrotoxicosis inequity information from epidemiology to outcomes. Stage 2 presents seven themes in an Indigenous flower conceptualisation: (a) recognisably Māori care, (b) differential experiences, (c) system access, (d) autonomy, (e) *whānau*/family, (f) communication, and (g) reciprocal relationships. Co-design *wānanga* developed a model of care incorporating six design features: (a) the foundational right to high quality healthcare, (b) safe environments, (c) support services, (d) staff development, (d) reciprocal relationships, and (e) resources. Conditional ethical approval means a clinical pilot will soon begin with feasibility findings able to be presented. Additionally, collaborative approaches to dissemination have developed whānau-informed outputs.

Conclusion: Indigenous-led research can facilitate power-sharing with *whānau*/families, supported by knowledgeable stakeholders,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

to create healthcare responsive to diverse Indigenous realities. It is imagined this will translate to better healthcare experiences and outcomes that could reach beyond thyroid care.

* *"Tōku Ara Oranga"–translating to 'My wellness path'*

References

1. Anderson I, Robson B, Connolly M, et al. Indigenous and tribal peoples' health (The Lancet–Lowitja Institute Global Collaboration): a population study. *Lancet*. 2016;388(10040): 131-157. http://doi.org/10.1016/S0140-6736(16)00345-7
2. Tamatea J. University of Auckland; 2018. https://reseachspace.auckland.ac.nz/items/b4e496d4-b8f6-45fb-a6ea-93406c9f6bb3
3. Smith LT. Zed Books; 2021. ISBN 9781877578281.
4. Huria T, Palmer SC, Pitama S, et al. Consolidated criteria for strengthening reporting of health research involving indigenous peoples: the CONSIDER statement. *BMC Med Res Methodol*. 2019;19:173. https://doi.org/10.1186/s12874-019-0815-8
5. Hopewell S, Chan A-W, Collins GS, et al. CONSORT 2025 statement: updated guideline for reporting randomised trials. *Nat Med*. 2025;31:1776-1783. https://doi.org/10.1038/s41591-025-03635-5

Abstract citation ID: lvag096.1736

EP1611 - ECE_2041 - National prevalence of thyroid disorders in North Macedonia: marked female predominance in a population-based registry study

Ana Talevska[1,2], Zaklina Cagoroska[3], Emilija Antova[4], Lisa Zottarelli[5], Colton Daniels[6], Larisa Ozeryansky[7], Sunil Thankam[7] and Ivica Smokovski[8]

[1]Internal Medicine, Klinicka Bolnica Dr Trifun Panovski, Bitola, North Macedonia; [2]Faculty of Medicine, Skopje, North Macedonia; [3]eHealth Directorate, Ministry of Health, Skopje, North Macedonia; [4]Medicinski Fakultet, Skopje, North Macedonia; [5]University of Tennesse, College of Social Work, Knoxville, United States; [6]Saint Mary's University, San Antonio, United States; [7]Univ Health System Inc., Knoxville, United States; [8]Univerzitet Goce Delchev-Medicinski Fakultet, Shtip, North Macedonia

Background: Thyroid disorders are among the most prevalent endocrine conditions worldwide, yet national-level epidemiological data from Southeast Europe remain limited. The Republic of North Macedonia has a history of iodine deficiency and recent concerns regarding changing dietary patterns, underscoring the need for comprehensive population-based data.

Objective: To estimate the national prevalence of thyroid disorders and to evaluate sex-, age-, and residence-specific patterns using data from the National e-Health System (NeHS).

Methods: A population-based cross-sectional analysis was performed using anonymized data from the NeHS, a nationwide electronic health platform integrating records from all levels of care. Individuals with recorded ICD-10 codes E00–E07 as of October 31, 2024 were identified. Prevalence estimates were calculated using official population denominators from the State Statistical Office and stratified by sex, age group, and urban or rural residence. Associations were assessed using odds ratios (ORs) with 95% confidence intervals (CIs).

Results: Among a total population of 1 836 713 individuals, 269 690 had a documented thyroid disorder, corresponding to an overall prevalence of 14.68%. Prevalence was substantially higher in women than in men (24.36% vs 4.85%), with a pronounced female predominance observed across all age groups and residential settings (overall OR 6.32; 95% CI 6.25-6.38). Thyroid disorder prevalence increased with age in both sexes, peaking in individuals aged 60-79 years (21.87%). Higher prevalence was observed in urban compared with rural areas (17.07% vs 10.85%). Hypothyroidism (ICD-10 E03) was the most frequent diagnosis, affecting 9.74% of the total population.

Conclusions: This first national-level registry-based study from North Macedonia demonstrates a high population burden of thyroid disorders with a marked and persistent female predominance and clear age- and residence-related patterns. These findings highlight substantial sex-specific disparities in thyroid disease and emphasize the importance of targeted screening and public health strategies in Southeastern Europe.

Abstract citation ID: lvag096.1737

EP1612 - ECE_2310 - When thyroid function is normal: MRI-guided diagnosis and management of endocrine orbitopathy

Maria Mathiopoulou and Maria Pisimisi

Hospital of Uster, Switzerland, Zurich, Switzerland

Background: Euthyroid endocrine orbitopathy (euthyroid thyroid-associated orbitopathy, TAO) represents a diagnostically challenging subset of thyroid eye disease, characterized by classical orbital manifestations in the absence of overt thyroid dysfunction. Atypical clinical presentations and normal thyroid biochemistry frequently delay diagnosis and increase the risk of irreversible visual complications. Advanced imaging, particularly orbital magnetic resonance imaging (MRI), has emerged as a critical tool for accurate disease characterization and risk stratification in this population.

Pathophysiology: Despite euthyroidism, disease mechanisms largely mirror Graves' orbitopathy and are driven by autoimmune activation of orbital fibroblasts, leading to excessive glycosaminoglycan accumulation, tissue edema, and remodeling of extraocular muscles and orbital fat. This immune-mediated process distinguishes euthyroid TAO from infectious, vascular, granulomatous, and infiltrative orbital disorders that may present with overlapping clinical features.

Diagnostic Approach and Imaging: Diagnosis remains one of exclusion and requires careful integration of clinical, laboratory, and imaging findings, particularly in patients with atypical muscle involvement or absent restrictive motility patterns. Orbital MRI plays a central role in this context due to its superior soft-tissue contrast, enabling reliable differentiation between active inflammatory disease (muscle edema, increased T2 signal intensity, and contrast enhancement) and inactive fibrotic disease. MRI is also uniquely suited for assessing tendon involvement, typically spared in TAO, and for identifying apical crowding and early dysthyroid optic neuropathy through direct visualization of optic nerve compression. While computed tomography remains valuable for anatomical detail and quantitative assessment of orbital structures, MRI provides critical functional and prognostic information that directly influences management decisions. Hybrid imaging modalities,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

such as SPECT/CT, may further complement anatomical imaging by assessing inflammatory activity in selected cases.

Clinical Implications and Management: Accurate MRI-based assessment of disease activity informs therapeutic strategy, supporting timely initiation of immunosuppressive therapy in active disease and appropriate surgical planning in fibrotic or sight-threatening stages. Given the risk of insidious optic nerve compromise, longitudinal imaging and structured follow-up are essential, even in patients with initially mild symptoms.

Conclusion: Euthyroid endocrine orbitopathy is an under-recognized but clinically significant entity with potential for serious visual morbidity. Incorporation of orbital MRI into diagnostic and prognostic pathways enhances diagnostic confidence, improves differentiation from mimicking conditions, and enables activity-guided, individualized management. These advantages support a central role for MRI in contemporary care models for euthyroid TAO and highlight its relevance for endocrinologists managing complex orbital disease.

Abstract citation ID: lvag096.1738

EP1613 - ECE_2424 - Fixed point observation of thyroid abnormalities after nuclear power plant explosions induced by giant earthquakes and thsunami

Takao Kunori[1,2]
[1]Surgery, Iwaki-city Medical Center, Thyroid Clinic, Iwaki City, Japan; [2]Surgery, Iwaki-city Medical Center, Iwaki, Japan

Background: Our clinic is located 45 km south of Tokyo Electric Fukushima Daiichi nuclear power plant (NPP), which exploded in East Japan Disaster (2011). Highest air dose was recorded as 20 micro Sievelt in our hospital. Significant number of pediatric thyroid cancer has been detected in this area, but not confirmed significant relation with the NPP accidents by DNA analysis. While adult data has not been sufficiently published. We reviewed pre- and post outpatient data of thyroid clinic to find NPP effects.

Patients and Methods: 7463 patients (2007-2025), age 54 ± 17 (3-96); female 83.7%), were examined. Chronological data: 5 terms were compred; group A, 2007-2010 (pre); B, 2011-14 (post1); C, 2015-2018 (post2); D, 2019-2022 (post3); E, 2023-2025 (post4). Disease: Nodular goiter was 2523 (solid), 1003 (cyst). Hyperthyroidismm (HY) was 1783 and Hashimoto (HA) was 531. Hormonal assay: Tg, anti-thyroglobulin (aTg), thyroid peroxidase antibody (TPO), anti-TSH receptor antibody (TSH-R) and thyroid stimulating antibody (TS). Diagnostic tools: Ultrasonography(US) and fine needle aspiration (FNA); classified 2(benign)-5(cancer). Signifiance was determined by Kai2 test or student-t test; probability (p) less than 0.05 was judged as significant.

Results: (1) Disease (%): Group A ($n = 559$); solid 40%, cyst 18%, HY 35%, HA 7.7%. Group B ($n = 616$); solid 40%, cyst 20%, HY 27%, HA 7.5%. Group C ($n = 451$); solid 40%, cyst 21%, HY 29%, HA 11%. Group D ($n = 55$); solid 47%, cyst 15%, HY 28%, HA 11%. Group E ($n = 345$); solid 48%, cyst 10%, HY 32%, HA 11%.

(2) Changes of autoimmunity*: TPO positive patients slightly increased from 23%(B), 25%(C), 33%(D), 40%(E) . aTg positive patients showed no particular changes; 33%(B), 25%(C), 28%(D), 35%(E). *Data of group A was not used by technical reason.

(3) Cytology(malignancy%): 9% (A) to 6%(B), 9%(C), 4%(D), 8%(E).

Conclusion: There was no observable changes in patients' analysis. These data suggest that the adverse effects of NPP accidents were as small as negligible.

Abstract citation ID: lvag096.1739

EP1615 - ECE_3412 - Urinary and serum iodine status and its association with inflammatory markers in a cohort of Romanian pregnant women

Robert Badan[1], Corina Delia[2,3], Ioana-Maria Crasan[2], Anisoara Cimpean[2], Alexandra Ichim[3], Mirela Daniela Haidautu[3], Beatrice Radu[2], Bogdan Pascu[3] and Elena Ionica[2]
[1]Giurgiu County Emergency Hospital, Giurgiu, Romania; [2]Departament of Biochemistry and Molecular Biology, University of Bucharest, Bucharest, Romania; [3]Laboratory of Biochemistry, National Institute for Mother and Child Health "Alessandrescu-Rusescu", Bucharest, Romania

Although salt iodisation programs are implemented in many countries, iodine deficiency among pregnant women persists in several regions of Romania and remains a significant public health concern. During pregnancy, the maternal thyroid must increase hormone production to meet both maternal and foetal requirements, particularly in the first trimester when the foetus depends entirely on maternal thyroxine (T4) (Spina et al., 2023; Pendersen et al., 1993).

The aim of this study was to evaluate urinary and serum iodine levels across pregnancy and to explore associations with inflammatory markers in a cohort of Romanian pregnant women. A total of 121 women were included and stratified by trimester: first ($n = 43$), second ($n = 42$), and third ($n = 36$). Urinary iodine concentration (UIC), serum iodine, thyroid function parameters (TSH, FT4), iron status, renal function markers (creatinine, urea), and inflammatory indices (C-reactive protein [CRP], white blood cell count [WBC]) were assessed. Iodine status was compared across trimesters, and Pearson correlation analyses, visualised in heatmaps, were performed to examine relationships between iodine measures and biochemical parameters in the overall cohort and within each trimester.

Analysis of a preliminary subset of 32 women showed a progressive decline in iodine status with advancing gestation. The median UIC decreased from 174 μg/L in the first trimester to 112 μg/L in the third trimester, and a higher proportion of women in late pregnancy fell below the World Health Organisation adequacy threshold of 150 μg/L. Serum iodine levels also declined in the third trimester compared with early pregnancy, although this difference did not reach statistical significance because of substantial interindividual variability. Thyroid function parameters remained largely stable, with no significant correlations between iodine measures and TSH or FT4.

Overall, UIC showed only weak associations with inflammatory markers across the entire cohort. However, in the third trimester, UIC showed a stronger positive correlation with CRP ($r \approx 0.6$) and aligned with WBC in heatmap analyses. These associations appeared to be driven by a small number of individuals with concurrently elevated iodine and inflammatory markers, potentially reflecting acute inflammatory states or recent supplementation. Mild to moderate iodine deficiency was prevalent, particularly in late gestation, despite universal salt iodisation.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

These findings underscore the importance of continuous monitoring of iodine status during pregnancy and support targeted strategies to ensure adequate iodine intake throughout gestation.

Abstract citation ID: lvag096.1740

EP1618 - ECE_2364 - Skin hyperpigmentation as a clinical manifestation of isolated hypothyroxinemia: a case report

Oleksandra Zavalniuk and Ilona Rudnieva
National Medical University named after O.O. Bogomolets, Kyiv, Ukraine

Introduction: Isolated hypothyroxinemia is defined as a reduction in free thyroxine levels with normal thyroid-stimulating hormone (TSH) and has long been considered a condition without clear clinical manifestations. However, accumulating evidence suggests that even with normal TSH, thyroid hormone deficiency at the tissue level may have clinical significance, including effects on skin status and pigment metabolism. Of particular interest is the role of iodine deficiency as a leading factor in the development of isolated hypothyroxinemia in women, as well as its possible association with hyperpigmentation of exposed skin areas. Clinical observations showing regression of pigmentation following correction of iodine status highlight the importance of a broader view of the clinical manifestations of this condition.

Aim of the Study: To present a clinical case illustrating a possible association between isolated hypothyroxinemia and skin hyperpigmentation and to evaluate the effect of iodine ицsupplementation.

Materials and Methods: A 35-year-old woman presented with progressive forehead hyperpigmentation lasting six months. Laboratory evaluation included prolactin, TSH, free thyroxine (fT4), vitamin D, and ferritin levels. TSH and prolactin levels were within the reference range, while fT4 was at the lower limit of normal. VitaminD, ferritin, and thyroid ultrasound findings were normal. Thyroid ultrasound was performed. Prophylactic potassium iodide was administered at a dose of 150 μg/day for six months.

Results: After six months of iodine supplementation, complete regression of forehead hyperpigmentation was observed, and euthyroid status was confirmed.

Conclusion: This case demonstrates that isolated hypothyroxinemia related to iodine deficiency may present with subtle cutaneous manifestations, such as forehead hyperpigmentation, which can be reversed with appropriate iodine supplementation. The findings emphasize the need to consider tissue-level thyroid hormone deficiency in women, even when TSH is normal, and highlight the clinical relevance of preventive iodine correction. Further experience with additional patients is needed to better understand the prevalence and spectrum of cutaneous manifestations in this condition.

Abstract citation ID: lvag096.1741

EP1621 - ECE_3888 - Ectopic mediastinal thyroid: a case report

Marta Almeida, Miguel Marques, Daniel Duarte, H. Francisca, Ricardo Capitão and Maria Carlos Cordeiro
Unidade Local de Saúde de Almada-Seixal, Almada, Portugal

Introduction: Ectopic thyroid tissue (ETT) is a rare developmental anomaly caused by abnormal embryological migration of the thyroid gland. Mediastinal involvement represents an uncommon presentation among ectopic thyroid cases. We present a case of multinodular ectopic mediastinal thyroid tissue discovered incidentally in a patient with prior hemithyroidectomy.

Case Presentation: A 55-year-old woman with a history of left hemithyroidectomy performed 10 years prior for colloid goiter presented with fatigue, mild dysphagia, cough, and recent-onset snoring following an upper respiratory infection. She had been maintained on levothyroxine 25 mcg with normal thyroid function. Family history was negative for thyroid malignancy and head/neck radiation exposure. Physical examination revealed 5 kg weight loss and night sweats without fever.

Investigations: Laboratory studies demonstrated euthyroid status (TSH 1.58 mIU/L, free T3 2.90 pg/mL, free T4 1.26 ng/dL) with undetectable calcitonin (2 pg/mL). Chest computed tomography revealed a well-defined, heterogeneous, contrast-enhancing mass in the superior anterior mediastinum measuring 51 × 38 × 46 mm, posterior to the manubrium sterni. The mass demonstrated multiple hypodense nodular areas. The residual right thyroid lobe appeared reduced in size with an apparent cleavage plane from the mediastinal lesion. Differential diagnosis included ectopic thyroid tissue vs thymoma.

Thyroid scintigraphy with Tc-99m pertechnetate confirmed diffuse hyperfunctioning of the right thyroid lobe and demonstrated anomalous uptake in the mediastinal mass corresponding to the CT findings. The mediastinal lesion showed heterogeneous tracer distribution consistent with multinodular ectopic thyroid tissue.

Management and Outcome: The patient was referred to thoracic surgery and underwent successful surgical resection without complications. Histopathological examination confirmed ectopic thyroid tissue. Separate fragments revealed involutional thymic tissue. The diagnosis of primary ectopic mediastinal thyroid was established, with no evidence of malignancy. After one year of follow-up, the patient showed complete resolution of all symptoms.

Conclusion: This case illustrates the diagnostic challenge of mediastinal masses in patients with thyroid disease history. Mediastinal ectopic thyroid tissue should be considered in the differential diagnosis of anterior mediastinal masses, particularly when scintigraphy demonstrates radiotracer uptake. The combined use of CT imaging and thyroid scintigraphy was essential for establishing an accurate preoperative diagnosis. Surgical resection remains the treatment of choice for symptomatic ectopic mediastinal thyroid. This case underscores the importance of maintaining a high index of suspicion for ectopic thyroid tissue, even in patients with prior thyroid surgery, as ectopic tissue may function independently of the orthotopic gland.

Abstract citation ID: lvag096.1742

EP1622 - ECE_2158 - Psychological distress in women with autoimmune thyroiditis assessed using GHQ-28 and the Hamilton Depression Rating Scale

Marcin Nosal
Collegium Medicum, Jan Dlugosz University, Częstochowa, Poland

Background: Autoimmune thyroiditis (AIT) is a endocrine disorder in women and is increasingly recognized as a condition associated not only with hormonal imbalance but also with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

inflammation, and psychological distress. Neuropsychiatric symptoms may persist even in euthyroid patients.[1-6]

Objective: This study aimed to evaluate general mental health and depressive symptoms in women with autoimmune thyroiditis using standardized psychometric tools.

Materials and Methods: Women diagnosed with AIT were assessed using the General Health Questionnaire (GHQ-28) to evaluate anxiety, and depression. Depressive symptom severity was measured with the Hamilton Depression Rating Scale (HAM-D). Coping strategies were additionally analyzed using the Brief COPE questionnaire.

Results: Participants showed significantly elevated GHQ-28 scores, indicating reduced psychological well-being, particularly in the domains of anxiety. HAM-D results revealed to depressive symptoms in a substantial proportion of patients, independent of thyroid hormone levels. Greater depressive severity was associated with fatigue, and subjective disease burden. Less adaptive coping strategies were more common among patients with increased psychological distress.

Conclusions: Women with autoimmune thyroiditis frequently experience clinically relevant psychological symptoms that are not fully explained by endocrine dysfunction. The combined use of GHQ-28 and HAM-D allows effective identification of patients at risk for depression. These findings support the need for routine psychological screening and an integrated psychoneuroendocrine approach in the management of autoimmune thyroid disease.

References

1. Ogłodek EA, Szota AM, Just MJ, Szromek AR, Araszkiewicz A. A study of chemokines, chemokine receptors and interleukin-6 in patients with panic disorder, personality disorders and their co-morbidity. *Pharmacol Rep*. 2016;68(4):756-763. https://doi.org/10.1016/j.pharep.2016.03.017
2. Grzesińska A, Ogłodek EA. Involvement of matrix metalloproteinases, inflammasome NLRP3, and gamma-aminobutyric acid pathway in cellular mechanisms of neuroinflammation in PTSD. *Int J Mol Sci*. 2025;26(12):5662. https://doi.org/10.3390/ijms26125662
3. Ogłodek EA, Just MJ, Moś DM, Just K, Frąszczak M, Araszkiewicz A. Decreased plasma paraoxonase-1 activity as a trait marker of depression. *Eur Neuropsychopharmacol*. 2016;26(2):S410-S411. https://doi.org/10.1016/S0924-977X(16)31376-1
4. Woźny-Rasała I, Ogłodek EA. Inflammatory and oxidative biological profiles in mental disorders: perspectives on diagnostics and personalized therapy. *Int J Mol Sci*. 2025;26(19):9654. https://doi.org/10.3390/ijms26199654
5. Paraniak-Gieszczyk B, Ogłodek EA. Impact of post-traumatic stress disorder duration on volumetric and microstructural parameters of the hippo-campus, amygdala, and prefrontal cortex: a multiparametric magnetic resonance imaging study with correlation analysis. *J Clin Med*. 2025;14(20):7242. https://doi.org/10.3390/jcm14207242
6. Paraniak-Gieszczyk B, Ogłodek EA. Neurobiological and existential profiles in posttraumatic stress disorder: the role of serotonin, cortisol, noradrenaline, and IL-12 across chronicity and age. *Int J Mol Sci*. 2025;26(19):9636. https://doi.org/10.3390/ijms26199636

Abstract citation ID: lvag096.1743

EP1624 - ECE_1645 - A rare overlap of Graves' disease and atypical subacute thyroiditis: a diagnostic and therapeutic challenge

Mariam Bulashvili, Ia Kavtiashvili and Nino Zavrashvili
Tbilisi Institute of Medicine, Tbilisi, Georgia

Introduction: Graves' disease is an autoimmune disorder that causes hyperthyroidism and is managed with antithyroid drugs, radioiodine therapy, or surgery. Subacute thyroiditis is a self-limiting inflammatory condition, often post-viral, that rarely coexists with Graves' disease. When present together, their clinical and biochemical overlap can complicate diagnosis and management.

Case Presentation: A 24-year-old male with a 5-year history of Graves' disease presented in January 2025 with significant weight loss (8-9 kg over 3 weeks), tremor, anxiety, tachycardia (100-130 bpm) and hypertension (140/85 mmHg). He had been on regular methimazole therapy, with relapses upon cessation. Although thyroidectomy was recommended two years prior, it was not pursued. At the presentation, the patient was taking methimazole 20 mg/day for the past five weeks. Laboratory evaluation revealed suppressed TSH <0.005 μU/mL, markedly elevated FT4 > 7.77 ng/dl (0.9-1.7), and FT3 3.25 ng/dl (0.26-0.44), Anti-TSHR 1.4 IU/l, consistent with thyrotoxicosis. CBC and CRP were normal. Thyroid ultrasound showed an enlarged thyroid (volume 60 cm^3). Methimazole was increased to 40 mg/day, and propranolol 40 mg three times daily was initiated.

After 20 days, follow-up testing showed persistent hyperthyroidism: TSH < 0.005 mIU/mL, FT4 > 7.77 ng/dl (0.9-1.7), FT3 1.8 ng/dl (0.26-0.44). The disproportionately elevated FT4/FT3 ratio raised suspicion of destructive thyroiditis. The patient reported a recent mild upper respiratory infection with sore throat and mild fever. A diagnosis of atypical subacute thyroiditis superimposed on Graves' disease was suspected, and methylprednisolone 32 mg/day was added to the regimen, which led to significant clinical improvement within 24 h.

By February 2025, the patient achieved a euthyroid state (FT4 1.66 ng/dl, FT3 0.2 ng/dl). Methimazole and methylprednisolone dosages were reduced. In March 2025, total thyroidectomy was performed successfully. The patient is on levothyroxine replacement therapy.

Conclusion: This case underscores a rare overlap of Graves' disease and subacute thyroiditis. Recognizing atypical thyroid function patterns, such as a high FT4/FT3 ratio, recent viral symptoms, and initiating corticosteroid therapy facilitate recovery and prepare patients for definitive treatment.

Abstract citation ID: lvag096.1744

EP1626 - ECE_2261 - Association between body mass index and ultrasound-derived thyroid parameters

Nino Turashvili[1,2]
[1]*Tbilisi State Medical University and Ingorokva Clinic of High Medical Technologies, Tbilisi, Georgia;* [2]*New Vision University, Tbilisi, Georgia*

Background: The relationship between obesity and thyroid morphology remains incompletely understood. Evidence regarding associations between body mass index (BMI) and ultrasound-derived thyroid parameters is limited, and potential sex-specific differences have not been fully clarified.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Aim: To investigate the association between BMI and thyroid ultrasound parameters in adults and to evaluate whether these associations differ between men and women.

Methods: This retrospective cross-sectional study included 152 adults aged 18-75 years. BMI was calculated using standard anthropometric measurements. Thyroid ultrasound examinations were performed to assess thyroid volume (cm^3), number of thyroid nodules, and size of the dominant thyroid nodule (mm). Thyroid volume was interpreted according to established upper reference limits. Thyroid-stimulating hormone (TSH) levels were within the normal range in all participants.

Associations between BMI and thyroid ultrasound parameters were assessed using Pearson's correlation coefficients. A P-value $< .05$ was considered statistically significant. Analyses were conducted in the overall population and separately in men and women.

Results: In the overall study population, BMI showed a weak but statistically significant positive correlation with thyroid volume ($r = 0.174$, $P = .032$). No significant associations were observed between BMI and thyroid nodule number or dominant nodule size (Table 1).

Table 1 Correlations between BMI and thyroid ultrasound parameters in the overall study population ($n = 152$).

Comparison	Pearson r	*P*-value
BMI vs thyroid volume	0.174	.032
BMI vs number of thyroid nodules	0.040	.625
BMI vs dominant nodule size	−0.033	.686

In analyses conducted separately in men and women, BMI was not significantly associated with thyroid volume, thyroid nodule number, or dominant nodule size (Tables 2 and 3).

Table 2 Correlations between BMI and thyroid ultrasound parameters in men ($n = 31$).

Comparison	Pearson r	*P*-value
BMI vs thyroid volume	0.235	.203
BMI vs number of thyroid nodules	−0.124	.507
BMI vs dominant nodule size	−0.265	.150

Table 3 Correlations between BMI and thyroid ultrasound parameters in women ($n = 121$).

Comparison	Pearson r	*P*-value
BMI vs thyroid volume	0.162	.077
BMI vs number of thyroid nodules	0.075	.416
BMI vs dominant nodule size	0.022	.809

Conclusions: Higher BMI was associated with a modest increase in thyroid volume in the overall population, while no associations were observed with thyroid nodular characteristics. These findings suggest that excess body weight may predominantly influence diffuse thyroid enlargement rather than focal nodular changes. Further studies are needed to clarify underlying mechanisms.

Abstract citation ID: lvag096.1745

EP1627 - ECE_3102 - Therapeutic management and outcomes of dysthyroid orbitopathy

Rekik Mona[1], Yoldez Ben Jemaa[1], Kmar Maaloul[1], Imene Kaibi[1], Nabila Rekik Majdoub[2] and Trigui Amira[1]
[1]*Habib Bourguiba Hospital, Sfax, Tunisia;* [2]*Hôpital Universitaire Hédi Chaker, Sfax, Tunisia*

Purpose: To evaluate therapeutic strategies and clinical outcomes of patients with dysthyroid orbitopathy, with particular emphasis on medical and surgical management and their impact on visual and functional prognosis.

Methods: We conducteed a retrospective study in Habib Bourguiba Hospital including patients diagnosed with dysthyroid orbitopathy and who were managed according to disease severity and activity. Therapeutic modalities were analyzed, including topical treatment, systemic corticosteroid therapy following EUGOGO recommendations, specific thyroid management in collaboration with endocrinology, and surgical intervention when indicated. Visual acuity, clinical signs, recurrence, complications, and long-term outcomes were assessed during follow-up.

Results: A total of nine patients with dysthyroid orbitopathy were included in the study. Medical treatment was the mainstay of management. Topical therapy using lubricants and intraocular pressure lowering agents was prescribed in 44.4% of patients. Systemic corticosteroid therapy was required in 33% of cases due to moderate-to-severe active disease. One patient with compressive optic neuropathy received high-dose intravenous methylprednisolone (1 g/day for three consecutive days), followed by oral tapering, while two patients were treated with weekly intravenous pulses according to EUGOGO protocols. Specific thyroid therapy was administered concomitantly in collaboration with endocrinology department in all patients with thyroid dysfunction. Surgical orbital decompression was performed in one patient presenting with compressive optic neuropathy and significant visual field loss. The mean follow-up duration was 10 months (range: 0-30 months). Final visual acuity remained stable in 77.8% of cases, improved in 11.1%, and worsened in 11.1%. Overall clinical evolution was favorable in 77.8% of patients, with complete recovery and no sequelae. However, recurrence occurred in 22.2% of cases, and residual sequelae were observed in 55.6%, including exposure keratopathy, ocular hypertension, and optic neuropathy (11.1%).

Conclusion: Appropriate therapeutic management of dysthyroid orbitopathy, guided by disease activity and severity, allows favorable outcomes in the majority of patients. Early initiation of systemic corticosteroids and timely surgical intervention in selected cases are crucial to prevent irreversible visual impairment. Long-term follow-up remains essential to detect recurrences and manage late complications.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1746

EP1629 - ECE_3607 - Effectiveness of iodine prophylaxis evaluated through iodine status in children and young adults living in residential care facilities in Lodz

Ewelina Sośnierz[1], Przemysław Śliwka[1], Dorota Kowalik-Zakrzewska[1], Sara Aszkiełowicz[1,2], Sylwester Smoleń[3], Marcin Pakosz[3], Alina Niewiadomska[4], Renata Stawerska[1,2], Anna Łupińska[1,2], Andrzej Lewiński[1] and Arkadiusz Zygmunt[1]

[1]Department of Endocrinology and Metabolic Diseases, Polish Mother's Memorial Hospital-Research Institute, Lódź, Poland; [2]Department of Developmental Age and Adult Endocrinology, Medical University of Lodz, Łódź, Poland; [3]Laboratory of Mass Spectrometry, Faculty of Biotechnology and Horticulture, University of Agriculture in Krakow, Kraków, Poland; [4]Laboratory Diagnostics Center, Polish Mother's Memorial Hospital-Research Institute, Łódź, Poland

Introduction: Poland is currently regarded as a country with sufficient iodine supply at the population level. However, iodine prophylaxis is a process whose effectiveness is influenced by numerous external factors; therefore, continuous monitoring of its efficacy is necessary. The aim of our study was to evaluate the effectiveness of the iodine prophylaxis model implemented in Poland since 1997.

Methods: We assessed urinary iodine concentration (UIC) in children and young adults from residential care facilities in central Poland. A total of 157 participants were examined in 2019, and 132 participants in 2023-2024. The participants were aged 6-20 years. The results were compared with goitre prevalence assessed on the basis of thyroid volume measured by ultrasound, as well as the thyroid volume–to–body surface area ratio (V/BSA). This ratio allows for a more reliable assessment of thyroid volume.

Results: The median urinary iodine concentration (UIC) was 237.04 ± 72.82 μg/dm^3 before creatinine normalisation and 89.49 ± 98.91 μg/g creatinine after normalisation. Based on unadjusted WHO cut-off values, 64% of participants had adequate or above-requirements iodine intake, while 24% exhibited mild iodine deficiency and 9% had moderate to severe deficiency. Using WHO cut-offs adjusted for the median creatinine concentration of the cohort, 53% of children had adequate or above-requirements iodine status, whereas 10% had excessive UIC, 31% had mild deficiency and <6% had moderate to severe deficiency. The median V/BSA ratio was 3.30 mL/m^2 (range: 1.14-15.72 mL/m^2). According to WHO reference standards, goitre prevalence was low (<5%), indicating no evidence of iodine-deficiency–related thyroid enlargement at the population level. Creatinine-normalised UIC was higher in boys than in girls (91.81 ± 108.86 vs 84.75 ± 82.16 μg/g creatinine). Small to moderate negative correlations were observed between UIC and body weight ($r = -0.351$; $P < .001$), BMI ($r = -0.231$; $P < .001$), BSA ($r = -0.407$; $P < .001$), thyroid volume ($r = -0.263$; $P < .001$) and V/BSA ($r = -0.138$; $P = .020$). When stratified by sex and age, younger children exhibited higher creatinine-normalised UIC, with a weak but significant negative correlation between UIC and age ($r = -0.153$; $P = .011$). Significant differences between age groups were observed ($P < .001$).

Conclusions: The iodine prophylaxis programme implemented in Poland remains effective at the population level, as reflected by adequate median urinary iodine concentrations and a low prevalence of goitre among children and young adults. These findings support the classification of Poland as a country with sufficient iodine supply.

Abstract citation ID: lvag096.1747

EP1630 - ECE_3818 - Graves' disease: ultrasonographic changes at diagnosis vs euthyroid state

Juan de Dios Barranco Ochoa, María Sánchez-Prieto Castillo, Marina Soria Becerra and Ana Segarra Balao

Endocrinology and Nutrition, Complejo Hospitalario de Jaén, Jaén, Spain

Introduction: Thyrotoxicosis is defined as the clinical state resulting from excess thyroid hormone levels. When caused by increased thyroid gland activity, it is termed hyperthyroidism, with Graves' disease (GD) being the most frequent etiology. The diagnosis of non-nodular hyperthyroidism may be challenging, as gold-standard diagnostic tests—such as thyroid scintigraphy and thyrotropin receptor antibodies (TRAb)—often involve delays. Thyroid ultrasonography allows bedside assessment and provides valuable diagnostic information.

Objectives: To evaluate ultrasonographic differences in patients with Graves' disease at diagnosis compared with the euthyroid state.

Materials and Methods: A prospective observational study was conducted including patients diagnosed with Graves' disease. GD was defined as primary hyperthyroidism with positive TRAb levels (>2 IU/mL) or diffuse uptake on thyroid scintigraphy in cases with negative or indeterminate TRAb results.

Biochemical evaluation (TSH, free T4, and TRAb) and thyroid ultrasonography were performed at the time of diagnosis. Ultrasonography was repeated after normalization of thyroid hormone levels. Clinical and laboratory data were recorded, along with qualitative ultrasonographic features (thyroid volume, echogenicity, and vascular pattern) and quantitative parameters, including peak systolic velocity of the inferior thyroid artery (ITA-PSV), measured both at diagnosis and at euthyroidism. Thyroid scintigraphy was performed in patients with suspected GD and negative or indeterminate TRAb results. Statistical analysis was carried out using SPSS version 25®.

Results: A total of 37 patients with Graves' disease were included, with a mean age of 44.4 ± 2.2 years; 33 were women (89%). Goiter was present in 91.7% of patients, and 91.9% reported symptoms of hyperthyroidism. At diagnosis, mean laboratory values were: TSH 0.03 ± 0.02 mIU/L, free T4 3.72 ± 1.61 ng/dL, and TRAb 9.47 ± 13.08 mIU/L.

On ultrasonography, increased thyroid volume was observed in 91.7% of patients, while decreased echogenicity was present in all cases. Regarding vascular patterns, increased thyroid vascularization (patterns 2 and 3) was observed in 97.3% of patients at diagnosis, compared with 71% at the euthyroid state.

Patients with Graves' disease showed statistically significant differences in ITA-PSV between diagnosis and euthyroidism (78.8 ± 20.1 cm/s vs 49.7 ± 12.8 cm/s; $P = .012$). The mean time to achieve normalization of thyroid hormone levels was 7.25 ± 1.6 months.

Conclusions: Thyroid ultrasonography is an essential tool in the management of hyperthyroidism. Measurement of inferior thyroid artery peak systolic velocity may serve as a useful marker for disease monitoring in Graves' disease.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1748

EP1631 - ECE_3859 - The prevalence of thyroid nodules in correlation with anthropometric and metabolic factors in euthyroid adult patients

Edlira Hoxha[1,2], Anila Shuka[1] and Arben Mitrushi[1]
[1]*Endocrinology, Morphology Department, Medicine University, Spacialty Polyclinic Nr.3, Tirana, Albania;* [2]*Endocrinology, Medicine Faculty, Specialty Polyclinic Nr.3, Medicine University, University of Medicine, Tirana, Albania*

Thyroid nodules are common in clinical practice. They begin like discrete lesions inside of structure of the gland that can be differentiated by radiological examinations. Most of them are benign and asymptomatic for the patient followed by normal hormonal balance. Epidemiologic studies have shown the prevalence of palpable thyroid nodules 5% in women and 1% in men living in iodine-sufficient countries. In contrast, high resolution ultrasound can detect 19%-65% of the thyroid nodules with higher frequencies in women and the elderly.

Genesis of nodules can be influenced by genetics and environmental factors. Most common risk factors in thyroid nodules are: age (high risk in children, adults under 30 years old and over 60 years old), iodine deficiency, history of radiation exposure or head/neck radiotherapy, smoking or alcohol, family history of thyroid cancer or MEN2. The recent studies have shown that high TSH values (those too in upper-normal range) is an important factor that influences nodules development. As well metabolic syndrome is related with a higher prevalence of thyroid nodules, especially in obese patients.

The aim of our study is to evaluate the prevalence of thyroid nodules and the association between thyroid hormone levels and anthropometric and metabolic parameters in the presence of this nodules in euthyroid adult subjects.

This is a prospective study during a period of one year, that includes 100 patients of the Specialty Polyclinic Nr.3 in Tirana, Albania. The patients came to control for another health disease like cardiovascular or diabetes mellitus type 2. We evaluated thyroid hormone levels like: TSH, FT4, FT3 and antithyroid peroxidase antibody. Also we evaluated the anthropometric and metabolic parameters.

Results: The prevalence of thyroid nodules was almost 30% among the patients. Female gender, TSH levels in the upper normal range, thyroid volume were independent risk factors for thyroid nodules. Metabolic syndrome (like obesity, Hypertension, dyslipidemia, insulin resistance) was associated the elevated thyroid volume and nodules prevalence.

Abstract citation ID: lvag096.1749

EP1632 - ECE_2352 - Amiodarone-induced thyrotoxicosis: a case report

Oumaima Dimassi, Ines Bayar, Ilef Guirar, Rawen Jaziri, Sana Abid, Ekram Hajji, Bilel Ben Amor, Héla Marmouch, Hanene Sayadi and Inès Khochteli
Department of Endocrinology and Internal Medicine, Fattouma Bourguiba University Hospital, Monastir, Tunisia

Introduction: Amiodarone is the most commonly used antiarrhythmic agent. It can lead to thyroid disease through two main mechanisms: intrinsic drug effects and the side effects due to its high iodine content. We report the case of amiodarone-induced thyrotoxicosis (AIT) with cardiothyrotoxicosis.

Observation: A 66-year-old male patient with cardiovascular and metabolic history (well-controlled hypertension, two episodes of acute coronary syndrome at the ages of 53 and 58, requiring the placement of drug-eluting stents, an ischemic stroke at the age of 61, prediabetes, and chronic kidney disease (stage 3A)).

At the age of 64, the patient was started on Amiodarone due to supraventricular tachycardia. Clinical examination upon admission showed: Grade 1 obesity; brisk deep tendon reflexes; heart rate at 120 beats per minute; no ocular signs; non-palpable thyroid. Electrocardiogram: rapid atrial fibrillation at 120 bpm.

Laboratory Tests: TSH at 0.15 µUI/mL; FT4 at 17 pmol/L; neutrophil count at 5400; negative anti-thyroperoxidase and anti-TSH receptor antibodies. Cervical ultrasound: thyroid of normal size; no thyroid nodules. Thyroid scintigraphy: “blank” result.

The patient was started on methimazole 20 mg/day and propranolol 40 mg/day, followed by prednisolone 30 mg/day, with good clinical and biological improvement, suggestive of type 2 AIT. However, type 3 (mixed type) cannot be ruled out.

Conclusion: Determining the type of AIT is crucial for better management. Although its treatment is complex, particularly due to “mixed” forms, euthyroidism is restored in the majority of cases with medical treatment.

Abstract citation ID: lvag096.1750

EP1634 - ECE_3104 - When cervical nodes speak first: two cases of papillary thyroid microcarcinoma revealed by lymphadenopathy

Assia Azzoune
Faculty of Medicine, Blida, Algeria

Introduction: The appearance of cervical lymphadenopathy is a real challenge for the doctor due to its varied benign or malignant etiologies; it can rarely reveal a previously asymptomatic papillary thyroid microcarcinoma which remains the most common cancer of the thyroid, accounting for up to 70% of cases. Ultrasound and cytology are crucial for diagnosis.

Cases:

1st case: a women 35 years old came to consult for a sensation of laryngeal tickling. She was stable. The cervical palpation reveals adenopathy of right lymph node chain III with a small right thyroid nodule. The thyroid and inflammatory tests were normal. Cervical ultrasound confirmed the presence of 01 cm lymphadenopathy as well as the 08 mm thyroid nodule classified EUTIRADS 4, cytology study finds malignant cellularity (Bethesda V) completed by a total thyroidectomy with lymph node dissection confirming the presence of a papillary thyroid carcinoma with lymph node metastasis.

2nd case: Mrs. A. L., 45 years old with overweight (BMI = 29 kg/m^2) consulted for left cervical discomfort. The patient was stable without any change in general condition or fever, cervical palpation revealed cervical lymphadenopathy of the left lymph node chain IV confirmed on cervical ultrasound which also showed an appearance of thyroiditis with 07 mm isthmic nodule classified

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

EUTIRADS 5. Biologically; antiTPO antibodies were positive. The aspiration cytology was malignant and the total thyroidectomy confirmed the presence of a papillary carcinoma on the isthmic nodule with lymph node metastasis on a background of Hashimoto's thyroiditis.

Discussion: The tumoral origin of cervical lymphadenopathy is predominantly represented by lymphomas and metastases from cancers of the upper aerodigestive tract. In 25% of cases, it is caused by thyroid carcinoma, particularly papillary thyroid carcinoma.[1] Cystic metastases from thyroid cancer have been reported in one out of ten cases, typically in individuals around 30 years of age.[2] The lymph node mass is usually solitary, most often located in levels IIa and III.[3] Thyroid abnormalities are identified during the diagnostic work-up in 75% of cases, mainly through cervical ultrasound followed by cytological confirmation.[4] The primary thyroid tumor is generally small—5.5 mm on average in a French series—with capsular involvement in 69% of cases.[5]

Conclusion: Through these two cases, we report an uncommon clinical situation in which the diagnosis of a papillary thyroid microcarcinoma was revealed by lymph node metastases. This highlights the importance of a thorough diagnostic work-up, which must systematically include cervical ultrasonography.

Abstract citation ID: lvag096.1751

EP1635 - ECE_3137 - Metabolic dysfunction–associated steatotic liver disease as the initial presentation of subclinical hypothyroidism

Marin Pecani[1] and Paola Andreozzi[2]
[1]*Department of Experimental Medicine, Sapienza University of Rome, Tirana, Albania;* [2]*Policlinico Umberto I University Hospital, Sapienza University of Rome, Rome, Italy*

Introduction: Metabolic dysfunction–associated steatotic liver disease (MASLD) is the most common chronic liver condition, with a worldwide prevalence of over 30% in adults. Most individuals with MASLD are asymptomatic, therefore, the diagnosis is often made incidentally through imaging studies or when elevated liver enzymes are detected. MASLD can be associated with subclinical hypothyroidism, particularly of autoimmune origin, and these two may conditionally exacerbate insulin resistance, dyslipidemia, or hepatic steatosis.

Case Report: A 35-year-old man (body mass index [BMI] 30.5 kg/m^2) was referred for further assessment after routine health screening revealed elevated liver enzymes. He reported fatigue and a gradual weight gain of 10 kg over the past four years, a sedentary lifestyle with long hours in the office, lack of exercise, and frequent consumption of refined carbohydrate-rich food and sweetened drinks. He denied alcohol use and smoking. Family history was positive for type 2 diabetes and hypertension. Physical examination showed central obesity (waist circumference 103 cm) and mildly elevated blood pressure (124/83 mmHg). Laboratory tests revealed increased levels of aspartate transaminase (AST, 53 U/L) and alanine transaminase (ALT, 61 U/L), fasting plasma glucose (FPG) 96 mg/dL, glycated hemoglobin (HbA1c) 5.7%, and dyslipidemia (total cholesterol 246 mg/dL, triglycerides 175 mg/dL, and HDL cholesterol 43 mg/dL). Viral hepatitis serology was negative. Thyroid function tests showed an elevated TSH (10.2 µIU/mL) with normal free T4 (0.98 ng/dL) and free T3 (2.5 pg/mL), along with positive anti-TPO antibodies (156 IU/mL), supporting the diagnosis of primary subclinical hypothyroidism. An ultrasound exam demonstrated grade 2 hepatic steatosis, and vibration-controlled transient elastography ruled out clinically significant fibrosis (stiffness 5.3 kPa). A diagnosis of MASLD, obesity, and autoimmune subclinical hypothyroidism was made. The patient was advised on calorie restriction, adherence to a Mediterranean diet, and regular exercise and started on levothyroxine. At six months, he achieved a 6 kg weight loss, TSH (2.4 µIU/mL), normalization of liver enzymes, and improved HbA1c (5.3%) and lipid profile.

Conclusion: MASLD and subclinical hypothyroidism have similar metabolic abnormalities that lead to metabolic dysfunction and increased cardiovascular disease risk. Therefore, timely diagnosis and effective treatment, including lifestyle modification and targeted therapy, are essential to prevent progression to advanced liver disease and systemic complications.

Abstract citation ID: lvag096.1752

EP1638 - ECE_1306 - Primary thyroid lymphoma: a case series from a tertiary care centre in Northern India

Prashant Hubballi, Subhash Yadav and Bibhuti Bhusan Mohanta
Endocrinology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

Introduction: Primary thyroid lymphoma (PTL) refers to a lymphoma which involves the thyroid gland with or without involving regional neck lymph nodes but without contiguous spread or distant metastases from other areas of involvement at the time of diagnosis. PTL is a very rare entity, necessitating accurate and early diagnosis, as its management is very much different from that of other neoplasms intrinsic to the thyroid.

Aims and Objective: In this study, we report cases of primary thyroid lymphoma for which we analysed clinical, pathological, and treatment aspects to contribute to a better understanding of this rare neoplasm

Materials and Methods: Cases diagnosed from 2014 to 2024 (10 years)were retrieved and clinical details were noted. Immunohistochemistry (IHC) was performed for immunophenotyping, and cases were classified according to the World Health Organization 2022 classification of haematolymphoid neoplasms

Results: Sixteen patients with PTL were identified, with mean age of 63.5 years (range 34-93 years) including ten males. Duration of symptoms ranged from 2-12 months with most common symptom being rapidly progressing painless goitre. Thyroid Peroxidase (TPO) antibody was positive in 8 patients. Diffuse large B cell lymphoma was most frequent type of NHL found and most commonly it was of nongerminal centre type. In immunochemistry, CD 20 was most common marker found (13 patients) and one pt had CD3 positivity for T cell lymphoma. 11 patients received R-CHOP regimen and one patient underwent left hemithyroidectomy. Five patients expired and four patients improved

Discussion and Conclusion: PTL is a very rare entity amongst lymphomas and even rarer in Indian population as there is lack of considerable data. PTL is rare, accounting for 5% of all thyroid neoplasms and 1%-2% of extranodal lymphomas. These tumours usually present with painless neck mass that rapidly increases in size

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

with/without compressive symptoms. The mean age of presentation is at 6th-7th decade of life, and a female predominance has been noted. DLBCL accounts for 50%-70% of all cases and 60%-90% arise in a background of Hashimoto's thyroiditis. Early diagnosis in the form of histopathological evaluation supplemented by immunochemistry is the gold standard for the diagnosis of PTL. Combined chemoradiotherapy (R-CHOP regimen/E-SHAP) appears to be the best treatment modality, irrespective of histological type, as PTL are considerably radiosensitive too. Overall survival rates with combination therapy are very good (more than 90%), and recurrence rates as low as 7.7% have been reported.

Abstract citation ID: lvag096.1753

EP1641 - ECE_2433 - When the eyes lead the diagnosis: Marine-Lenhart syndrome with subclinical hyperthyroidism and unilateral exophthalmos

Teodora Nastasa[1], Nada Akad[1,2], Anca Matei[1,2], Georgiana Constantinescu[1,2], Alexandru Florescu[1,2] and Stefana Bilha[1,2]
[1]*Saint Spiridon County Hospital, Iaşi, Romania;* [2]*"Grigore T Popa" University of Medicine and Pharmacy, Iaşi, Romania*

The coexistence of hyperfunctioning thyroid nodules is estimated to occur in 0.26%-4.1% of patients with Graves disease (GD), a clinical entity referred to as Marine–Lenhart syndrome (MLS). Due to its rarity, clear diagnostic criteria and standardized therapeutic management strategies have not yet been established.

We present the case of a 47-year-old woman referred for right upper eyelid retraction, right unilateral exophthalmos, diffuse conjunctival congestion and minimal bilateral chemosis. Contrast-enhanced cranio-cerebral CT and MRI were performed for orbitopathy assessment, revealing no significant pathological abnormalities on imaging, thus ruling out potential causes of proptosis.

Laboratory evaluation revealed negative anti–thyroid peroxidase antibodies (TPOAb) and anti–TSH receptor antibodies (TRAb), with positive thyroid-stimulating immunoglobulins (TSI) and subclinical hyperthyroidism, characterized by borderline TSH levels and normal free-T4 concentrations. Thyroid ultrasound revealed two nodular lesions, a microcyst and a TI-RADS 3 thyroid nodule, within a diffusely heterogeneous, hypoechoic thyroid parenchyma, with an overall normal thyroid volume and vascularisation. Thyroid scintigraphy with technetium-99m pertechnetate ($99mTcO_4$) demonstrated a hyperfunctioning nodule, accounting for approximately 32% of total thyroid uptake.

The patient was diagnosed with type 1 MLS, associated with moderate inactive (CAS 2) thyroid eye disease (TED). Any active therapeutic interventions were postponed given the rare condition of subclinical hyperthyroidism status, inactive TED and the absence of cervical compressive symptoms. Clinical, biochemical and imaging follow-up were recommended.

At subsequent evaluation, a >50% increase in nodular volume was observed, along with progression of ultrasound features to a TI-RADS 5, with a maximum diameter at the borderline threshold for fine-needle aspiration biopsy (FNAB). FNAB was performed, leading to a Bethesda II cytological result. TSH was within normal limits (TSH = 1.06 mUI/mL). Follow-up in 6 months was recommended.

This case highlights a type 1 MLS presentation with moderate, inactive thyroid eye disease and only subclinical biochemical hyperthyroidism, justifying close clinical, biochemical and imaging monitoring. Clinically significant orbitopathy may occur even when classical thyroid autoimmunity markers (TRAb, TPOAb) are negative, with TSI positivity supporting the autoimmune background.

Abstract citation ID: lvag096.1754

EP1642 - ECE_2510 - When the skin reveals the diagnosis: pretibial myxedema in Graves' disease

Hakan Ömer Karataş[1] and Banu Ocak[2]
[1]*Internal Medicine, Van Gürpınar State Hospital, Van, Turkey;* [2]*Marmara University School of Medicine, Marmara University Pendik Research and Education Hospital, Internal Medicine, İstanbul, Turkey*

Background: Graves' disease is a multisystem autoimmune disorder with cardiovascular, neuropsychiatric and dermatological manifestations that may result in fragmented evaluation across multiple specialties and lead to delayed diagnosis. In such settings, cutaneous manifestations may serve as a unifying clinical clue that prompts reassessment of the overall clinical picture. The aim of this case is to illustrate the diagnostic value of pretibial myxedema in patients with fragmented multisystem presentations of Graves' disease.

Methods: Case presentation.

Case Presentation: A 47-year-old woman was referred to our outpatient clinic by her family physician for evaluation of progressive pretibial and ankle edema. Over the preceding year, she experienced restlessness, anxiety, sweating and weight loss along with tremor, leading to consultations across multiple specialties. She had been followed by psychiatry for 18 months with a diagnosis of anxiety disorder and treated with selective serotonin reuptake inhibitors (SSRI). She also presented repeatedly to the emergency department with palpitations and fever, where sinus tachycardia was documented on electrocardiograms and empirical antibiotic treatments were administered. Neurological evaluation for progressive tremor and neuropathic pain included electromyography demonstrating entrapment neuropathy and cranial imaging, which was unremarkable, after which levodopa was empirically initiated with a preliminary diagnosis of Parkinson's disease.

Physical examination revealed bilateral non-pitting edema over the pretibial regions and dorsal ankles, warm and moist skin and fine tremor. Resting heart rate was 115 bpm. Cardiac, renal, hepatic and venous evaluations did not identify an alternative cause for edema. Laboratory evaluation showed suppressed thyroid-stimulating hormone (0.0001 μIU/mL), markedly elevated free triiodothyronine (22.2 ng/L) and free thyroxine (5.61 ng/dL) with increased thyroid-stimulating immunoglobulin levels. Thyroid ultrasonography demonstrated diffuse enlargement with heterogeneous parenchyma.

Graves' disease was diagnosed and treatment with methimazole and propranolol was initiated. With treatment, autonomic symptoms resolved, free thyroxine levels normalized and pretibial myxedema showed regression, while previously prescribed SSRI and levodopa therapies were discontinued. The patient remains clinically stable under ongoing outpatient follow-up.

Conclusion: Pretibial myxedema is an uncommon but specific manifestation of Graves' disease with a clear pathophysiological basis in autoimmune fibroblast activation and glycosaminoglycan deposition in the dermis and subcutaneous tissue. It should be recognized not merely as a late or rare finding but as a valuable diagnostic clue that may precede or outshine other features of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

thyrotoxicosis. This case underscores the importance of careful physical examination and early consideration of thyroid dysfunction in patients with fragmented multisystem presentations to prevent diagnostic delay, unnecessary investigations and polypharmacy.

Abstract citation ID: lvag096.1755

EP1643 - ECE_3146 - Emotional regulation and existential well-being in women with autoimmune thyroiditis: findings based on CECS and LAP-R

Marcin Nosal
Collegium Medicum, Jan Dlugosz Uniwersity, Częstochowa, Poland

Background: Autoimmune thyroiditis is a chronic disorder affecting not only physical health but also existential functioning. Persistent symptoms, uncertainty regarding disease progression, and treatment contribute to distress and reduced quality of life. Emotional suppression and impaired meaning-making may play an important role in adaptation to chronic illness. This study aimed to assess emotional regulation patterns and existential attitudes in women with autoimmune thyroiditis using the Courtauld Emotional Control Scale (CECS) and the Life Attitude Profile–Revised (LAP-R).[1-6]

Materials and Methods: Women with autoimmune thyroiditis were evaluated using the CECS, measuring suppression of anxiety, and depressed mood, and the LAP-R, assessing purpose in life, existential coherence, life acceptance, and attitudes toward death. Additional tools, including Brief COPE and PSSI-5, supported interpretation of emotional functioning and coping styles.

Results: Participants demonstrated increased emotional suppression, particularly in anxiety and sadness. Higher CECS scores were associated with lower existential fulfillment, reduced sense of life meaning, and poorer psychological adaptation. Women showing stronger emotional inhibition reported greater subjective disease burden and less effective coping, indicating a link between emotional suppression and reduced existential well-being.

Conclusions: Emotional regulation and existential factors play an important role in autoimmune thyroiditis. Combined use of CECS and LAP-R offers valuable insight beyond standard endocrine evaluation. Psychological interventions focused on emotional expression, meaning-making, and adaptive coping may improve patient and quality of life.

References

1. Woźny-Rasała I, Ogłodek EA. Inflammatory and oxidative biological profiles in mental disorders: perspectives on diagnostics and personalized therapy. *Int J Mol Sci*. 2025;26(19):9654. https://doi.org/10.3390/ijms26199654
2. Paraniak-Gieszczyk B, Ogłodek EA. Impact of post-traumatic stress disorder duration on volumetric and microstructural parameters of the hippo-campus, amygdala, and prefrontal cortex: a multiparametric magnetic resonance imaging study with correlation analysis. *J Clin Med*. 2025;14(20):7242. https://doi.org/10.3390/jcm14207242
3. Paraniak-Gieszczyk B, Ogłodek EA. Neurobiological and existential profiles in posttraumatic stress disorder: the role of serotonin, cortisol, noradrenaline and IL-12 across chronicity and age. *Int J Mol Sci*. 2025;26(19):9636. https://doi.org/10.3390/ijms26199636
4. Grzesińska A, Ogłodek EA. Involvement of matrix metalloproteinases, inflammasome NLRP3, and gamma-aminobutyric acid pathway in cellular mechanisms of neuroinflammation in PTSD. *Int J Mol Sci*. 2025;26(12):5662. https://doi.org/10.3390/ijms26125662
5. Ogłodek EA, Just MJ, Just K, Mos DM, Grzesinska AD, Araszkiewicz A. Peroxiredoxin-1 and peroxiredoxin-3 as indicators of sickness behaviour in patients with varying levels of depression severity. *Eur Neuropsychopharmacol*. 2017;27:S622-S623. https://doi.org/10.1016/S0924-977X(17)31177-X
6. Ogłodek EA, Just MJ, Moś DM, Just K, Frąszczak M, Araszkiewicz A. Decreased plasma paraoxonase-1 activity as a trait marker of depression. *Eur Neuropsychopharmacol*. 2016;26(2):S410-S411. https://doi.org/10.1016/S0924-977X(16)31376-1

Abstract citation ID: lvag096.1756

EP1644 - ECE_3464 - When “definitive” isn’t final: late recurrence of Graves’ disease after total thyroidectomy

Zin Tun, Saira Yousaf, Sarishka Singh, Denise Tapa and Hassan Ibrahim
Diabetes and Endocrinology, Cambridge University Hospitals, Wolfson Diabetes & Endocrinology Centre, Cambridge, United Kingdom

Introduction: Radioactive iodine (RAI) and total thyroidectomy are established definitive treatments for Graves’ disease, with total thyroidectomy offering rapid and durable control of hyperthyroidism. Recurrence of Graves’ disease following complete thyroidectomy is considered exceptionally rare and is usually attributable to residual or ectopic thyroid tissue rather than failure of the surgical approach itself. We present a rare case of late recurrent Graves’ thyrotoxicosis occurring more than a decade after total thyroidectomy.

Case Presentation: A 57-year-old female with a history of refractory Graves’ disease underwent total thyroidectomy in 2008. She subsequently developed hypothyroidism and was stabilised on 125 µg of levothyroxine once daily.

In 2022, after fourteen years of stability, the patient presented with classic thyrotoxic symptoms including insomnia, palpitations, heat intolerance, diaphoresis, and 3 kg weight loss. She also reported dry skin and gritty eyes. Despite reducing levothyroxine dose gradually to 25 µg daily she remained biochemically thyrotoxic. Review of her records revealed subclinical hyperthyroidism dating back to 2019.

Thyroid stimulating immunoglobulin (TSI) level has been persistently more than 40 IU/L (normal < 0.56 IU/L). A thyroid ultrasound identified 8 mm residual thyroid tissue in the left lower thyroid bed. Fine needle aspiration confirmed benign thyroid tissue (Thy2). A technetium uptake scan revealed multiple foci of uptake in the neck (13 mm anterior to the cartilage, a small 5 mm right paratracheal nodule and 2 small nodules in the left thyroid bed).

Levothyroxine was discontinued and carbimazole 10 mg daily was commenced. While thyroid function tests initially normalised the persistently high TSI levels prompted a transition to a block and replace regimen. MRI of the orbits ruled out active thyroid eye disease.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Repeat surgery was deemed clinically inappropriate after discussion with the ENT team. Patient was offered radioactive iodine, but she expressed a preference for long term medical management.

Conclusion: Recurrence of thyrotoxicosis following total thyroidectomy is a rare but significant complication. This case demonstrates the challenges of managing a persistent autoimmune drive despite surgical intervention. High TSI titres necessitate long term vigilance as even minimal residual tissue can grow over time and become hyper-functional under sustained autoimmune stimulation. Imaging with ultrasound and uptake scans is essential for localising remnants.

Abstract citation ID: lvag096.1757

EP1645 - ECE_3586 - Comparative analysis of inflammatory biomarkers in women with hypothyroidism and diminished ovarian reserve

Fotima Makhmudova[1,2] and Khurshida Nasirova[2]
[1]Tashkent, Uzbekistan; [2]Tashkent State Medical University, Tashkent, Uzbekistan

This study empirically investigated the relationship between thyroid function and ovarian reserve in women of reproductive age, incorporating key hormonal markers and inflammatory indicators. A one-way Analysis of Variance (ANOVA) was conducted to compare three distinct groups: the control group (practically healthy women, $n = 20$), women with decreased ovarian reserve (DOR) and hypothyroidism ($n = 40$), and women with DOR and euthyroidism ($n = 40$). Data on Thyroid-Stimulating Hormone (TSH), Anti-Müllerian Hormone (AMH), Follicle-Stimulating Hormone (FSH), C-reactive protein (CRP), Complement C3, and Ceruloplasmin were analyzed. Significant differences were observed across groups for TSH ($F(2,97) = 54.245$, $P < .001$), AMH ($F(2,97) = 323.365$, $P < .001$), CRP ($F(2,97) = 101.497$, $P < .001$), Complement C3 ($F(2,97) = 34.264$, $P < .001$), and Ceruloplasmin ($F(2,97) = 46.734$, $P < .001$). Post-hoc analyses revealed significantly higher TSH and lower AMH in the group with DOR and hypothyroidism compared to both the control group and the group with DOR euthyroidism. CRP, Complement C3, and Ceruloplasmin were also markedly elevated in the DOR with hypothyroidism group, suggesting an inflammatory component. FSH and age did not show significant inter-group differences. These findings underscore the critical impact of thyroid dysfunction on ovarian reserve and highlight the potential role of inflammatory markers in compromised reproductive health.

Keywords thyroid function, ovarian reserve, hypothyroidism, diminished ovarian reserve, infertility

Abstract citation ID: lvag096.1758

EP1646 - ECE_1678 - Potential use of tocilizumab in glucocorticoid-resistant Thyroid Eyes Diseases

Tatsiana Mokhort[1], Ksenia Palavinkina[2], Alena Mokhort[1] and Natalia Likharad[3]
[1]Endocrinology, Belarusian State Medical University, Minsk, Belarus; [2]Minsk City Clinical Endocrinology Center, Minsk, Belarus; [3]Endocrinology, 1th City Clinical Hospital, Minsk, Belarus

Objective: to evaluate the efficacy of tocilizumab (TZM) in the treatment of glucocorticoid-resistant Thyroid eyes Diseases (TED)

Materials and Methods: 7 female patients with glucocorticoid-resistant TED were observed on the background of compensated Graves' disease (6) and 1 with compensated hypothyroidism after surgical treatment of Graves' disease. Treatment with TZM (8 mg/kg, intravenously, once a month No. 3) was initiated after a course of pulse therapy with methylprednisolone (total dose 8000-13 500 mg) without significant clinical effect with a score of 4-5 points on a 7-point CAS scale. After a course of TZM treatment, all patients subjectively assessed changes in their quality of life, indicating significant improvement after 1-3 months. The CAS scores returned to normal (up to CAS 1) in all patients. The disappearance of spontaneous pains, pain when trying to look up, redness of the eyelids and conjunctiva, swelling of the eyelids, caruncle/plica inflammation, and chemosis was noted. At the same time, there was an improvement in vision, a decrease in intraocular pressure, and a significant decrease in the manifestations of diplopia (only 1 patient retained Gorman type 2 diplopia). When assessing the tolerability of treatment, 1 patient had an infection, and 2 patients had neutropenia, which had no significant effect on the treatment. With the consent of the patients, visual changes of the eyes are presented before and after TZM therapy.

Conclusion: The effectiveness of TZM in reducing CAS in patients with glucocorticoid-resistant TED has been demonstrated, which allows it to be used for the activity of TED manifestations.

Abstract citation ID: lvag096.1759

EP1650 - ECE_1167 - Correlation between iron deficiency in women with autoimmune thyroiditis depending on the functional status of the thyroid gland

Ilona Rudnieva[1], Iuliia Komisarenko[1], Galyna Mykhalchyshyn[1], Nazarii Kobyliak[1,2] and Viktoriia Yerokhovych[1]
[1]Bogomolets National Medical University, Kyiv, Ukraine; [2]Medical Laboratory CSD, Kyiv, Ukraine

Introduction: Iron is an essential micronutrient for sustaining vital physiological functions. It plays a key role in oxygen transport, energy metabolism, as well as in the functioning of the immune and nervous systems.

According to the World Health Organization, iron deficiency is the most widespread micronutrient disorder globally: approximately

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

30% of the population has anemia, predominantly due to iron deficiency. Women of reproductive age are particularly vulnerable, with up to 40% showing signs of iron depletion.

Women with autoimmune thyroiditis (AIT) are at an even higher risk of developing iron deficiency due to several contributing factors: chronic inflammation, impaired micronutrient absorption, and frequently associated hypothyroidism, which suppresses erythropoiesis.

Therefore, investigation the relationship between iron levels and thyroid function in women with AIT is relevant for early detection of latent deficiency and prevention of related complications.

Aim of the Study: To assess the presence of latent iron deficiency in women diagnosed with autoimmune thyroiditis, taking into account the functional status of the thyroid gland.

Materials and Methods: The study involved 50 female patients aged till 18-73 years, all of them had a confirmed the autoimmune thyroiditis. All participants underwent laboratory testing, which included the determination of ferritin levels (as an indicator of iron stores), as well as thyroid-stimulating hormone (TSH), free thyroxine (fT4), and free triiodothyronine (fT3) levels, using the immunochemiluminescence method for venous blood samples.

Results: Latent iron deficiency (reduced ferritin without overt anemia) was identified in 40% of the examined patients. Among them:

- 13 women (26%) were under 49 years of age;
- 3 women (6%) were over 49 years of age.

Among reproductive-age women with confirmed iron deficiency:

- 3 women (6%) had AIT with overt primary hypothyroidism;
- 4 women (8%) had AIT with subclinical hypothyroidism;
- 6 women (12%) had AIT with euthyroid status.

Among women over 49 years of age:

- 1 patient (2%) had AIT with overt hypothyroidism;
- 1 (2%) had subclinical hypothyroidism;
- 1 (2%) had euthyroidism.

Conclusions: 1. Latent iron deficiency was identified in 40% of women with autoimmune thyroiditis, indicating a high prevalence of this condition in the studied population. 2. The highest proportion of iron deficiency was observed among women of reproductive age—26%. 3. Most cases of iron deficiency occurred in patients with the euthyroid form of AIT—12%, suggesting that this subgroup may be underdiagnosed due to the absence of obvious thyroid dysfunction.

Abstract citation ID: lvag096.1760

EP1651 - ECE_3381 - Pembrolizumab-induced secondary adrenal insufficiency and thyroid dysfunction

Tamara Janic[1], Luka Ciric[1], Mirjana Stojkovic[1,2], Bojan Markovic[1], Nata Joksimovic[1], Jovana Babic[1], Biljana Nedeljkovic Beleslin[1,2], Jasmina Ciric[2] and Milos Zarkovic[1,2]
[1]Department of Thyroidology, Clinic of Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Centre of Serbia, Belgrade, Serbia; [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Pembrolizumab is a monoclonal antibody that blocks the programmed death receptor-1 (PD-1) on T cells and prevents cancer cells expressing PD-L1 ligand from using this pathway for suppression of the host immune system. It is successfully used for the treatment of various malignancies. Pembrolizumab allows T-cell reactivation leading to a more potent antitumor immune response. T-cell overactivity due to increased proliferation and a Th1/Th2 balance shift may cause autoimmune-driven destruction of endocrine tissues with or without autoantibody-mediated dysfunction. We present a 67-year-old male with a history of BRAF-negative metastatic melanoma with unknown primary, which was diagnosed by the examination of an enlarged cervical lymph node. Treatment with pembrolizumab was started and stable partial response achieved. After the fourth cycle of treatment (after 3 months), an increased level of FT4 was found (28 pmol/L), with suppressed TSH and undetectable TPOAb. A thyroid ultrasound showed a few spongiform micronodules. The treatment with low dose of methimazole was started in local hospital. After four months (eleven cycles of treatment) the patient presented to the emergency department due to extreme fatigue, hypotension, nausea and weight loss. Serum cortisol measured sporadically during the treatment was normal, but at the time of presentation a significant decrease of cortisol (38 nmol/L) and ACTH (1.8 ng/L) was found. Also, hypothyroidism on 5 mg of methimazole was registered, with FT4 5.95 pmol/L and TSH 94 mIU/L, undetectable TPOAb and TRAb 2.2 U/L (normal < 1.75). The treatment with hydrocortisone and levothyroxine was successfully introduced. Except for slightly higher FSH, gonadal hormones were normal. Aldosterone was 2.7 ng/dl, renin 1.5 uIU/mL, both normal. Although TgAb was transitory found slightly increased, only TRAb remained permanently 2.2 U/L for 20 months until now, with normal thyroid hormones on 37.5 mcg of levothyroxine. Among pembrolizumab-induced endocrinopathies the most common is thyroiditis, mostly presented as thyrotoxicosis followed by long-term hypothyroidism. Hypophysitis may lead to central hypothyroidism, secondary adrenal insufficiency and hypogonadism. Primary adrenal insufficiency and diabetes mellitus type 1 are rare complications. Since those conditions may be life-threatening, regular monitoring of thyroid hormones, cortisol and glucose levels during and after the treatment with pembrolizumab is essential.

Abstract citation ID: lvag096.1761

EP1652 - ECE_3575 - Unilateral Graves' disease: a case report

Chayma Besrour[1], Wiem Helali[2], Hiba Bettaieb[3], Manel Boudokhane[3], Rim Bourguiba[2] and Syrine Bellakhel[2]
[1]Endocrinology, Internal Security Forces Hospital Marsa, Tunis, Tunisia; [2]Internal Medecine, Internal Security Forces Hospital Marsa, Tunis, Tunisia; [3]Rhumatology, Internal Security Forces Hospital Marsa, Tunis, Tunisia

Introduction: Graves' disease is an immune system condition that affects the thyroid gland and responsible for an excess of hormones production that causes hyperthyroidism. Usually it affects the entire thyroid gland, only few cases reported the involvement of one lobe.

Case Presentation: Herein we report the case of 31-year-old female patient ,with no medical history , who consulted for weight loss, palpitations and asthenia for 2 months. Clinical examination

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

showed no abnormalities in the cervical area. Laboratory investigations confirmed thyrotoxicosis with suppressed thyroid stimulating hormone < 0.001 μU/L. Anti-TSH receptor antibodies were negative. Neck Ultrasound showed a right thyroid lobe enlarged and heterogeneous with increased vascularization ,and left lobe were both normal in size. A Tc99m pertechnetate thyroid scan showed an enlargement of the right thyroid lobe with diffuse intense uptake, whereas the left lobe was totally suppressed. A diagnosis of unilateral Graves' disease was made. The patient was treated with methimazole.

Discussion: Anti-TSH receptor antibodies are the classic autoantibodies that mimic TSH role, and they're present in almost 90 % of Graves' disease case.

Some patients can initially test negative despite having thyrotoxicosis but they may convert later on, suggesting timing or assay sensitivity issues or difference in structural or local expression of sodium-iodide symporters.

Abstract citation ID: lvag096.1762

EP1657 - ECE_1650 - Multiparametric ultrasound–based algorithm for evaluating overt thyrotoxicosis in diffuse thyroid disorders

Stefania-Alexandra Bunceanu[1], Bena Andreea[2], Roxana Pui[1,3] and Stoian Dana[2]
[1]*Department of Doctoral Studies, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania;* [2]*Timisoara, Romania;* [3]*Endocrinology, Spitalul Clinic Judetean de Urgenta Timisoara, Timisoara, Romania*

Introduction: Thyrotoxicosis, defined as an excess of circulating thyroid hormones, encompasses a heterogeneous group of disorders, most commonly related to diffuse thyroid disease (DTD). In current clinical practice, distinguishing hyperfunctional etiologies, particularly Graves' disease (GD), from destructive causes such as subacute thyroiditis, hashitoxicosis, postpartum thyroiditis, or drug-induced thyroiditis remains challenging. This diagnostic uncertainty can delay accurate diagnosis and prompt treatment initiation. The aim of this study was to improve etiologic discrimination in thyrotoxicosis by implementing a multiparametric ultrasound (MPUS) algorithm.

Methods: This prospective study was conducted between January 2022 and January 2024 in a specialized endocrinology center in Timișoara, Romania. A total of 100 patients with newly diagnosed thyrotoxicosis were enrolled, alongside 25 controls. All participants underwent a stepwise MPUS assessment, including B-mode ultrasound, shear-wave elastography (SWE), and spectral Doppler evaluation. Contrast-enhanced ultrasound (CEUS) was reserved for cases in which the etiology remained uncertain after the preceding steps. For each pathology subtype, the reference standard was established using biochemical markers and/or confirmatory tests, in accordance with current guideline recommendations.

Results: Among 125 participants, 25 were controls and 100 were diagnosed with DTD. The MPUS algorithm provided definitive etiologic classification in 98/100 DTD cases. At the initial assessment, B-mode hypoechogenicity showed good performance for identifying DTD (ROC AUC = 0.810). As the second step of the proposed algorithm, SWE revealed markedly increased parenchymal stiffness in subacute thyroiditis (SWE > 52 kPa; $P < .001$; ROC AUC = 0.990). Subsequently, spectral Doppler reliably separated GD from destructive thyrotoxicosis using inferior thyroid artery peak systolic velocity measurements; a cut-off of 54.8 cm/s identified GD (ROC AUC = 0.962; $P < .001$), whereas destructive disorders typically measured < 32.7 cm/s. Finally, CEUS correctly classified 26/28 equivocal cases; hyperfunctioning etiologies showed shorter time-to-peak and higher peak enhancement than destructive patterns. Using quantitative time–intensity curve thresholds: washout AUC (WoAUC) > 1867, wash-in AUC (WiAUC) > 205.8, and mean time–intensity curve (mTIC) > 12, CEUS discriminated hyperfunctioning disease with 88.2% sensitivity, 100% specificity, and 92.9% overall accuracy.

Conclusion: The proposed MPUS algorithm integrating grayscale ultrasound, SWE-based stiffness assessment, spectral Doppler, and selective quantitative CEUS demonstrated high diagnostic performance for etiologic classification in this cohort. If confirmed in larger prospective studies, this approach may facilitate earlier etiologic diagnosis, guide targeted management, and reduce reliance on radionuclide scintigraphy.

Abstract citation ID: lvag096.1763

EP1659 - ECE_1015 - Warthin-like papillary thyroid carcinoma associated with BRAF V600E and TERT promoter mutations: a case report

Yotsapon Thewjitcharoen[1], Waralee Chatchomchuan[1], Ekgaluck Wanothayaroj[1], Veekij Veerasomboonsin[2] and Somboon Keelawat[3]
[1]*THEPTARIN Diabetes, Thyroid and Endocrine Center, Vimut-Theptarin Hospital, Bangkok, Thailand;* [2]*Radiology, Vimut-Theptarin Hospital, Bangkok, Thailand;* [3]*Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

Background: Warthin-like Papillary Thyroid Carcinoma (WL-PTC) is a rare subtype of PTC, officially recognized as a distinct entity since 2017. It is characterized by the presence of papillary architecture with prominent lymphocytic stroma within fibrovascular core, resembling the Warthin tumor of the salivary gland. WL-PTC typically carries an excellent prognosis. However, due to its rarity, molecular profiling in WL-PTC remains limited. We present an unusual case of WL-PTC with coexisting *TERT* and *BRAF V600E* mutations.

Clinical Case: A 56-year-old Thai woman with no known underlying disease presented with left thyroid nodule for 6 months without other symptoms. Ultrasound showed a large heterogeneous hypoechoic nodule involving the entire left lobe (2.4 × 1.9 × 3.3 cm) and an ill-defined hypoechoic nodule in the right lobe (1.4 × 0.9 × 1.7 cm). Fine-needle aspiration (FNA) at left lobe yielded a Bethesda class V result. The patient underwent total thyroidectomy with lymph node dissection at another hospital. Histopathological examination revealed WL-PTC in the left lobe and Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) in the right lobe. Given the favorable prognosis of both tumors, the patient was advised against radioactive iodine (RAI) therapy. However, she sought a second opinion regarding the need for RAI. A follow-up neck ultrasound revealed multiple sub-centimeters, suspicious cervical lymph nodes (LNs) metastasis. Repeated neck exploration with modified radical neck dissection was subsequently performed. Pathology confirmed metastatic PTC with oncocytic features inside LNs (7/37 nodes). Molecular analyses for *BRAF* V600E and *TERT* promoters (C228T

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

and C250T) were detected by pyrosequencing technique. High-dose RAI ablation (150 mCi) was administered and the patient recovered well without recurrent disease at 24 months later.

Conclusions: WLPTC is an uncommon subtype of papillary thyroid carcinoma, accounting for less than 0.2% of all PTCs but with generally good prognosis. However, LNs metastasis with aggressive molecular alterations such as BRAF V600E and TERT mutations should be considered and thoroughly evaluated to guide treatment decisions. Further investigations are required to elucidate the prognostic impact of coexisting *BRAF* V600E and *TERT* mutations in this rate tumor subtype.

Abstract citation ID: lvag096.1764

EP1662 - ECE_3427 - Morphological features of thyroid dysfunction during combined therapy for breast cancer

Makhbuba Azimova and Khurshida Nasirova
Endocrinology, Tashkent State Medical University, Tashkent, Uzbekistan

Breast cancer (BC) is one of the most common malignancies among women worldwide and requires multimodal treatment approaches. Combined therapy, including chemotherapy, hormone therapy, and targeted treatment, significantly improves survival; however, it is often accompanied by systemic adverse effects. Thyroid dysfunction represents an important complication that may worsen patients' quality of life and reduce treatment tolerance. The study of morphological and functional changes in the thyroid gland during combined therapy for breast cancer remains clinically relevant.

Purpose: To evaluate morphological, laboratory, and clinical manifestations of thyroid dysfunction in patients with breast cancer undergoing combined therapy, taking into account tumor histological grade, molecular subtype, and proliferative activity.

Materials and Methods: The study included 136 patients with histologically confirmed breast cancer treated with combined therapy between 2021 and 2024. Thyroid function was assessed by measuring serum levels of thyroid-stimulating hormone (TSH), free thyroxine (fT4), free triiodothyronine (fT3), and anti-thyroid peroxidase antibodies (anti-TPO). Cytomorphological examination of the thyroid gland was performed in 14 patients using fine-needle aspiration biopsy specimens obtained from thyroid nodules after four cycles of chemotherapy and/or within 30 days after completion of combined treatment. Morphological evaluation included nuclear atypia, karyopyknosis, proportion of binucleated cells, and apoptotic index. Immunohistochemical analysis of breast tumor tissue assessed estrogen and progesterone receptor status, HER2/neu expression, and Ki-67 proliferation index.

Results: Patients receiving combined therapy demonstrated significantly elevated TSH levels and reduced fT4 and fT3 concentrations compared with the control group ($P < .001$). Higher TSH levels and lower fT4 values were observed in patients with invasive breast cancer compared to ductal carcinoma in situ, suggesting early manifestations of subclinical hypothyroidism. Morphological analysis revealed destructive changes in thyroid tissue, including nuclear atypia and increased apoptotic activity, predominantly after multiple chemotherapy cycles. Clinical manifestations of thyroid dysfunction were more frequent in patients with luminal B subtype and high proliferative activity (Ki-67 > 35%), including palpitations, neck discomfort, apathy, and sensation of a "lump" during swallowing. No statistically significant association was found between histological tumor grade (G1–G3) and severity of thyroid dysfunction.

Conclusion: Thyroid dysfunction in breast cancer patients undergoing combined therapy is more closely associated with molecular tumor subtype and proliferative activity than with histological tumor aggressiveness. These findings support the necessity of regular thyroid function monitoring in patients with breast cancer, particularly those with aggressive molecular subtypes, to ensure timely detection and correction of endocrine disorders.

Abstract citation ID: lvag096.1765

EP1664 - ECE_3925 - Rapidly enlarging thyroid nodule in an asymptomatic patient from an endemic goiter region: a case report

Ivanna Zaliska
Emergency Department, Ivano Frankivsk City Central Clinical Hospital, Ivano Frankivsk, Ukraine

Background: Thyroid nodules are common, particularly in endemic goiter regions. Environmental factors, including potential radiation exposure following the Chernobyl disaster, as well as challenges in healthcare access during the ongoing war in Ukraine, highlight the importance of early detection and monitoring. Incidentally detected thyroid nodules may demonstrate rapid growth and require timely evaluation.

Case Description: An asymptomatic female patient was referred by her primary care physician for thyroid ultrasonography during routine evaluation. Initial imaging revealed a small thyroid nodule. During follow-up, the nodule demonstrated rapid enlargement, raising suspicion for malignancy. The patient subsequently underwent total thyroidectomy, followed by radioiodine therapy as part of postoperative management.

Conclusion: This case highlights the importance of careful monitoring of incidentally detected thyroid nodules, particularly in high-risk regions. Rapid growth may necessitate surgical intervention and multidisciplinary management. Early detection and coordinated care remain essential to ensure optimal patient outcomes.

Abstract citation ID: lvag096.1766

EP1665 - ECE_3582 - Influence of ethnicity on prevalence of hypothyroidism in women with gestational diabetes and its relationship with metabolic parameters and pregnancy outcomes

Laura Vitale[1], Pamela Senesi[1,2], Guido Adda[2], Anna Ferrulli[1,2] and Livio Luzi[1,2]
[1]*Department of Biomedical Science for Health, University of Milan, Milan, Italy;* [2]*Department of Endocrinology, Nutrition and Metabolic Diseases, IRCCS Multimedica, Sesto San Giovanni, MI, Italy*

Background: Hypothyroidism and diabetes mellitus (DM) are the most common endocrine disorders in pregnancy and are associated with increased perinatal and postnatal morbidity. Adequate levothyroxine replacement and optimal glycaemic control reduce adverse pregnancy outcomes. The aetiology of hypothyroidism in pregnancy differs by ethnicity; for instance, iodine deficiency is more common in northern Asian populations, whereas

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

autoimmune thyroiditis predominates among Caucasians, albeit with exceptions. As ethnicity may affect incidence of both hypothyroidism in pregnancy (HP) and gestational diabetes mellitus (GDM), this study aims to evaluate its impact on type of hypothyroidism, glycaemic metabolism and pregnancy outcomes.

Materials and Methods: 105 women of different ethnicities [35 Caucasian (C), 35 North African (NA) and 35 Asian (A)] with GDM were included and the following parameters were retrospectively analysed:

- pre-existing hypothyroidism or HP,
- risk factors for GDM (maternal age, pre-gestational BMI, family history of DM, previous GDM),
- metabolic parameters [fasting glucose, glycated haemoglobin (HbA1c), oral glucose tolerance test (OGTT)],
- delivery characteristics (labour induction, caesarean section).

Results: Pre-existing hypothyroidism was more prevalent in Asian women (mostly secondary to autoimmune thyroiditis in our cohort), whereas Caucasians developed HP more frequently (C 26%, A 5%, NA 8%; $P = .055$), and exhibited higher HbA1c levels when compared with C without HP (33.00 ± 2.87 vs 30.05 ± 5.89 mmol/mol). Baseline fasting glucose values during OGTT were significantly higher in groups A and NA compared with group C (A vs C, $P = .02$; NA vs C, $P = .03$). Groups NA and A showed a trend toward higher HbA1c levels (NA 35.0 ± 4.8, A 34.3 ± 3.7, C 31.91 ± 3.5 mmol/mol; NA vs C $P = .003$, A vs C $P = .014$) and higher pre-gestational BMI compared with group C (NA 27.7 ± 0.9, A 25.9 ± 0.7, C 25.4 ± 1.1 kg/m^2; $P = .07$).

Conclusions: Higher rate of HP and higher HbA1c levels in group C suggests a negative impact of hypothyroidism on glucose metabolism. Lower fT4 and higher TSH levels may interfere with insulin synthesis and secretion and may induce insulin resistance by reducing peripheral insulin sensitivity due to excessive glucose–fatty acid cycling, which impairs insulin-mediated increases in blood flow to insulin-sensitive tissues.

Higher maternal age emerged as a major GDM risk factor in Caucasians, while higher pre-gestational BMI played a predominant role in groups A and NA, consistent with higher glycaemic parameters that demonstrate a greater tendency towards insulin resistance in these two groups. Family history of DM and previous GDM were confirmed as ethnicity-independent risk factors. No significant differences in delivery outcomes were observed.

Abstract citation ID: lvag096.1767

EP1667 - ECE_3765 - HLA allele associations with Hashimoto's thyroiditis in Albanian patients

Dorina Ylli[1], Megi Lekbello[1], Erkena Shyti[2], Marjeta Kermaj[1], Violeta Hoxha[1], Donika Kasemi[2], Zamira Ylli[1] and Genc Sulcebe[2]
[1]*University of Medicine Tirana, Tirana, Albania;* [2]*Research Center of Biotechnology and Genetics, Tirana, Albania*

Background: Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disease and is strongly influenced by genetic susceptibility, particularly within the human leukocyte antigen (HLA) region. Population specific data on HLA related risk and protection remain limited in Southeast Europe and particularly in Albania.

Methods: We performed a case control study including 50 patients diagnosed with Hashimoto's thyroiditis (diagnosis based on positive thyroid autoantibodies (anti-TPO and/or anti-Tg) and/or characteristic ultrasound features) and 208 controls. High-resolution HLA typing was performed for class I (HLA-A, B, C) and class II (HLA-DRB1, HLA-DQB1) loci. Allele frequencies were compared using Fisher's exact test, and odds ratios (OR) were calculated.

Results: Marked differences in HLA class II allele distribution were observed between patients and controls. The HLA-DQB1*03:01 allele was significantly overrepresented in Hashimoto patients (OR ≈ 8.25, $P < .001$), representing the strongest disease association. The HLA-DQB1*02:01 allele was also significantly associated with HT (OR ≈ 3.17, $P = .009$). At the DRB1 locus, DRB1*12:01 showed a significant association with disease susceptibility (OR ≈ 13.2, $P = .024$). Several alleles, including DRB1*14:01, were more frequent among controls than patients, however, these differences did not reach statistical significance, indicating a possible but unconfirmed protective effect.

Conclusions: This study identifies strong associations between Hashimoto's thyroiditis and specific HLA class II risk alleles in the Albanian population, while also suggesting the presence of potentially protective alleles that did not reach statistical significance. These findings emphasize the complex role of HLA class II variants in both susceptibility and protection in autoimmune thyroid disease and support the need for larger population studies.

Abstract citation ID: lvag096.1768

EP1668 - ECE_1130 - Thyroid dysfunction due to chronic stress caused by military operations

Yana Kocherzhynska-Halis
Family Doctor's Office, Odesa, Ukraine

For thousands of years, humans have lived in a dynamic environment full of potential dangers. While fear and stress were crucial for the survival of our ancestors, today they are largely considered harmful factors that threaten both our physical and mental health. The hypothalamus plays a crucial role in initiating hormonal responses to stressful stimuli through the hypothalamic-pituitary-adrenal (HPA) axis. Connected to the prefrontal cortex and limbic structures, especially the amygdala and hippocampus, the hypothalamus acts as a central hub, integrating the physiological aspects of the stress response. However, in addition to the well-known role of the hypothalamic-pituitary-thyroid (HPT) axis, the hypothalamus can also involve the hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-gonadal (HPG) axes, as well as through the secretion of growth hormone, prolactin, dopamine, and oxytocin. Experimental studies in animals and humans illustrate the effects of various forms of stress on the thyroid gland and the regulation of thyroid hormone (TH) through the thyrotropic multi-loop control loop. The hypothalamic-pituitary-thyroid (HPT) axis is part of the physiological stress system and mediates key regulators of metabolic activity during the stress response. Genetically predisposed individuals are more responsive to stressors, and their psychological response is greatly enhanced. This results in a significant increase in serum TH levels as soon as a negative stressor occurs. Physical stressors are used to induce psychological stress all of which affect thyroid function. In addition, somatic diseases can also affect the thyroid gland or be associated with thyroid dysfunction. Within the framework of observation in practice over the past year

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

11.2024-11.2025, 35 patients were examined for TSH levels, 30 women and 5 men, aged 30-65 years and a questionnaire was conducted on the impact of stress on their health. The survey included a clear framework for the occurrence of stress and the development of complaints that may have been associated with thyroid diseases. All patients who noted a significant deterioration according to the questionnaire during the war were sent for TSH control, according to the results of TSH level violations and further examination of patients, it was found: diffuse toxic goiter 12 patients, Autoimmune thyroiditis, including hypothyroidism in 9 patients. This work represents an analysis of previously conducted studies and observations in personal clinical practice of the impact of chronic stress caused by military operations on the development of thyroid dysfunction and the need for screening for the disease in countries where military operations are underway.

Abstract citation ID: lvag096.1769

EP1670 - ECE_1101 - Reappraisal of the role of ultrasonography-guided fine needle aspiration biopsy in the management of autonomously hyperfunctioning thyroid nodules

Hee Kyung Kim[1], Ho-Cheol Kang[1,2], Jeehee Yoon[1], Ji Yong Park[1], A. Ram Hong[1], Sun Kyung Song[3] and Suk Bong Yun[4]

[1]Chonnam National University Medical School, Hwasun-gun, South Korea; [2]Division of Endocrinology and Metabolism, Department of Internal Medicine, Chonnam National University Medical School, Chonnam University Hwasun Hospital, Hawsun, South Korea; [3]Internal Medicine, Presbyterian Medical Center, Jeonju, South Korea; [4]Rehabilitation Medicine, Presbyterian Medical Center, Jeonju, South Korea

Background: Autonomously hyperfunctioning thyroid nodules are generally believed to have very low chances of malignancy. Clinical guidelines recommend not performing fine needle aspiration biopsy (FNAB) on these lesions irrespective of their size. However, a reappraisal of the need to perform FNAB is warranted because recent studies suggest the malignancy rate of toxic nodules may have been underestimated.

Methods: We reviewed patients with toxic nodules who visited Chonnam National University Hwasun Hospital from 2003 to 2023. A control group was selected from the population with nontoxic nodules who underwent FNAB in 2023. Laboratory tests and ultrasonographic findings of the nodules were analyzed.

Results: Toxic nodules were more likely to be single (77.8% vs 38.4%, $P < .001$) and larger (3.94 cm vs 1.78 cm, $P < .001$) compared to nontoxic nodules. Nontoxic nodules tended to exhibit ultrasonographic features associated with a higher malignancy risk (K-TIRADS 3: 28.0%, K-TIRADS 4: 28.4%, K-TIRADS 5: 42.0%) compared to toxic nodules (K-TIRADS 3: 55.6%, K-TIRADS 4: 42.6%, K-TIRADS 5: 1.9%). The malignancy rate was higher in nontoxic nodules (25.6% vs 3.7%, $P < .001$), but the malignancy rate in other nodules or the contralateral thyroid gland was similar (16.7% vs 9.2%, $P = .139$). This resulted in a malignancy rate of 16.7% for toxic nodules and 25.6% for nontoxic nodules ($P = .014$).

Conclusion: We believe that when deciding whether to perform FNAB for thyroid nodules, ultrasonographic findings should take priority over serum TSH levels.

Abstract citation ID: lvag096.1770

EP1671 - ECE_2171 - A network meta-analysis of the therapeutic efficacy for moderate to severe active thyroid-associated ophthalmopathy

Aihua Liu[1], Fanrui Meng[1], Yixin Gao[1], Haining Wang[1,2], Hongwei Gao[1] and Tianpei Hong[1]

[1]Beijing, China; [2]Endocrinology and Metabolic Disease, Peking University Third Hospital, Beijing, China

Objective: To evaluate the safety and efficacy of various treatment modalities for thyroid-associated ophthalmopathy through a network meta-analysis.

Methods: A literature search was conducted in multiple databases including PubMed, Web of Science, EMBASE, and Cochrane Library up to December 31, 2024, for randomized controlled trials involving patients with moderate to severe active thyroid-associated ophthalmopathy. The quality of the included studies was evaluated using the Cochrane Risk of Bias tool (RoB 2). Network meta-analysis based on the frequentist approach was performed using RevMan 5.3 and STATA 15.0 software. The primary outcome measures were overall response rate, clinical activity score (CAS), proptosis, palpebral fissure height, diplopia, and adverse reactions.

Result: Eventually, we included 26 eligible randomized controlled studies, involving a total of 1561 participants, covering a total of 16 intervention methods, including intravenous glucocorticoid injection (IVGC), oral glucocorticoid (OGC), retrobulbar glucocorticoid injection (TA), orbital radiotherapy (OR), somatostatin analogues (SSA), and biological agents such as tislelizumab, etc. Network analysis showed that tislelizumab outperformed the placebo in improving clinical activity scores, exophthalmos degree, and overall response rate. Glucocorticoid combined with statins and mycophenolate mofetil treatment could improve the exophthalmos degree, quality of life score, and diplopia score of patients.

Conclusion: Compared with no treatment, tiotropium bromide shows a significant effect in increasing the overall treatment response rate. The method of oral mycophenolate mofetil or statins combined with intravenous glucocorticoid administration is more effective in improving exophthalmos and diplopia in patients. Although some treatment methods have shown good effects in the treatment of thyroid-associated ophthalmopathy, the adverse reactions that occur raise safety concerns, and a more ideal balance between the efficacy and safety of the treatment methods needs to be sought.

Abstract citation ID: lvag096.1771

EP1679 - ECE_3542 - Sex differences in agranulocytosis reporting among patients on antithyroid drugs: a retrospective EudraVigilance study

Aia Nana[1], Alexandru-Ioan Draghici[2], Ioana-Elena Tarabasanu-Mihaila[3], Mahir Khalil Ibrahim Jallo[4], Shatha Faisal Al Aqarbeh[5] and Rania Al-Mukhtar[6]

[1]Thumbay University Hospital, Ajman, United Arab Emirates; [2]Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania; [3]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [4]Department of Endocrinology, Thumbay University Hospital, Ajman, United Arab Emirates; [5]Near East University, Cyprus; [6]King's College London, London, United Kingdom

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Agranulocytosis is a rare but serious adverse event of antithyroid drugs (ATDs). We decided to evaluate clinical outcomes and reporting patterns of agranulocytosis with methimazole (MMI), carbimazole (CBZ), and propylthiouracil (PTU) with an emphasis on gender disparities.

Methods: Individual Case Safety Reports (ICSR) of MMI, CBZ OR PTU use were extracted from EudraVigilance. Agranulocytosis was categorized using MEDRA Preferred Terms. The reports were classified by drug and sex. Overall and sex specific reporting disproportionality was evaluated using reporting odd ratios (ROR) with 95% confidence intervals, each drug being compared to a pooled group made out of the other members of the category. Clinical outcomes were summarized by drug (recovered, not recovered, fatal). Reporter type and geographical origin of reports (European Economic Area vs non-EEA) were described.

Results: Recovery was reported in 71% of methimazole, 74% of carbimazole, and 75% of propylthiouracil agranulocytosis cases. Fatal outcomes were uncommon, occurring in 4%, 5%, and 3% of cases, respectively.

Disproportionality analysis identified varying reporting patterns for agranulocytosis among antithyroid drugs. Carbimazole showed a significantly increased signal (ROR 1.15, 95% CI 1.03-1.29), whereas propylthiouracil was associated with a significantly lower signal (ROR 0.72, 95% CI 0.61-0.86). Methimazole showed no disproportional reporting overall (ROR 1.01, 95% CI 0.91-1.12).

Although limited by a low number of male cases, sex-stratified analyses showed potential differences in reporting patterns. Among males, no statistically significant disproportionality was observed. Carbimazole showed a numerically higher ROR (1.27, 95% CI 0.98-1.64), while methimazole showed a lower ROR that did not show statistical significance (0.80, 95% CI 0.63-1.01). Propylthiouracil showed no disproportional reporting (ROR 1.08, 95% CI 0.75-1.56).

Among females, carbimazole remained significantly associated with higher disproportionality reporting (ROR 1.15, 95% CI 1.01-1.31), propylthiouracil showed lower reporting (ROR 0.75, 95% CI 0.62-0.92), and methimazole showed no disproportionality (ROR 0.99, 95% CI 0.88-1.11).

Hospital care providers submitted 97% of the reports. Reporting from the European Economic Area accounted for 40% of methimazole, 78% of carbimazole, and 70% of propylthiouracil cases.

Conclusion: This EudraVigilance analysis revealed drug- and sex-specific differences in agranulocytosis reporting among antithyroid drugs. Carbimazole showed increased reporting and propylthiouracil decreased reporting, largely driven by female reports, while methimazole showed no signal. Most cases recovered and fatal outcomes were rare. Despite limitations of spontaneous reporting, these findings support drug- and sex-specific clinical vigilance.

Abstract citation ID: lvag096.1772

EP1700 - LBA_ECE_1289 - Pituitary gigantism due to a novel AIP variant with an under-recognised ocular manifestation

Vishnou Mourougavelou[1,2,3], Erik Benyei[1], Panagiotis Drakos[1], Naz Raoof[4], Fresht Naomi[5], Anouk Borg[6] and Marta Korbonits[1,2]

[1]Faculty of Medicine and Dentistry, Queen Mary University of London, William Harvey Research Institute, Centre for Endocrinology, London, United Kingdom; [2]Department of Endocrinology, Barts Health NHS Trust—Barts & the London Hospitals, London, United Kingdom; [3]Barts Health NHS Trust, London, United Kingdom; [4]Department of Opthalmology, Barts Health NHS Trust—Barts & the London Hospitals, London, United Kingdom; [5]Department of Oncology, University College London Hospitals NHS Foundation Trust, London, United Kingdom; [6]Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, London, United Kingdom

Background: Pituitary gigantism is typically caused by growth hormone (GH)-secreting pituitary neuroendocrine tumours. Germline heterozygous loss-of-function variants in the aryl hydrocarbon receptor-interacting protein (*AIP*) gene are the most common genetic cause and are associated with large, invasive tumours and relative resistance to first-generation somatostatin analogues.

Case Presentation: A 17-year-old male initially presented with a slipped capital femoral epiphysis. Despite a height exceeding 2 m, the diagnosis of gigantism was delayed by six months, during which he experienced rapid linear growth, headaches, and declining academic performance. While he had markedly elevated GH levels (>100 µg/L), his insulin-like growth factor-1 (IGF-1; 1.64× upper limit of normal [ULN]) was only modestly raised. This discordance was attributed to coexisting hypopituitarism, including secondary hypothyroidism, adrenal insufficiency, and hypogonadotropic hypogonadism (undetectable testosterone; bone age 14 years at a chronological age 18.5 years).

Magnetic resonance imaging demonstrated a 37 × 36 × 25 mm pituitary macroadenoma with cavernous sinus invasion and suprasellar extension compressing the anterior visual pathway. Initial treatment with first-generation somatostatin analogues achieved limited biochemical control (GH: 58.9 µg/L; IGF-1: 654 µg/L; 1.34x ULN). Following transsphenoidal surgery, histopathology revealed a sparsely granulated somatotrophinoma with a Ki-67 index of 1%-2% and a low mitotic index. There was a significant remnant within the cavernous sinus. GH (29.6 µg/L) and IGF-1 (540 µg/L, 1.11x ULN) levels improved but did not normalise.

Genetic testing identified a novel truncating *AIP* variant (c.259C>T; p.Gln87Ter). Postoperative management included escalating doses of pegvisomant (currently 270 mg/week), thyroxine, hydrocortisone, testosterone replacement, and subsequent proton beam radiotherapy. After radiotherapy, the patient developed eye pain, and an ophthalmological assessment diagnosed posterior (“foamy”) blepharitis, with preserved visual function, fields, colour vision, and normal intraocular pressures. This was attributed to acromegaly-related meibomian gland dysfunction rather than radiation exposure, and symptoms improved with topical treatment with eye drops.

Discussion: There are several learning points in this case:

1. Slipped capital femoral epiphysis is a well-described complication of childhood-onset GH excess.
2. Given his epiphysis was open, and he grew by 3 centimetres within the few months whilst awaiting surgery, the best postoperative medical treatment was deemed to be pegvisomant. Testosterone therapy would be the optimal solution, but it could cause an initial temporary growth acceleration.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

3. The ocular manifestation of posterior blepharitis seems to be under-recognised in patients with GH-excess.
4. Genetic testing helped us to make therapeutic decisions (early pegvisomant and proton beam therapy).

Abstract citation ID: lvag096.1773

EP1701 - LBA_ECE_1166 - Clinicopathologic characteristics and recurrence risk factors in parathyroid carcinoma: a multi-institutional retrospective study in Korea

So Hee Lee[1], Yu-Mi Lee[2], Jae Hyun Park[3], Su-Jin Kim[4], Hyeok Jun Yun[5] and Jong Ju Jeong[6]

[1]Department of Surgery, Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea; [2]Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [3]Department of Surgery, Yonsei University Wonju College of Medicine, Wonju-si, Gangwon-do, South Korea; [4]Department of Surgery, Seoul National University Hospital, Seoul, South Korea; [5]Department of Surgery, Gangnam Severance Hospital, Seoul, South Korea; [6]Department of Surgery, Severance Hospital, Seoul, South Korea

Background: Parathyroid carcinoma is a rare endocrine malignancy, due to its rarity, prognostic factors and optimal surgical strategies remain incompeletely defined. This study aimed to evaluate clinicopathological characteristics and outcomes and to identify risk factors for recurrence.

Methods: We conducted a retrospective multicenter study across six tertiary hopitals in Korea. Patients without surgical treatments or those whose initial surgery was not performed at the respective institution were excluded. A total of 81 patients with pathologically confirmed parathyroid carcinoma between 1990 and 2024 were included. Clinicopathological data and outcomes were analyzed. Recurrence-free surgival was assessed, and Cox regression analysis was performed to identify risk factors for recurrence.

Results: The mean follow-up periods was 74.8 months. The mean age was 50.6 years, and 58% were female. Hypercalcemia was present in 81.5% of patients, while 17.3% were normocalcemic. Markedly elevated PTH levels (>1000 pg/mL) were observed in 38.5%. Primary hyperparathyroidism was present in 82.7% of patients, and 12.4% had secondary or tertiary hyperparathyroidism.

Ultrasonography detected 97.3% of cases, and MIBI scans were positive in 88.7%. Focused parathyroidectomy was performed in 77.8% of patients; among these, combined thyroidectomy was performed in 53.1% and central compartment neck dissection(CCND) in 50.6%. Subtotal or total parathyroidectomy was performed in 11.1% of patients, including concomitant thyroidectomy in 4.9%, CCND in 6.2%, and lateral neck dissection in 1.2%.

The mean tumor size was 28.4 mm. Capsular invasion was observed in 86.5%, including direct invasion into the thyroid gland in 19.8%. Vascular invasion was identified in 22.2%. Regarding the Ki-67 index, 12.4% of patients had values of 5%-10%, and 6.2% had values >10%. Most tumors were T1 (80.2%) and nodal metastasis was present in 4.9%. Synchronous distant metastasis was observed in 3 patients: two had lung metastases, and one had both lung and bone metastases.

During follow-up, eleven patients developed recurrence, most commonly in cervical lymph node(54.5%) and lung(63.6%). Nine patients undewent reoperation. Seven patients died during follow-up, including four disease-related death. The 5-year overall survival rate was 89.2% and 5-year disease-specific survival rate was 97.0%.

On multivariate analysis, lymph node metastasis was an independent risk factor for recurrence (HR 6.22, 95% CI 1.27-30.37, $P = .024$), while combined thyroidectomy showed a trend toward reduced recurrence risk but did not reach statistical significance.

Conclusion: Parathyroid carcinoma showed favorable long-term survival with a relatively low recurrence rate. Lymph node metastasis was the only independent predictor of recurrence, highlighting the importance of nodal assessment.

Abstract citation ID: lvag096.1774

EP1703 - LBA_ECE_1126 - Improvement of symptomatic postprandial reactive hypoglycemia with a nutraceutical based on white mulberry, fenugreek, inulin, niacin, xhromium, zinc, and *Lactiplantibacillus plantarum* A7

Inmaculada Molinero-Marcos[1], Borja Santana-Ojeda[1], Sara Andrada-Diaz[2], Claudia Arnas-Leon[1,3], Ricardo Jose de Leon-Durango[1], Agnieszka Kuzior[3], Irene Hernandez-Hernandez[1], Carmen Acosta-Calero[4], Jennifer Maria Perez-Rivero[5] and Francisco Javier Martinez-Martin[1,3]

[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Medical Advisory, Bioksan Naturalmente Juntos, Las Palmas de Gran Canaria, Spain; [3]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain; [4]Cardiology, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [5]Centro de Salud de Escaleritas, Las Palmas, Spain

Background and Objectives: Symptomatic postprandial reactive hypoglycemia is associated with hyperinsulinism and prior gastric surgery. Although rarely severe—except in occasional cases such as arrhythmia—it can significantly impair patients' quality of life. Current management includes dietary measures and, in some cases, off-label use of alpha-glucosidase inhibitors such as acarbose. These agents are effective in blunting postprandial hyperglycemia and reducing subsequent hyperinsulinemia, but their use is often limited by poor gastrointestinal tolerability.

White mulberry (*Morus alba*) contains 1-deoxynojirimycin, a potent competitive inhibitor of alpha-glucosidase. A nutraceutical has been developed combining a standardized white mulberry leaf extract, fenugreek (*Trigonella foenum-graecum*), inulin, *Lactiplantibacillus plantarum* A7, niacin, chromium, and zinc.

This study aimed to evaluate the tolerability and efficacy of this nutraceutical in patients with symptomatic postprandial reactive hypoglycemia, as well as its impact on quality of life.

Methods: We recruited patients diagnosed with symptomatic postprandial reactive hypoglycemia who had failed dietary management and had declined or were intolerant to treatment with acarbose. All participants presented documented symptomatic hypoglycemic episodes (<70 mg/dL), confirmed by capillary blood glucose measurements using test strips or continuous/

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

intermittent glucose monitoring. Patients were instructed to take one capsule of the nutraceutical daily before the main meal (usually lunch) with a glass of water. Episodes of hypoglycemia were registered and reported. Quality of life was assessed at baseline and after 3 months of treatment using the EuroQoL-5D-3L questionnaire.

Results: Fifteen patients were recruited (8 women; mean age 57 ± 9 years). Twelve had a history of gastric surgery (5 sleeve gastroplasty, 4 gastric by-pass, 2 fundoplication for reflux, 1 resection of gastric lymphoma), one had long COVID as a potential cause of reactive hypoglycemia, and two had prediabetes without another obvious cause. Five patients had previously received acarbose (off-label) with poor tolerance.

After 3 months of treatment, 12 out of 15 patients reported a clear clinical improvement. The frequency of hypoglycemic episodes decreased from 2.7 ± 1.2 to 0.3 ± 0.2 episodes per week (−89%, $P < .001$). Quality of life scores improved from 0.65 ± 0.12 to 0.84 ± 0.15 ($P = .008$).

Self-reported tolerability was excellent in 7 patients, good in 6, and acceptable in 2.

Conclusions: This nutraceutical was well tolerated and reduced symptomatic reactive hypoglycemia episodes by nearly 90%, significantly improving quality of life scores. Although originally designed for prediabetes and diabetes management, it may also represent a useful option in this therapeutic niche.

Abstract citation ID: lvag096.1775

EP1704 - LBA_ECE_1301 - FDG-avid lipid-poor adrenal incidentaloma mimicking malignancy: a rare cortisol-secreting black adrenal adenoma

Eirini Melidou[1], Artemis Kyriakidou[1], Maria Grammatiki[1], Litsa Rakitzi[1,2], Triantafyllia Koletsa[3], Stylianos Apostolidis[4] and Kalliopi Kotsa[1]

[1]*Division of Endocrinology and Metabolism—Diabetes Center, 1st Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA University Hospital, Thessalonki, Greece;* [2]*University Hospital AHEPA, Thessaloniki, Greece;* [3]*Laboratory of General Pathology and Pathological Anatomy, Aristotle University of Thessaloniki, Thessaloniki, Greece;* [4]*1st Propedeutic Surgical Department, Aristotle University of Thessaloniki, AHEPA University Hospital, Thessaloniki, Greece*

Objective: To report a rare case of a cortisol-secreting black adrenal adenoma detected during investigation of elevated carcinoembryonic antigen (CEA) levels.

Case Presentation: A 58-year-old woman with a history of total hysterectomy with bilateral salpingo-oophorectomy at age 47 for a uterine smooth muscle tumor of uncertain malignant potential (STUMP) was evaluated for persistently elevated CEA levels (12.3 ng/mL; reference < 6.5) detected during routine gastroenterological screening. Gastrointestinal endoscopy was normal. Computed tomography revealed a 22-mm left adrenal nodule and a thyroid nodule. Findings remained stable on follow-up imaging. 18F-FDG PET-CT demonstrated moderate metabolic activity in the thyroid nodule (SUV_{max} 3.2) and increased uptake in the adrenal lesion (SUV_{max} 7.3), raising suspicion of malignancy. Magnetic resonance imaging confirmed a 21 × 19 mm left adrenal mass without signal loss on chemical-shift sequences, consistent with a lipid-poor lesion and raising the possibility of metastatic disease. The patient was referred for endocrine evaluation. Hormonal assessment revealed hypercortisolism with abnormal suppression tests (overnight dexamethasone suppression test 1 mg: cortisol 20.5 μg/dL; low-dose dexamethasone suppression test: cortisol 21.27 μg/dL) and suppressed ACTH (<1.5 pg/mL), confirming ACTH-independent hypercortisolism. Twenty-four-hour urinary metanephrines and normetanephrines were normal, excluding pheochromocytoma, while renin, aldosterone and androgen levels were within normal limits. Clinically, the patient had hypertension, easy bruising and hair thinning without overt Cushingoid features. Thyroid ultrasound showed a 1.68-cm TIRADS-3 nodule with normal thyroid function and calcitonin. The patient underwent laparoscopic left adrenalectomy.

Follow-up: Postoperatively, hydrocortisone replacement was tapered and discontinued within two months. At follow-up visits at two and four months, blood pressure and hormonal parameters were normal. Histopathological examination confirmed an adrenocortical adenoma with intracytoplasmic lipofuscin deposition, consistent with a black adrenal adenoma. No malignant features were identified and Ki-67 <1% confirmed low proliferative activity.

Conclusion: Black adrenal adenomas are extremely rare benign tumors characterized by lipofuscin deposition. They are usually nonfunctioning adrenal incidentalomas, while cortisol or aldosterone secretion is uncommon. Because lipid-poor appearance and increased FDG uptake may mimic malignancy, careful endocrine evaluation and histopathological confirmation are essential. Surgical resection is curative and associated with excellent prognosis.

Abstract citation ID: lvag096.1776

EP1705 - LBA_ECE_1103 - Wernicke's encephalopathy following GLP-1 receptor agonist use for weight loss: a case report

Anne Milligan[1] and Joseph Timmons[1,2]

[1]*University Hospital Wishaw, Lanarkshire, United Kingdom;* [2]*Glasgow, United Kingdom*

Wernicke's encephalopathy (WE) is a neurological emergency resulting from vitamin B1 (thiamine) deficiency. It's classic triad of symptoms -oculomotor dysfunction, ataxia and altered mental status- are present in only 16% of patients, making it a chronically under-diagnosed condition. Whilst WE is most commonly associated with chronic alcoholism, malnourishment (for example, starvation, extreme dieting, hyperemesis gravidarum and bariatric surgery) and hyper-catabolism (for example, cancer) are among other, far less recognised, states in which WE can develop. An emerging subgroup at risk of developing WE, is those taking glucagon-like peptide 1 receptor agonists (GLP-1RA). The therapeutic role of GLP-1RAs in obesity management has been increasingly recognised and endorsed over recent years. We will discuss a case of a patient presenting with non-specific neurological symptoms in the context of recent GLP-1RA use, and subsequent significant weight loss, who saw rapid resolution of symptoms with intravenous (IV) thiamine replacement. This case highlights the importance of nutritional supplementation with GLP-1RAs and the need for early consideration of a WE diagnosis in patients receiving GLP-1 receptor agonists, allowing prompt and sufficient treatment, and prevention of irreversible neurological damage.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1777

EP1706 - LBA_ECE_1386 - The great masquerader: pheochromocytoma presenting as type 2 diabetes mellitus

Ricardo Jose de Leon-Durango[1], Borja Santana-Ojeda[1], Inmaculada Molinero-Marcos[1], Claudia Arnas-Leon[1,2], Alba Hernandez-Lazaro[1,3], Marta Sánchez[1], Agnieszka Kuzior[2], Carmen Acosta-Calero[4], Fabianna Genesi[5] and Francisco Javier Martinez-Martin[1,2]

[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain; [3]Servei d'Endocrinologia i Nutricio, Parc Taulí Hospital Universitari, Sabadell, Barcelona, Spain; [4]Cardiology, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [5]Centro de Salud de Arucas, Arucas, Las Palmas, Spain

Background: Catecholamine excess in pheochromocytoma can induce hyperglycemia occasionally mimicking type 2 diabetes mellitus (T2DM). Although typically symptomatic, some tumors remain clinically silent. We report an incidental, asymptomatic pheochromocytoma presenting as apparent type 2 diabetes, which remitted following tumor resection.

Case Presentation: A 56-year-old woman with a normal body mass index was referred to our Endocrinology Clinic following the incidental discovery of an indeterminate left adrenal mass on abdominal CT, performed during the evaluation of recurrent abdominal pain. The lesion measured 3.4 cm in maximum diameter, with a density of 30-40 Hounsfield units. The patient was normotensive, had no history of tremor or tachycardia, and showed no Cushingoid features.

Five years earlier, she had been diagnosed with T2DM, presenting with polydipsia, polyuria, and marked hyperglycemia. Latent autoimmune diabetes in adults (LADA) was excluded based on negative anti-GAD antibodies. Glycemic control had been acceptable (HbA1c 6.8%) with diet, regular exercise, metformin, sitagliptin, and a relatively high dose of basal insulin (approximately 0.75 U/kg), after failure to achieve adequate control without insulin.

Adrenal evaluation revealed a normal cortisol suppression test and normal aldosterone, renin, and aldosterone-to-renin ratio. However, plasma metanephrines and chromogranin A were markedly elevated (metanephrine 412 pg/mL, normetanephrine 335 pg/mL, chromogranin A 324 ng/mL). An MIBG scan confirmed a left pheochromocytoma without evidence of additional lesions. The tumor was successfully removed via robotic laparoscopic adrenalectomy without complications. Histopathological analysis confirmed a pheochromocytoma with low malignant potential (PASS score 3).

Postoperatively, the patient developed frequent hypoglycemic episodes, predominantly nocturnal. Basal insulin doses were progressively reduced and eventually discontinued, followed by withdrawal of sitagliptin and metformin.

Ten months after surgery, the patient remains asymptomatic, with normal plasma metanephrines and chromogranin A levels. Her diabetes has apparently remitted, with an HbA1c of 5.6% in the absence of pharmacological treatment.

Discussion: This case illustrates an atypical presentation of pheochromocytoma, lacking classical adrenergic symptoms and identified incidentally. Catecholamine excess (particularly in epinephrine secreting tumors, as in our case) can induce hyperglycemia through increased hepatic glucose production, impaired insulin secretion, and insulin resistance, thereby mimicking T2DM. The requirement for relatively high insulin doses despite normal BMI may represent a clinical clue. The marked improvement and eventual remission of diabetes following tumor resection support a causal relationship.

Conclusions: Pheochromocytoma should be considered in atypical or difficult-to-control diabetes. Recognition of this reversible cause of hyperglycemia is essential, as surgical treatment may lead to complete remission.

Abstract citation ID: lvag096.1778

EP1707 - LBA_ECE_1349 - Uncontrolled hyperthyroidism mimicking pseudo-hypoandrogenism: SHBG-mediated peripheral androgen resistance in a male with poorly controlled Graves' disease

Inmaculada Molinero-Marcos[1], Borja Santana-Ojeda[1], Claudia Arnas-Leon[1,2], Ricardo Jose de Leon-Durango[1], Alba Hernandez-Lazaro[1], Agnieszka Kuzior[2], Carmen Acosta-Calero[3], Maria del Pino Perez-García[4], Paula Maria Fernandez-Trujillo-Comenge[1] and Francisco Javier Martinez-Martin[1,2]

[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain; [3]Cardiology, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [4]Family & Community Medicine, Centro de Salud San Gregorio, Telde, Las Palmas, Spain

Background: Uncontrolled hyperthyroidism robustly increases hepatic sex hormone-binding globulin (SHBG) synthesis via direct T3 stimulation, leading to elevated total testosterone with paradoxically normal or low free testosterone. This creates a state of functional peripheral androgen resistance (pseudo-hypoandrogenism) without primary hypogonadism, often overlooked and prompting unnecessary urologic investigations for androgen-secreting tumors.

Case Presentation: A male patient with Graves' disease diagnosed in 2022, marked by persistent non-adherence and loss to follow-up, was referred from Urology in September 2025 for persistently elevated total testosterone (>2× upper limit of normal) without virilizing features. Biochemical evaluation confirmed severe uncontrolled hyperthyroidism (free T4 3.07 ng/dL, TSH undetectable) without clinically evident ophthalmopathy. Total testosterone was markedly elevated, yet free testosterone remained within normal range; gonadotropins (LH/FSH) were normal, testicular ultrasound unremarkable, and tumor markers negative. SHBG was strikingly elevated, attributable solely to sustained thyrotoxicosis. The patient exhibited classic hyperthyroid symptoms (tachycardia, tremor) but was not receiving antithyroid therapy.

Discussion and Management: This presentation exemplifies SHBG-driven discordance in androgen profiling, where hyperthyroidism induces a reversible, functional hypoandrogenic state by sequestering testosterone. It averted invasive workup for neoplasm and highlighted the pitfalls of interpreting total

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

testosterone in isolation. Given poor adherence, absent active ophthalmopathy, and recurrent loss to follow-up, definitive radioiodine (^{131}I) therapy was recommended as the optimal strategy to achieve euthyroidism, normalize SHBG, restore physiologic androgen balance, and prevent future complications.

Conclusions: This case emphasizes two pivotal clinical pearls: (1) always contextualize elevated total testosterone with SHBG and thyroid status to avoid misdiagnosis of androgen excess; and (2) prioritize definitive ^{131}I ablation in non-adherent Graves' patients without contraindicating ophthalmopathy. Multidisciplinary endocrinology-urology collaboration proved essential in steering accurate diagnosis and targeted therapy.

Abstract citation ID: lvag096.1779

EP1708 - LBA_ECE_1373 - Atypical presentation of acute thyroiditis masking recurrent laryngeal carcinoma—a case report

Radina Dimitrova[1], Zhenya Ruseva[1], Mira Siderova[1], Georgi Davidov[2], Rumen Nenkov[3] and Lyuben Stoev[4]
[1]*Second Department of Internal Medicine, Medical University of Varna, Clinic of Endocrinology and Metabolic Diseases, Varna, Bulgaria;* [2]*Department of Neurosurgery and ENT, Medical University of Varna, Clinic of ENT, Varna, Bulgaria;* [3]*Department of Surgery, Medical University of Varna, Clinic of Thoracic surgery, Varna, Bulgaria;* [4]*Department of General and Clinical Pathology, Forensic Medicine and Deontology, Medical University of Varna, Varna, Bulgaria*

Introduction: Acute thyroiditis usually manifests with sudden onset of fever, neck pain and tenderness. However, atypical painless forms pose substantial diagnostic challenges as they can resemble or coexist with regional malignancies. Here, we present a rare case of severe necrotizing thyroiditis that has masked a late recurrence of laryngeal cancer.

Case Report: A male patient presented with a rapid growing anterior neck mass, progressive dysphagia and dyspnea. Notably, the patient had a history of laryngeal carcinoma (pT2NxMx) treated surgically five years prior and deemed in remission. No neck pain or fever was reported.

Laboratory findings revealed markedly elevated inflammatory markers and constellations for thyrotoxicosis. Computed tomography (CT) revealed large polylobulated formation involving the entire thyroid gland (suspected abscess 30 × 71 × 82 mm). Due to diagnostic uncertainty, fine-needle biopsy (FNA) was performed, yielding a greenish, malodorous aspirate. Cytology demonstrated cells with marked signs of necrosis. Despite the aspirate's suspicious features and empiric triple antibiotic therapy, microbiology cultures remained sterile.

Due to the mechanical airway obstruction and high mediastinitis risk the patient underwent urgent surgery with team of thoracic and otorhinolaryngology specialists.

Intraoperatively, around 100 mL of thick purulent discharge was evacuated. Histopathology confirmed acute thyroiditis, with recurrent laryngeal carcinoma infiltrating left laryngeal part as an incidental finding.

Conclusion: This case highlights the potential for severe necrotizing thyroiditis to present without the classic "red flag" symptoms (fever, pain, tenderness). Concurrent or etiologic recurrent laryngeal carcinoma emphasizes the need for rigorous diagnostic evaluation in patients exhibiting obstructive symptoms. Sterile cultures despite purulent-appearing aspirate should prompt consideration of malignancy-associated necrosis over primary infection. Expedited surgical intervention is critical to avert airway compromise and delineate overlapping pathologies when clinical and microbiological data are discordant.

Keywords a MNABYVCUTE thyroiditis, laryngeal carcinoma, neck mass, dyspnea, thyroid abscess

Abstract citation ID: lvag096.1780

EP1709 - LBA_ECE_1124 - Tocilizumab in refractory pretibial myxedema: new therapeutic frontiers?

Silvia Corrias, Federica Diana, Francesca Sedda, Claudia Corda, Giuseppe Giannaccare, Stefano Mariotti, Francesco Boi and Giulia Lanzolla
Cagliari, Italy

Introduction: Pretibial myxedema (PTM), is a rare extrathyroidal manifestation of Graves' disease (GD), occurring in approximately 1%-4% of patients and with concomitant Graves' Orbitopathy (GO) present in nearly all reported cases. It presents as bilateral non-pitting edema of the pretibial region, occasionally accompanied by hyperkeratotic and hyperpigmented papules and plaques.

Case Report: We report the case of a GD female patient treated with total thyroidectomy in 2022. In November 2024, following the development of moderate-to-severe active GO, first-line therapy with high-dose intravenous glucocorticoids (ivGCs) was initiated. At baseline, the patient presented with bilateral proptosis of 25 mm, eyelid aperture of 18 mm, intermittent diplopia and CAS 6/7. Six months after ending treatment, partial response was observed: CAS improved to 4/7 and eyelid aperture reduced to 16 mm, while proptosis remained unchanged at 25 mm. However, at one-year follow-up, disease worsening was documented, with CAS returning to 5/7, persistent proptosis of 25 mm, eyelid aperture of 16 mm and inconstant diplopia in supraversion and lateroversion. Concurrently, the patient had developed bilateral PTM approximately 18 months after thyroidectomy, refractory to topical corticosteroids and occlusive bandaging.

Given the inadequate and non-sustained response of GO to first-line therapy, tocilizumab (8 mg/kg monthly infusion for 6 months) was initiated in July 2025. After 6 months of treatment, marked improvement in GO was observed: proptosis reduced to 23 mm (OD) and 22 mm (OS), eyelid aperture decreased to 13 mm, diplopia became intermittent, and CAS improved to 2/7. Notably, the patient reported rapid and significant improvement of PTM following the first infusion, with progressive marked reduction of edema and local symptoms confirmed at subsequent visits. No significant adverse events were recorded.

Discussion: The pathogenesis of PTM remains incompletely understood, but it is considered an autoimmune condition likely sharing key immunomediated mechanisms with GO. Interleukin-6 (IL-6) is a key pro-inflammatory cytokine implicated in GO pathogenesis, and tocilizumab, a monoclonal antibody targeting the IL-6 receptor, has demonstrated efficacy in moderate-to-severe active GO refractory to ivGCs. To our knowledge, this is the first reported case of PTM successfully treated with tocilizumab. Given the shared pathogenetic background of GO and PTM, IL-6 inhibition may represent an effective

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

therapeutic option not only for ivGC-refractory GO but also for refractory PTM, by targeting fibroblast activation and underlying autoimmune inflammatory cascade. Further studies are warranted to confirm the therapeutic role of tocilizumab in PTM and to define optimal treatment protocols.

Abstract citation ID: lvag096.1781

EP1711 - LBA_ECE_1420 - Comparable biochemical outcomes after surgery or radioactive iodine therapy for biopsy-proven nodal recurrence in differentiated thyroid cancer

Beril Turan Erdogan[1], Fatma Dilek Dellal Kahramanca[1], Furkan Savas[2], Zuhal Kandemir[3], Ayse Yilmaz[4], Cevdet Aydin[5], Oya Topaloglu[5], Reyhan Ersoy[5] and Bekir Cakir[5]

[1]Department of Endocrinology and Metabolism, Ankara Bilkent City Hospital, Ankara, Turkey; [2]Department of General Surgery, Ankara Bilkent City Hospital, Ankara, Turkey; [3]Department of Nuclear Medicine, Faculty of Medicine, Ankara Yildirim Beyazit University, Ankara, Turkey; [4]Department of Pathology, Ankara Bilkent City Hospital, Ankara, Turkey; [5]Department of Endocrinology and Metabolism, Faculty of Medicine, Ankara Yildirim Beyazit University, Ankara, Turkey

Background: The optimal treatment of biopsy-proven cervical lymph node recurrence in differentiated thyroid cancer (DTC) has not been established. Although surgery is the preferred approach for structural disease, RAI therapy is used in selected patients. Comparative data on biochemical outcomes between these modalities remain scarce.

Methods: We conducted a retrospective cohort study of 104 adult patients with pathologically confirmed nodal recurrence of DTC treated between 2019 and 2025 at Ankara Bilkent City Hospital. Patients received either surgical resection ($n = 72$) or RAI therapy ($n = 32$) as the initial treatment. The primary outcome was anti-thyroglobulin antibody (AntiTg) negativity at 1 year; secondary outcomes included AntiTg status at last follow-up, need for additional treatment, and time to biochemical event.

Results: One-year AntiTg negativity was achieved in 22/32 patients (68.8%) in the RAI group and 49/72 (68.1%) in the surgery group ($P = 1.000$). AntiTg negativity at last follow-up was 74.1% vs 66.1% ($P = .628$). Additional treatment rates were similar (64.5% vs 71.4%, $P = .645$). Median 1-year Tg was 3.39 ng/mL (RAI) vs 1.17 ng/mL (surgery) ($P = .129$). Kaplan–Meier analysis showed no difference in time to AntiTg positivity (log-rank $P = .894$). On multivariable analysis, treatment modality was not associated with 1-year biochemical response (adjusted OR = 0.88, 95% CI 0.34-2.28), whereas baseline AntiTg negativity was the strongest predictor of response ($P < .001$).

Conclusion: In patients with biopsy-proven nodal recurrence of DTC, surgery and RAI yielded comparable biochemical outcomes. Baseline AntiTg status, rather than treatment modality, was the primary predictor of response. In selected patients with limited nodal disease, RAI may be a reasonable alternative to surgery, with AntiTg status serving as a key prognostic marker.

Table Primary and secondary outcomes according to initial treatment strategy.

Outcome	RAI *n*/*N* (%)	Surgery *n*/*N* (%)	RR (95% CI)	OR (95% CI)	*P* value
1-year AntiTg negativity (primary)	22/32 (68.8)	49/72 (68.1)	1.01 (0.76-1.34)	1.03 (0.42-2.53)	1.0
No additional treatment needed	20/31 (64.5)	50/70 (71.4)	0.90 (0.67-1.22)	0.73 (0.30-1.79)	.645
Last follow-up AntiTg negativity[a]	20/27 (74.1)	37/56 (66.1)	1.12 (0.84-1.50)	1.47 (0.53-4.08)	.628
1-year Tg level (ng/mL)	median (IQR)	3.39 (1.90-5.39)	1.17 (0.41-4.51)	-	.129

RR and OR presented with 95% CI.
Percentages based on available data. AntiTg negativity defined per institutional reference range.
Anti-tg, Anti-Thyroglobulin Antibodies; tg, Thyroglobulin.
[a]Most recent available follow-up measurement for each patient.

Abstract citation ID: lvag096.1782

EP1713 - LBA_ECE_1229 - Adrenal adenoma causing apparent 21-hydroxylase deficiency: a case report of a non-classic congenital adrenal hyperplasia mimic

Sandra Urbina Solano[1], Marta Iturregui Guevara[1] and Mariana Jesús Gomes Porras[1,2,3]

[1]Endocrinology and Nutrition, Regional University Hospital of Málaga, Malaga, Spain; [2]Institute of Biomedical Research of Málaga (IIBIMA), BIONAND Platform, Málaga, Spain; [3]Biomedical Research Networking Center for Diabetes and Associated Metabolic Diseases (CIBERDEM), group CB07/08/0019, Málaga, Spain

We present the case of a 40-year-old man who consulted for a six-month history of gynecomastia and decreased libido, without medication use or apparent testicular abnormalities. Initial laboratory findings were consistent with hypogonadotropic hypogonadism (FSH 0.55 mIU/mL, LH 1.15 mIU/mL, estradiol 88 pg/mL, testosterone 1.22 ng/mL), with normal TSH and prolactin levels. Semen analysis and testicular ultrasound were unremarkable. Pituitary MRI showed no abnormalities.

Topical testosterone therapy was initiated, resulting in minimal clinical improvement. Follow-up laboratory testing at three months demonstrated further suppression of gonadotropins and testosterone (FSH 0.35 mIU/mL, LH 0.46 mIU/mL, estradiol 49 pg/mL, testosterone 1.01 ng/mL). Therapy was then switched to intramuscular testosterone every three weeks for 8 months. After a six-week washout period, hormone levels worsened (FSH < 0.3 mIU/mL, LH 0.50 mIU/mL, estradiol 97 pg/mL, testosterone 0.88 ng/mL). Intramuscular testosterone therapy was continued for eight months, and during the treatment, gynecomastia resolved, and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

libido returned. After discontinuation, spontaneous normalization of serum testosterone levels (2.91 ng/mL) was observed, while 17-hydroxyprogesterone levels remained elevated (5.32 ng/mL).

An ACTH stimulation test demonstrated results consistent with non-classic congenital adrenal hyperplasia. An abdominal CT scan was performed to exclude neoplasia, which revealed a left adrenal lesion 26 × 29 mm with attenuation <10 HU, suggestive of an adrenal adenoma. Therefore, the most likely diagnosis was non-classic congenital adrenal hyperplasia with an associated adrenal lesion. However, negative genetic testing for variants in CAH-related genes leads to consideration of the possibility of an androgen-secreting adrenal tumor, a rare entity.

Finally, a left adrenalectomy was performed, and histopathological analysis confirmed an adrenal adenoma. Three months after surgery, serum 17-hydroxyprogesterone and androstenedione levels normalized. An ACTH stimulation test demonstrated recovery of normal 21-hydroxylase activity.

Abstract citation ID: lvag096.1783

EP1717 - LBA_ECE_1183 - Effectiveness and safety of palopegteriparatide in clinical practice: a real-world experience from a Spanish region

Jorge González Prieto[1], Laura María Martín Flores[1], Jesús Manuel Morán López[2], Juan Manuel Parra Barona[3], Marelis Triana Borroto[4] and Francisco Morales Pérez[1]
[1]*Hospital Universitario de Badajoz, Badajoz, Spain;* [2]*Hospital Virgen Del Puerto, Plasencia, Spain;* [3]*Hospital De Mérida, Mérida, Spain;* [4]*Hospital Campo Arañuelo, Navalmoral de la Mata, Spain*

Introduction: Chronic hypoparathyroidism is a rare endocrine disorder characterized by hypocalcemia and impaired calcium-phosphate homeostasis, traditionally managed with oral calcium and active vitamin D. However, conventional therapy is often associated with poor biochemical control, fluctuations in serum calcium, and renal complications. Palopegteriparatide, a long-acting parathyroid hormone analog, has emerged as a novel therapeutic option, although real-world data remain limited.

Methods: This multicenter retrospective observational study included adult patients with chronic hypoparathyroidism treated with palopegteriparatide in routine clinical practice in Extremadura, Spain. Demographic, clinical, and biochemical data, including calcium-phosphate parameters, renal function, and treatment requirements, were collected before and after treatment initiation. Comparisons were performed using the Wilcoxon signed-rank test ($P < .05$).

Results: Eight patients were included (62% female), with a mean age of 52.4 ± 15.9 years and hypoparathyroidism duration of 13.3 ± 8.7 years. Baseline PTH was 5.81 ± 2.91 pg/mL and 25-hydroxyvitamin D 29.4 ± 12.0 ng/mL. Mean treatment duration with palopegteriparatide was 3.5 ± 1.5 months. Etiology was postsurgical in 75% and idiopathic in 25%. Indications for treatment were recurrent hypocalcemia (75%), renal impairment (50%), nephrolithiasis (37%), and prior hospitalizations due to calcium disturbances (25%).

Following treatment initiation, corrected calcium increased significantly from 7.77 ± 0.91 to 9.33 ± 0.56 mg/dL ($P = .017$), while no significant changes were observed in serum phosphorus (4.70 ± 0.99 to 4.24 ± 0.79 mg/dL; $P = .246$) or estimated glomerular filtration rate (76.0 ± 26.4 to 84.8 ± 24.6 mL/min/1.73 m^2; $P = .500$). Calcium carbonate requirements markedly decreased from 5962 ± 7277 to 275 ± 511 mg/day, and calcitriol was discontinued in all patients. After treatment optimization, normalization of corrected calcium and serum phosphorus was achieved in 100% of cases.

All patients (100%) reported high satisfaction after switching from conventional therapy to palopegteriparatide. Regarding safety, one patient experienced transient pruritus at the injection site, and 75% presented mild episodes of hypo- or hypercalcemia, all of which resolved without requiring emergency or hospital care.

Conclusions: Palopegteriparatide treatment in patients with chronic hypoparathyroidism was associated with rapid and effective normalization of calcium homeostasis, allowing discontinuation of conventional therapy. Despite the small sample size, a significant improvement in corrected calcium levels was observed, with consistent biochemical control achieved in all patients. Treatment was well tolerated and was associated with high patient satisfaction. These findings support palopegteriparatide as an effective and well-accepted therapeutic option in the management of hypoparathyroidism.

Abstract citation ID: lvag096.1784

EP1719 - LBA_ECE_1405 - Clinical case: resistance to thyroid hormone syndrome in a patient after treatment for papillary thyroid carcinoma

Viktoria Sadovskaya
Endocrinology and Metabolic Disorders, Fomin Clinic, Moscow, Russia

Background: Resistance to thyroid hormone (RTH) syndrome is a rare genetic disorder most commonly caused by mutations in the THRB gene. Diagnosing RTH in patients after thyroidectomy for thyroid cancer is challenging because the clinical picture of thyrotoxicosis during high-dose levothyroxine therapy may be misinterpreted as iatrogenic hyperthyroidism, while inappropriate dose reduction carries a risk of tumor progression.

Clinical Case: A 30-year-old female patient. She had a history of multinodular goiter; in January 2023, fine-needle aspiration biopsy revealed papillary thyroid carcinoma (pT1bN1M0). Total thyroidectomy with central lymph node dissection was performed, followed by radioactive iodine therapy (3700 MBq) in March 2023. After surgery she was started on levothyroxine replacement.

She complained of hair loss, hot flashes, and tachycardia. Attempts to adjust the levothyroxine dose were complicated by extreme fluctuations in TSH levels:

- on 88 µg/day, TSH was 49.06 µIU/mL;
- on 112-125 µg/day, TSH ranged from 15.7 to 1.25 µIU/mL.

Target TSH suppression (<0.1 µIU/mL) could not be achieved. While taking 125 µg/day, TSH was 1.23 µIU/mL and free T4 was elevated to 1.92 ng/dL, with normal levels of anti-TPO and anti-TG antibodies.

Given the discrepancy between high levothyroxine doses, failure to achieve adequate TSH suppression, and clinical signs of thyrotoxicosis, resistance to thyroid hormone was suspected. Genetic testing confirmed a mutation in the THRB gene, establishing the diagnosis of RTH.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusion: Resistance to thyroid hormone should be considered in post-thyroidectomy patients when target TSH suppression cannot be achieved with high levothyroxine doses and the clinical picture combines features of thyrotoxicosis with biochemically elevated free T4. Genetic confirmation helps avoid unnecessary dose escalation and reduces the risk of treatment-related adverse effects.

Abstract citation ID: lvag096.1785

EP1720 - LBA_ECE_1145 - Booking HbA1c as a marker of preconception care delivery in women with type 2 diabetes: a service evaluation from a UK centre

Charlotte Jones, Fareeha Ikram, Dilawar Khan, Nomaira Hassan and Ammara Naeem
Croydon University Hospital, Diabetes and Endocrinology department, London, United Kingdom

Background: Optimising glycaemic control prior to conception is critical in reducing adverse maternal and neonatal outcomes in women with type 2 diabetes mellitus (T2DM). Despite clear national and international recommendations advocating structured preconception care, real-world delivery remains inconsistent. Recent evidence further highlights persistent gaps between guideline recommendations and clinical practice. We evaluated booking HbA1c as a pragmatic marker of preconception care effectiveness in our population.

Methods: We conducted a retrospective service evaluation of women with T2DM booked for antenatal care at a single UK centre over a 12-month period (August 2024—August 2025). Data were extracted from electronic health records, including demographics, preconception care indicators (documented counselling and 5 mg folic acid use), diabetes management, and HbA1c at booking and 28 weeks' gestation. Pregnancy outcomes, including gestational age at delivery and birthweight centiles, were also analysed.

Results: Forty-four pregnancies were identified. Mean maternal age was 33 years, with a diverse ethnic distribution (White 14%, Asian 29%, Black 29%, other 28%). Mean booking BMI was 32 kg/m^2.

Mean booking HbA1c was 60 mmol/mol, with only 10/44 (23%) achieving the recommended target of ≤48 mmol/mol. Booking took place between 5-20 weeks at an average of 9 weeks. Most women were on metformin, insulin, or a combination (27%, 11% and 34% respectively) with the remaining on diet (14%) or on other oral medication not recommended in pregnancy (14%) that were stopped at booking.

Evidence of preconception care was limited: 2/44 (5%) had documented preconception counselling, and 10/44 (23%) were recorded as taking 5 mg folic acid prior to conception.

Women with target booking HbA1c demonstrated more favourable outcomes, with a higher proportion of term deliveries (88% vs 69%) and infants with birthweight within the 10th–95th centile (100% vs 65%) compared to those above target.

Conclusions: This evaluation demonstrates substantial gaps in the delivery and documentation of preconception care for women with T2DM, reflected in suboptimal glycaemic control at booking. Although limited by sample size, our findings show a consistent signal towards improved perinatal outcomes in women achieving target HbA1c prior to pregnancy.

In the context of growing evidence highlighting deficiencies in preconception care uptake, our data reinforce the need for system-level interventions, including strengthened primary—secondary care collaboration, improved identification of women of reproductive age with type 2 diabetes, and accessible, funded preconception pathways. Booking HbA1c represents a simple and clinically meaningful metric to monitor and drive improvements in preconception care delivery.

Abstract citation ID: lvag096.1786

EP1721 - LBA_ECE_1237 - Brown adipose tissue status modifies the dynamic proteomic response to cold exposure in humans

Filip Bossowski[1], Dominik Cysewski[2], Tomasz Kowalczyk[2], Magdalena Bossowska[1], Katarzyna Miniewska[3], Edyta Adamska-Patruno[4], Adam Krętowski[1] and Katarzyna Maliszewska[1]
[1]Department of Endocrinology, Diabetology and Internal Medicine, Medical University of Bialystok, Bialystok, Poland; [2]Centre of Regenerative Medicine, Medical University of Bialystok, Bialystok, Poland; [3]Department of Medical Biochemistry, Medical University of Bialystok, Bialystok, Poland; [4]Clinical Research Centre, Medical University of Bialystok, Bialystok, Poland

Background: Brown adipose tissue (BAT) activation is a potential therapeutic target for metabolic disorders, yet the effects of BAT on the circulating proteome are not well characterized. This study examined whether BAT status is associated with a distinct baseline proteomic signature at rest and whether it alters the proteomic response to acute cold stimulation.

Methods: Twenty-five healthy, non-smoking Caucasian men (median age 25-28 years) were recruited and completed a standardized 120-minute cold exposure protocol. BAT activity was quantified by 18F-FDG PET/MR imaging. Participants were classified as BAT-positive (BAT(+), $n = 17$) or BAT-negative (BAT(−), $n = 8$) using a glucose uptake rate threshold of $>2.0\ \mu mol \cdot (100\ g)^{-1} \cdot min^{-1}$; groups were matched for age and BMI. Plasma samples collected at 0, 60, and 120 minutes were analyzed with a targeted proteomics panel. The assay used 804 stable-isotope-labeled standard reference peptides to quantify 582 human plasma proteins. Differential abundance was assessed with linear models using empirical Bayes moderation, testing baseline differences and BATxTime interactions.

Results: At baseline (0 min), no proteins differed significantly between groups after false discovery rate (FDR) correction, indicating that BAT status was not associated with a distinct baseline plasma proteomic signature at rest. In contrast, longitudinal analyses over 120 minutes identified BATxTime interaction effects consistent with BAT-dependent divergence during cold exposure. Thirty-three proteins showed a nominal BATxTime interaction ($P < .05$), with opposite-direction trajectories in BAT(+) versus BAT(−) subjects. Vinculin showed the strongest interaction (interaction FDR = 0.076): levels increased in BAT(+) subjects (log2FC approximately +5.6) but decreased in BAT(−) subjects (log2FC approximately −8.0) during cold exposure. Sensitivity analyses showed that these interaction effects persisted after adjustment for BMI.

Conclusions & Clinical Relevance: BAT status dictates a highly dynamic, rather than static, proteomic response to thermogenic stress. The extreme divergence of vinculin provides a direct, systemic readout of acute cytoskeletal remodeling and focal adhesion turnover occurring strictly in BAT(+) individuals during activation.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Clinically, rather than relying on radioactive imaging, tracking the plasma trajectories of vinculin and associated mechanotransduction proteins offers a novel foundation for the liquid biopsy-based therapeutic monitoring of BAT-activating pharmacotherapies in metabolic disease.

Abstract citation ID: lvag096.1787

EP1723 - LBA_ECE_1257 - Vanishing Testes Syndrome (VTS): emerging insights from a pediatric case series

Vasiliki Siampanopoulou[1], Sofia Lekka[2], Maria Tzoraki[2,3], Maria Kafetzi[4], Georgia Pepe[5] and Elpis Vlachopapadopoulou[2]

[1]Unit of Endocrinology, First Department of Internal Medicine, National and Kapodistrian University of Athens, Laiko General Hospital of Athens, Athens, Greece; [2]Department of Endocrinology, «P. and A. Kyriakou» Children's Hospital of Athens, Athens, Greece; [3]Endocrinology-Growth and Development, Children's Hospital "P. & A. Kyriakou", Athina, Greece; [4]Biochemical Department, «P. and A. Kyriakou» Children's Hospital of Athens, Athens, Greece; [5]Genekor Medical SA, Athens, Greece

Introduction: Congenital anorchia, also known as VTS, is a rare cause of primary hypogonadism in boys and is characterized by the absence of functional testicular tissue in individuals with a 46,XY karyotype. Early diagnosis is essential to ensure appropriate hormonal, surgical, and psychosocial management.

Objective: To present a case series of five pediatric patients with congenital anorchia and their management including pubertal induction and final height.

Methods: A retrospective study of five boys who presented with bilateral anorchia at a tertiary pediatric endocrinology clinic.

Results: All patients presented with normal penile size without hypospadias, shallow scrotum and non-palpable testes. Laboratory evaluation showed a 46,XY karyotype, consistent with 46XY,DSD, hypergonadotropic hypogonadism [median value of LH = 15.25 mIU/mL (min:10, max:202) and FSH = 119 mIU/mL (min:15, max:253) respectively] and undetectable testosterone levels. Median age at diagnosis was 14 months (min: 3, max: 40). Imaging did not reveal functional testicular tissue; in some cases, atrophic testicular remnants were detected, suggesting an intrauterine vascular event or torsion. Findings were confirmed by ultrasonography in all patients and by laparoscopy in two.

All patients received testosterone replacement therapy during puberty; median age of initiation: $12^{6/12}$ years (min: $11^{9/12}$ years, max: $14^{11/12}$ years), with a gradual dose titration, resulting in growth acceleration, normal penile size, and development of secondary sexual characteristics. Four patients reached their final height [median = 170 cm (min: 165, max: 172)], corresponding to the 5^{th}-25^{th} percentiles. One patient was below target height ($H_{final}/H_{target} = 169/178 \pm 5$ cm), while three were within their respective target height ranges (H_{final}/H_{target}: $172/178 \pm 5$ cm, $165/167 \pm 5$ cm, $171/176 \pm 5$ cm). One patient has not yet reached final height (chronological age: $11^{9/12}$), but is currently at the 75th percentile ($H_{current}/H_{target} = 153/170 \pm 5$ cm).

Testicular prostheses were placed in three patients at a median age of 16 years (min: 15, max: $17^{3/12}$ years). One patient is below the recommended age and one declined due to personal preferences. Whole exome sequencing (WES) was performed in one patient and did not identify pathogenic variants among the 118 genes included in the analyzed panel.

Conclusions: Congenital anorchia represents a heterogeneous condition with variable pathogenetic mechanisms. Systematic clinical and hormonal evaluation, combined with operative evaluation is essential for the diagnosis. This case series highlights the importance of early diagnosis and timely testosterone treatment to achieve normal pubertal development and growth. Nowadays, incorporating comprehensive genetic testing into the diagnostic approach for patients with vanishing testes syndrome is valuable to clarify the etiology and optimize management.

Abstract citation ID: lvag096.1788

EP1724 - LBA_ECE_1232 - Genetically confirmed HNF1A-MODY with severe autoimmune β-cell failure: evidence for a true overlap phenotype

Ayse Nur Gul and Meliha Melin Uygur

Department of Endocrinology, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Turkey

Background: Maturity-Onset Diabetes of the Young (MODY) is a monogenic form of diabetes characterized by non-autoimmune β-cell dysfunction, most commonly due to HNF1A mutations. In contrast, Type 1 Diabetes Mellitus results from immune-mediated β-cell destruction and is defined by the presence of pancreatic autoantibodies. These entities are traditionally considered mutually exclusive; however, emerging evidence suggests that overlapping mechanisms may occur, challenging the current classification paradigm.

Case Presentation: A 47-year-old man was diagnosed with diabetes at age 29 and initially classified as type 1 diabetes. He presented with weight loss without documented ketoacidosis. His body mass index was 28.6 kg/m^2. Family history revealed diabetes in multiple maternal relatives, suggesting a hereditary component. He was treated from diagnosis with basal–bolus insulin therapy using multiple daily injections (MDI). Despite long-term treatment, glycaemic control progressively deteriorated (HbA1c from 9.1% at diagnosis to 10.3% currently), and microvascular complications including diabetic retinopathy and peripheral neuropathy developed. Immunological evaluation showed strongly positive anti-glutamic acid decarboxylase antibodies (209 U/mL), while islet cell antibodies were initially positive but became negative during follow-up. Fasting C-peptide was <0.10 ng/mL, indicating near-complete β-cell failure. Genetic testing identified a pathogenic HNF1A mutation, confirming HNF1A-MODY. Sulfonylurea therapy was not initiated due to the severe insulin-deficient phenotype.

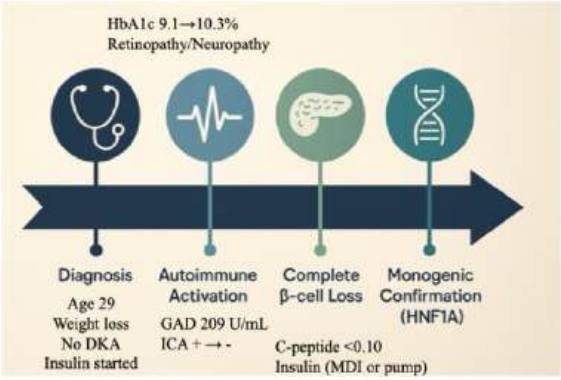
Discussion: This case demonstrates a true overlap between HNF1A-MODY and autoimmune diabetes, characterized by coexistence of a monogenic β-cell defect and profound immune-mediated β-cell destruction. Unlike classical HNF1A-MODY, which is associated with preserved endogenous insulin secretion and high sensitivity to sulfonylureas, this patient exhibited complete insulin deficiency and a clinical course indistinguishable from long-standing autoimmune diabetes. A plausible explanation is a sequential dual-hit mechanism, whereby chronic β-cell dysfunction due to HNF1A mutation increases cellular stress and immunogenicity, facilitating autoimmune activation in genetically susceptible individuals.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusion: Autoimmune diabetes does not exclude monogenic diabetes, even in genetically confirmed HNF1A-MODY. In patients with atypical features, strong family history, or discordant clinical progression, overlapping mechanisms should be considered. Recognition of this phenotype has important implications for diabetes classification, therapeutic decision-making, and genetic counselling, supporting a shift toward a more integrated, mechanism-based approach.

FEATURE	TYPICAL HNF1A-MODY	THIS CASE
Antibodies	Negative	Strongly positive
C-peptide	Preserved	Absent
Treatment	Sulfonylurea	Insulin
Course	Mild-progressive	Severe

Phenotypic Divergence Between Classical HNF1A-MODY and Overlap Diabetes.



Sequential Dual-Hit Model of β-Cell Failure.

Keywords HNF1A-MODY, autoimmune diabetes, overlap phenotype, monogenic diabetes

Abstract citation ID: lvag096.1789

EP1725 - LBA_ECE_1089 - A wolf in sheep's clothing: unmasking CAH in a "PCOS" patient with co-occurring POTS and Ehlers-Danlos syndrome

Rana Almudhammed[1,2]
[1]*Department of Biochemistry and Internal Medicine, Diyala College of Medicine, Private Clinic, Baghdad, Iraq;* [2]*Physiology and Internal Medicine, Diyala College of Medicine, Diyala, Iraq*

24 year old female presented with a five-year history of irregular menstrual cycles, oligomenorrhea alternating with menorrhagia, lower facial acne, and hirsutism. She also reported symptoms of chronic sleepiness, tiredness, brain fog, occasional palpitations, orthostatic intolerance, exercise intolerance and easy fatiguability.

Clinical signs included facial lower face acne, mild hirsutism, no androgenetic alopecia, no central obesity or signs of insulin resistance, no striae or other skin manifestation.

Examination revealed joint hypermobility, skin laxity, widespread joint pain, no joint swelling, she exhibited unexplained, non-traumatic easy bruising.

The patient denies any symptoms of depression or anxiety.

2. Clinical and Laboratory Findings: Examination revealed a lean phenotype with no signs of insulin resistance. Evaluation using the Beighton score confirmed a diagnosis of hypermobile Ehlers-Danlos Syndrome (hEDS) as described by Rhumatologist.

C REACTIVE PROTEIN	Normal
ACTH	26
Stimulated Cortisol	550 nmol/L
Hemoglobin (Hb)	12 g/dL
Blood Pressure (BP)	110/70 mmHg
Total Testosterone	0.9 ng/mL
DHEAS	1000 i.u.
Prolactin	19 ng/mL
TSH	2.5 mIU/L
Stimulated 17(OH) Progesterone	1300 ng/dl
HbA1C	5.0%
LH	6.5 mIU/mL
FSH	4.5 mIU/mL

Genetic confirmation chromosome 6: ***CYP21A2*** and ***TNXB***. confirmed the diagnosis of Non-Classical Congenital Adrenal Hyperplasia CAH×. Additionally, symptoms of hypovolemia and palpitations led to the diagnosis of Postural Orthostatic Tachycardia Syndrome (POTS) as it is closely related to EDS .

4. Clinical Outcome: The patient reported significant improvements in quality of life, including enhanced focus, attention, and the ability to maintain her academic performance and daily activities.

This case demonstrates that POTS is often underdiagnosed in young females and can severely impact quality of life. Furthermore, NCCAH should be considered as a differential diagnosis for hyperandrogenism in lean patients, especially when symptoms overlap with connective tissue and autonomic disorders.

Abstract citation ID: lvag096.1790

EP1728 - LBA_ECE_1445 - Takotsubo cardiomyopathy revealing pheochromocytoma: a case of severe catecholamine-induced cardiomyopathy with dramatic recovery after adrenalectomy

Aye Aye Khine, Elfreda Baker, Khurram Qayyum and Shiva Mongolu
Hull University Teaching Hospital NHS Trust, Hull, United Kingdom

Background: Pheochromocytoma is a rare catecholamine-secreting tumor with diverse cardiovascular presentations. Excess catecholamines may induce stress cardiomyopathy with severe but potentially reversible myocardial dysfunction. Early recognition is essential to enable appropriate alpha-blockade and curative surgery.

Case Presentation: A 61-year-old woman with type 2 diabetes, hypertension, and active smoking presented with persistent vomiting following metformin up-titration. She was found

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

to have stage 3 acute kidney injury and markedly elevated troponin (1484-1624 ng/L). ECG showed widespread T-wave inversion.

Echocardiography demonstrated severe left ventricular (LV) systolic dysfunction. Cardiac MRI confirmed severe LV impairment (LVEF 21%) and LV thrombus with features consistent with stress-induced cardiomyopathy and normal coronary angiography. An incidental 7 cm right adrenal mass was identified in initial cardiac MRI.

Biochemical evaluation showed markedly elevated plasma metanephrines (>25 000 pmol/L) and urinary metanephrines (metanephrine 124.4 µmol/24 h; normetanephrine 86.5 µmol/24 h). Initial adrenal CT scan revealed thick-walled centrally necrotic right adrenal lesion of 7 × 6.2 cm suspicious for pheochromocytoma. Subsequent MIBG imaging confirmed a catecholamine-secreting tumor. Genetic testing for pheochromocytoma/ paraganglioma (11-genes panel) was negative.

The patient had highly labile blood pressure with episodes of severe hypertension (180/136 mmHg) alternating with hypotension (77/56 mmHg). Alpha-blockade (doxazosin) was cautiously introduced with close hemodynamic monitoring. Fluid therapy was administered cautiously due to severe LV dysfunction. Following clinical stabilization with alfa and beta blockage, she underwent elective laparoscopic adrenalectomy after three months of diagnosis. Histology confirmed pheochromocytoma (PASS 1, Ki-67 <1%).

Post-operatively, cardiac function improved significantly, with LVEF recovering from 21% to 54% at three months, alongside resolution of myocardial oedema and LV thrombus.

Discussion: Pheochromocytoma-related cardiomyopathy is mediated by catecholamine excess causing myocardial stunning via microvascular spasm and direct toxicity. Management is challenging when severe cardiac dysfunction coexists with haemodynamic instability. Careful initiation and titration of alpha-blockade remain essential even in patients with hypotension, requiring multidisciplinary management involving endocrinology, cardiology, anaesthesia, and surgery. Definitive tumour removal often results in marked cardiac recovery.

Conclusion: Pheochromocytoma can present as severe reversible Takotsubo-like cardiomyopathy. Early diagnosis and coordinated management, including alpha-blockade and surgical resection, can lead to substantial cardiac recovery.

Abstract citation ID: lvag096.1791

EP1729 - LBA_ECE_1452 - When PCOS is not PCOS: a diagnostic pitfall of non-classical congenital adrenal hyperplasia

Aye Aye Khine, Elfreda Baker, Khurram Qayyum and Najeeb Shah
Hull University Teaching Hospital NHS Trust, Hull, United Kingdom

Background: Non-classical congenital adrenal hyperplasia (NCCAH) due to partial 21-hydroxylase deficiency is an important differential diagnosis of polycystic ovary syndrome (PCOS). Both conditions may present with hyperandrogenic features including hirsutism, acne, and menstrual irregularities. Failure to recognize NCCAH may delay appropriate endocrine counselling and reproductive planning. Measurement of basal and ACTH-stimulated 17-hydroxyprogesterone (17-OHP) is recommended when adrenal androgen excess is suspected.

Clinical Case: A 24-year-old woman was referred to a PCOS clinic with hirsutism and oligomenorrhoea. She reported facial and periareolar hair growth and had a prior history of acne. She was using a levonorgestrel intrauterine system for contraception and had no current fertility concerns. Her BMI was 22.5 kg/m^2 and blood pressure was 110/70 mmHg. Secondary sexual characteristics were normal and there was no history of salt-wasting.

Initial biochemical evaluation demonstrated elevated adrenal androgens with androstenedione 11.1 nmol/L and DHEAS 19.5 µmol/L. Total testosterone was 2.2 nmol/L with a free androgen index of 6.1. Basal 17-hydroxyprogesterone was elevated at 50.8 nmol/L. A short synacthen test initially demonstrated adequate adrenal reserve (cortisol 337-485 nmol/L), but stimulated 17-OHP was not measured. Repeat testing showed baseline 17-OHP 19.6 nmol/L rising to 180.8 nmol/L following ACTH stimulation, confirming NCCAH. Cortisol response remained appropriate (264-455 nmol/L).

The patient had initially been treated for presumed PCOS with anti-androgen therapy including spironolactone and later topical eflornithine and finasteride for persistent hirsutism. Glucocorticoid therapy was not initiated following diagnosis due to preserved cortisol reserve and absence of fertility concerns.

Conclusion: This case highlights NCCAH as an important PCOS mimic. Elevated basal 17-OHP should prompt ACTH-stimulated testing to avoid misdiagnosis. Early recognition allows appropriate counselling regarding long-term endocrine follow-up and reproductive implications. This case emphasises the importance of screening for non-classical congenital adrenal hyperplasia in women presenting with hyperandrogenic features suggestive of PCOS, particularly when basal 17-hydroxyprogesterone is elevated.

Abstract citation ID: lvag096.1792

EP1730 - LBA_ECE_1107 - Impact of pharmacological therapeutic transition in obesity: analysis of anthropometric variations and metabolic profile

Ignacio Nocete Aragón[1,2], Leopoldo Garcia-Valdecasas Vazquez[1], Alejandro Tomás Pérez[1], Alejandra Salomé Criollo Posso[1], Natalia Díez Fernández[1] and Vanessa Capristán Díaz[1]
[1]*Endocrinology, Hospital Universitario General de Villalba, Collado Villalba, Spain;* [2]*Endocrinología y Nutrición, Hospital Universitario General de Villalba, Collado Villalba, Spain*

Background: The sequential use of GLP-1 and GLP-1/GIP receptor agonists is increasingly common in clinical practice to manage obesity and metabolic disorders. However, real-world data evaluating the efficacy of transitioning between these therapies remains limited. This study aimed to assess the anthropometric and metabolic outcomes of switching incretin-based treatments in a real-world clinical setting.

Methods: A retrospective cohort study was conducted on 64 patients (71.9% female; mean age 54.4 ± 12.5 years). Clinical parameters, including weight, body mass index (BMI), fasting glucose, LDL cholesterol, and gamma-glutamyl transferase (GGT), were evaluated at three specific time points: baseline, time of medication switch, and final follow-up. The primary transitions involved Liraglutide, Semaglutide, and Tirzepatide.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Statistical analyses included paired t-tests and multivariable linear regression adjusted for age, sex, treatment duration, and specific drug type.

Results: The primary clinical reason for switching therapies was insufficient efficacy (64.0%). During the initial treatment phase (mean duration 283 days), patients achieved highly significant reductions in weight (−8.29 kg; $P < .001$), BMI (−2.93; $P < .001$), and fasting glucose (−7.84 mg/dL; $P < .001$). Following the medication switch, patients experienced further significant clinical improvements. Transitioning from Liraglutide to Tirzepatide resulted in the most substantial additional weight loss (−11.97 kg; $P = .004$). Alternatively, switching from Semaglutide to Tirzepatide yielded a significant secondary reduction in fasting glucose (−7.68 mg/dL; $P = .022$). Multivariable analysis demonstrated that female sex was a significant independent predictor of greater BMI reduction during the post-switch phase ($P = .027$). LDL cholesterol levels remained stable throughout the study without significant variations.

Conclusions: Switching between incretin-based therapies is a highly effective clinical strategy to overcome weight-loss plateaus and enhance metabolic control. Escalating treatment to a dual agonist (Tirzepatide) provides profound rescue efficacy, particularly in glycemic control and absolute weight loss. Furthermore, female patients appear to derive a significantly greater anthropometric benefit from this sequential treatment strategy compared to males.

Abstract citation ID: lvag096.1793

EP1731 - LBA_ECE_1116 - An unusual case of hypogonadotrophic hypogonadism due to Erdheim Chester disease related pituitary hypophysitis

Kalyani Nagarajah[1,2] and Emmanuel Kofi Obuobie[1,2]
[1]Endocrinology, Aneurin Bevan Health Board, Newport, United Kingdom; [2]Endocrinology and Diabetes, Aneurin Bevan Health Board, Newport, United Kingdom

Background: Erdheim–Chester disease (ECD), is a rare cause of non-Langerhans histiocytosis. These cells may infiltrate the hypothalamic-pituitary tissues and retroperitoneum, leading to central diabetes insipidus, progressive anterior pituitary failure, and ureteral obstruction with hydronephrosis.[1-3] Male hypogonadism may also be a feature of this condition.

Case: A 52-year-old man with histologically confirmed ECD/Langerhans cell histiocytosis overlap presented for routine endocrine evaluation. He had been diagnosed with Hypopituitarism including arginine vasopressin deficiency, bilateral hydronephrosis and chronic kidney disease stage 3 due to persistent retroperitoneal fibrosis, diverticular disease, and depression. Treatment regimen consisted of cobimetinib for systemic disease, desmopressin 100 μg nocte for polyuria management, and transdermal testosterone gel for established central hypogonadism. Pituitary MRI identified characteristic stalk infundibular thickening without discrete lesion. He was Clinically stable with controlled polydipsia, testicular atrophy, and preserved visual fields, biochemical assessment revealed low-normal IGF-1, normal prolactin/TSH, therapeutic testosterone concentration (13.6 nmol/L), and indeterminate 9 am cortisol (190 nmol/L).[5] Guideline-directed 250 μg Short Synacthen testing was arranged to assess corticotroph function, which was reported as within normal range.[5] Adrenal insufficiency was then ruled out.

Discussion: hypogonadotropic hypogonadism c with diabetes insipidus and stalk thickening, is a recognised feature of ECD and gonadal histiocytosis has been noted in some patients.[1,2] Our patient had a pattern of results consistent with central hypogonadism due to Pituitary hypophysistis. Endocrinology guidelines advocate testosterone replacement and monitoring pituitary, haematologic, prostatic, and cardiovascular profiles.[8]

Conclusion: ECD constitutes an uncommon but well recognised of secondary male hypogonadism due to hypophysitis, and it is important that clinicians are made aware of this association. Testosterone therapy, adrenal stimulation assessment, and planned neuroimaging provide comprehensive endocrine management for this multisystem disorder.[1-9]

Abstract citation ID: lvag096.1794

EP1732 - LBA_ECE_1444 - Grave's–Hashimoto overlap with suspicious thyroid nodules: navigating diagnostic timing and thionamides therapy in the setting of baseline neutropenia on anakinra

Azmi Mohammed, Rawan Alghawi and Zainab Alabdurubalnabi

Graves' disease and Hashimoto thyroiditis lie on a spectrum of autoimmune thyroid disease and may coexist in the same patient. Overlapping stimulatory and destructive autoimmune mechanisms may produce a fluctuating biochemical profile, complicating monitoring and therapeutic decision-making. Thionamides, such as carbimazole, remain first-line therapy in patients who defer definitive treatment; however, their use is challenging in the presence of pre-existing leukopenia and neutropenia due to the risk of agranulocytosis.

We report a 44-year-old female with Familial Mediterranean fever (FMF) on anakinra, presenting with hair loss, weight loss and overt thyrotoxicosis. Thyroid function test demonstrated: (TSH < 0.008 μIU/mL, FT4 1.97 ng/dL [0.7-1.48], FT3 12.6 pg/mL [1.58-3.91]). Thyroid peroxidase antibodies were elevated at 197.69 IU/mL (<5.3), and thyroid-stimulating immunoglobulin (TSI) was positive at 3.4 (<1.3), supporting the diagnosis of overlapping autoimmune thyroid disease.

Ultrasound demonstrated bilateral nodules, including a 3.2 cm left-sided mixed solid–cystic nodule with microcalcifications (TI-RADS 4) and a smaller right-sided 1 cm TI-RADS 3 nodule. The suspicious nodule required fine-needle aspiration; however, this was deferred until she was rendered euthyroid and her thyroiditis had settled. Cytology during inflammatory phases may be non-diagnostic due to lymphocytic infiltration. Serial ultrasound surveillance at 6-month intervals was therefore undertaken to exclude interval progression while allowing time to achieve euthyroidism.

Management was complicated by anakinra-associated chronic leukopenia and neutropenia (baseline absolute neutrophil count 0.6-1.5 × 10^9/L). Carbimazole was initiated at 5 mg on alternate days (neutrophil count 0.7 × 10^9/L at initiation) and cautiously up-titrated to a maximum required dose of 15 mg daily, with close haematological monitoring. Euthyroidism was achieved without infectious complications, and neutrophil counts during treatment ranged between 0.7-2.2 × 10^9/L.

FNA of the dominant nodule, performed after restoration of euthyroidism, confirmed a benign follicular lesion (Bethesda II). At her last follow-up, the patient remained clinically stable

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

on low-dose therapy, with normal thyroid function tests and declining TSI (2.1 after 14 months). A total treatment duration of 18 months is planned.

This case highlights four key challenges: autoimmune overlap with fluctuating thyroid function, limitations of cytology during thyroiditis, the need to delay invasive investigation until biochemical control is achieved, and the safe use of thionamides in baseline cytopenia. It underscores the importance of individualised management, careful haematological surveillance, and multidisciplinary coordination.

Abstract citation ID: lvag096.1795

EP1733 - LBA_ECE_1473 - The role of pembrolizumab immunotherapy in metastatic adrenocortical carcinoma: a case series study

Kyriaki Gkoufa[1], Ariadni Spyroglou[1], Maria Theochari[1], Odysseas Violetis[2], Panagiota Konstantakou[1], Dionysia Kolomodi[1], Georgios Kyriakopoulos[1], Konstantinos Iliakopoulos[1], Konstantinos Bramis[1], Pantelis Antonakis[1], Georgios Sotiropoulos[1], Christos Papadimitriou[1], Manousos Konstadoulakis[1], George Mastorakos[1], Dimitra Argyro Vassiliadi[1] and Krystallenia Alexandraki[1]

[1]Aretaieion Hospital, National & Kapodistrian University of Athens, Athens, Greece; [2]Maroussi, Greece

Background: Adrenocortical carcinoma (ACC) is a rare endocrine malignancy with a poor prognosis in advanced stages. Standard first-line treatment for metastatic disease involves mitotane and cytotoxic chemotherapy (EDP-M); however, therapeutic options following progression are limited. Immunotherapy with immune checkpoint inhibitors, such as the anti-PD-1 agent pembrolizumab, has shown potential in solid tumors, particularly those with high microsatellite instability (MSI-H) or deficient mismatch repair (dMMR). This study presents the clinical experience, safety, and outcomes of patients treated with pembrolizumab at a specialized Endocrine Unit of a University Hospital.

Methods: This retrospective observational case series study analyzed a cohort of seven adult patients with metastatic ACC followed between 2020 and 2026. Among them, three patients receiving pembrolizumab as salvage therapy for advanced disease were evaluated. Data collection included demographic profiles, clinical and histopathological characteristics, progression-free survival (PFS), overall survival (OS), and treatment-related toxicity.

Results: Case 1: A 30-year-old female with functional, symptomatic ENSAT stage IV ACC (pulmonary, hepatic, bone metastases) and Ki-67 35%-40% (Weiss score 8). Following surgery, adrenolytic therapy, and chemotherapy, pembrolizumab was initiated three years post-diagnosis. Treatment was discontinued after a single administration due to severe drug-induced hepatitis. Although a partial reduction in pulmonary metastases occurred, the brief treatment duration precluded a definitive attribution of this response to immunotherapy.

Case 2: An 89-year-old female with functional ENSAT stage IV ACC (pulmonary, diaphragmatic, nodal, perirenal involvement) and a Ki-67 index of 50% (Weiss score 8), received pembrolizumab postoperatively alongside mitotane as salvage therapy. Efficacy could not be assessed as the patient succumbed shortly after initiation; death was attributed to rapid disease progression.

Case 3: A 56-year-old female with symptomatic ENSAT stage IV oncocytic ACC (renal, hepatic, IVC involvement) with low grade malignancy (Weiss score 4, Ki-67 15%). Following surgery and standard therapies, she received pembrolizumab for two years. She achieved a sustained initial response with disease progression occurring 2 years later.

Conclusion: Pembrolizumab demonstrates heterogeneous outcomes in metastatic ACC. While it may provide prolonged disease control in selected patients. The risk of severe immune-related adverse events, should be considered. Immunotherapy remains a viable second/third line option, though, optimal patient selection and predictive biomarker identification are essential.

Abstract citation ID: lvag096.1796

EP1735 - LBA_ECE_1201 - CYP11B2 immunohistochemistry-defined subtypes and clinical outcomes after adrenalectomy in primary aldosteronism

Anna Casteràs Roman[1,2], Veronica Engracia Rodríguez[1], Sheila Bermejo[3], Andres Cardona-Arias[1], Betina Biagetti[1], Juzzy Tatiana Zuñiga[4] and Carmela Iglesias[4]

[1]Endocrinology Department, Vall d'Hebron University Hospital, Barcelona, Spain; [2]Endocrinology, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [3]Nephrology Department, Vall d'Hebron University Hospital, Barcelona, Spain; [4]Pathology Department, Vall d'Hebron University Hospital, Barcelona, Spain

Background: CYP11B2 (aldosterone synthase) immunohistochemistry has enabled a more precise histopathological subtyping of primary aldosteronism (PA) after adrenalectomy. However, the relationship between CYP11B2-defined subtypes and clinical presentation or postoperative outcomes remains unclear.

Objectives: To assess the association between CYP11B2-based histopathological findings and preoperative characteristics, as well as clinical and biochemical outcomes after unilateral adrenalectomy according to PASO criteria.

Methods: Retrospective study including 21 patients who underwent adrenalectomy for PA over the last 10 years. Clinical, biochemical and hormonal variables were analyzed alongside CYP11B2 immunohistochemistry findings according to HISTALDO criteria: solitary aldosterone-producing (AP) adenoma (>1 cm), AP-nodule <1 cm (HE+ CYP11B2+), AP-micronodule <1 cm (HE-, CYP11B2+), micronodular hyperplasia (multiple nodules/micronodules), AP-diffuse hyperplasia. Statistical analysis was further based on the presence of solitary adenoma with or without associated hyperplasia. Outcomes at 1 year were assessed using PASO criteria.

Results: A total of 21 patients were included (52.4% male), with a median age at surgery of 53 years [IQR 48-59.5]. Median duration of hypertension was 10 years [IQR 5.5-23.5]. Hypokalemia was present in 20/21 patients (2.8 mmol/L[IQR 2.5-3.1]). Median aldosterone was 36.6 ng/dL[IQR 30.7-87.7], plasma renin activity (PRA) 0.3 ng/mL/h [IQR 0.3-0.48]) and ARR 143.1 [IQR 89.6-239.5]. CT identified an adrenal adenoma in all cases (median size 1.7 cm [IQR 1.1-2]).

CYP11B2 immunohistochemistry revealed adenoma alone in 23.8%, adenoma plus micronodular hyperplasia in 42.9%,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

micronodular hyperplasia in 23.8%, and other patterns in 9.6%. No association was observed between histopathological subtype and preopertative variables such as age, gender or HTA grade or duration. In 6 cases, the adrenal adenoma identified on CT was either not confirmed on histopathology or lacked CYP11B2 expression.

All patients normalized potassium levels after surgery. Complete biochemical remission (including PRA >1) was achieved in 31.3% and complete clinical remission (BP normalization) in 38.1%. Antihypertensive treatment decreased significantly (median 3 to 1 drugs, $P < .001$), and mineralocorticoid receptor antagonist use decreased from 20 to 2 patients. CYP11B1-subtype did not predict clinical or biochemical outcomes. Female sex was associated with higher rates of hypertension remission (87.5% vs 12.5%) P .008.

Conclusions: Mixed CYP11B2-defined patterns are common in PA and are not adequately captured by current classifications. Histopathological subtype did not predict postoperative outcomes in our study. While hypokalemia is consistently corrected, blood pressure response remains variable, with female sex emerging as the only predictor of clinical remission.

Abstract citation ID: lvag096.1797

EP1736 - LBA_ECE_1259 - Four-year BMI trajectories and weight regain after bariatric surgery using prespecified regain definitions: a procedure-comparative analysis

Elamin Abdelgadir[1,2], Fatheya Alawadi[1,2], Alaaeldin Bashier[1,2] and Fauiza Rashid[1,2]
[1]*Mohammed Bin Rashid University for Medicine and Health Sciences, Dubai, United Arab Emirates;* [2]*Dubai Hospital, Dubai, United Arab Emirates*

Background: Long-term bariatric outcomes are often complicated by heterogeneous weight-regain definitions and incomplete follow-up. We characterised BMI trajectories and regain prevalence through year 4 using three operational definitions.

Methods: BMI was evaluated at baseline, 6 months, and 1-4 years after index primary SG, MGB/OAGB, or RYGB. Missing values were imputed. Nadir BMI was defined as the minimum postoperative BMI across 6 months to 4 years, and last BMI was standardised as year-4 BMI. Weight regain was defined as: (A) ≥25% regain of lost BMI relative to nadir; (B) ≥5 BMI units increase from nadir; (C) ≥2 BMI units increase from 1-year BMI. Regain prevalence was summarised by procedure; a multivariable logistic regression evaluated procedure associations with Definition A.

Results: Median time-to-nadir was 24 months. At year 4, regain prevalence (Definition A) was 22.2% (SG), 17.2% (MGB/OAGB), and 25.9% (RYGB). Using Definition B, prevalences were 7.5%, 6.7%, and 8.2%, respectively. In adjusted modelling, MGB/OAGB had lower odds of regain vs SG (OR 0.57; 95% CI 0.46-0.72; $P = .0000$).

Conclusion: Regain prevalence at year 4 depended materially on the operational definition used, yet MGB/OAGB demonstrated more favourable durability across definitions. Harmonised regain definitions and risk-stratified long-term follow-up are warranted.

Table 1 Weight regain prevalence at 4 years by definition (imputed; standardised year-4 BMI).

Procedure	*n*	Median time-to-nadir (months)	Def A (%)	Def B (%)	Def C (%)
SG	1447	24	22.2	7.5	23.0
MGB/OAGB	899	24	17.2	6.7	19.0
RYGB	632	24	25.9	8.2	21.2

Figure 1

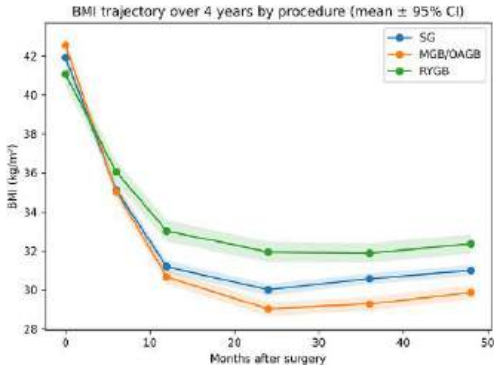
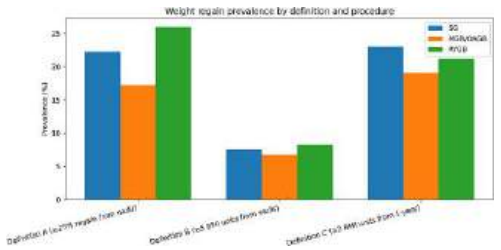


Figure 2



Abstract citation ID: lvag096.1798

EP1742 - LBA_ECE_1175 - Prediabetes management with a nutraceutical based on white mulberry leaf, fenugreek, inulin, niacin, chromium, zinc and a probiotic: effects on metabolic and cardiovascular risk

Claudia Arnas-Leon[1,2], Sara Andrada-Diaz[3], Agnieszka Kuzior[2], Ana Maria Sanchez Garcia[2], Juan Fernandez-Jimenez[2], Irene Hernandez-Hernandez[1,2], Facundo Marcelo Guerrero-Kesselman[2], Borja Santana-Ojeda[1], Inmaculada Molinero-Marcos[1] and Francisco Javier Martinez-Martin[1,2]
[1]*Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain;* [2]*Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain;* [3]*Medical Advisory, Bioksan Naturalmente Juntos, Las Palmas de Gran Canaria, Spain*

Background and Objective: Prediabetes is a serious public health concern worldwide. Acarbose, an α-glucosidase inhibitor, has been shown to prevent type 2 diabetes (T2DM) and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

reduce blood pressure, incident hypertension, and cardiovascular risk in subjects with prediabetes (STOP-NIDDM trial). White mulberry (*Morus alba*) contains 1-deoxynojirimycin, a potent competitive α-glucosidase inhibitor. A nutraceutical combining standardized white mulberry leaf extract, fenugreek (*Trigonella foenum-graecum*, an AMPK activator), inulin (soluble fiber), *Lactiplantibacillus plantarum* A7 (probiotic), niacin (vitamin B3), chromium and zinc (trace elements) has been developed for patients with prediabetes.

This study evaluated the tolerability and efficacy of this formulation on metabolic profile, blood pressure, and cardiovascular risk (SCORE2) in subjects with prediabetes, with change in insulin resistance (HOMA2-IR) as the primary endpoint.

Methods: In this open-label study, adults with prediabetes received the nutraceutical once daily for 6 months, with an interim visit at 3 months. Body mass index (BMI), blood pressure, fasting glucose, insulin, lipid profile, and HOMA2-IR were assessed at each visit.

Results: Of 144 recruited patients, 113 (78.5%) completed the study (71 women; mean age 56.4 ± 6.7 years). HOMA2-IR decreased from 1.659 ± 0.721 to 1.269 ± 0.581 (−23.5%, $P < .001$). Fasting glucose decreased by 7.6 mg/dL ($P < .001$) and HbA1c by 0.22% ($P < .001$). Normoglycemia was achieved in 33 patients (29.2%, $P < .001$), while 3 (2.65%, p NS) developed T2DM. Body weight and BMI remained unchanged.

Significant improvements were observed in lipid profile: total cholesterol (−5.3%, $P = .002$), non-HDL cholesterol (−9.94%, $P < .001$), LDL cholesterol (−10.5%, $P < .001$), triglycerides (−19.3%, $P < .001$), and HDL cholesterol (+11.83%, $P < .001$). Systolic and diastolic blood pressure decreased by 5.7 (4.11%, $P < .001$) and 4.2 mmHg (4.92%, $P = .005$), respectively.

The SCORE2-estimated cardiovascular risk decreased from 4.23 ± 1.98% to 3.58 ± 1.76% (−15.4%, $P < .001$). The proportion of patients classified as low cardiovascular risk increased from 56% to 72% ($P = .005$).

Mild gastrointestinal adverse effects were reported in some patients; however, no discontinuations or serious tolerability issues occurred.

Conclusions: This white mulberry leaf-based nutraceutical was well tolerated and significantly improved glycemic control, lipid profile and blood pressure in patients with prediabetes. The reduction of the SCORE-2 cardiovascular risk index was significant, with one out of six patients progressing from the moderate/high to the low risk category. In the absence of approved pharmacological treatments for prediabetes in the European Community, it may represent a useful adjunct to lifestyle modification.

Abstract citation ID: lvag096.1799

EP1743 - LBA_ECE_1356 - Coronary heart disease in patients with type 2 biabetes: the role of traditional, behavioral and atherogenic risk factors in a large multicenter study

Ozge Telci Caklili[1], Ibrahim Demirci[2], Cem Haymana[3], Hulya Hacisahinogullari[4], Faruk Kilinc[5], Ayhan Karakoç[6], Ramazan Sari[7], Ilker Tasci[8], Serpil Salman[9], Canan Ersoy[10], Fahri Bayram[11], Ilhan Satman[12], Alper Sonmez[2] and Temd Study Group[13]

[1]Kocaeli City Hospital, Kocaeli, Turkey; [2]Ankara Guven Hospital, Ankara, Turkey; [3]Gulhane Training and Research Hospital, Ankara, Turkey; [4]Faculty of Medicine, Istanbul University, Istanbul, Turkey; [5]Fırat University, Elazig, Turkey; [6]Gazi University, Ankara, Turkey; [7]Akdeniz University, Antalya, Turkey; [8]Ufuk University, Ankara, Turkey; [9]Department of Internal Medicine, Faculty of Medicine, Istanbul Health and Technology University, Istanbul, Turkey; [10]Uludag University, Bursa, Turkey; [11]Private Practice, Kayseri, Turkey; [12]VKV American Hospital, Istanbul, Turkey; [13]Various Hospitals, Ankara, Turkey

Background: Type 2 diabetes mellitus (T2DM) substantially increases the risk of coronary artery disease (CAD) through insulin resistance, inflammation, and related complications. In this large, nationally representative multicenter study, we investigated behavioral and metabolic risk factors associated with CAD in T2DM.

Materials and Methods: This cross-sectional study was conducted across Türkiye, including 70 endocrine clinics in 36 cities. Adults with T2DM followed at the same center for at least one year were included. Sociodemographic, anthropometric, clinical, laboratory, and lifestyle data were recorded using a standardized web-based system.

Results: A total of 5707 patients with diabetes were recruited, of whom 4956 (86.8%) had T2DM (mean age 58.9 ± 10.0 years; 59.8% women). CAD status was available in 4750 patients, among whom 1061 (22.3%) had CAD.

CAD was more frequent in men than women (30.4% vs 16.9%, $P < .001$). Patients with CAD were older (62.8 ± 8.6 vs 57.8 ± 10.2 years, $P < .001$) and had longer diabetes duration (16.1 ± 8.8 vs 12.2 ± 7.7 years, $P < .001$). Body mass index was lower (31.2 ± 5.8 vs 31.8 ± 6.8 kg/m^2, $P = .005$), whereas waist circumference was higher (106.7 ± 13.7 vs 105.1 ± 14.1 cm, $P = .004$).

Lower income was associated with CAD (23.4% vs 19.5%, $P = .003$), whereas smoking and exercise were not ($P = .219$ and $P = .977$). Hypertension was associated with CAD (28.2% vs 14.5%, $P < .001$). Systolic blood pressure was higher (126.1 ± 13.6 vs 124.3 ± 13.6 mmHg, $P = .004$), while diastolic pressure did not differ ($P = .603$). HbA1c was higher in the CAD group (8.27 ± 1.94 vs 7.84 ± 1.89%, $P < .001$), and hypoglycemia was more frequent (24.6% vs 20.8%, $P = .002$).

In multivariable logistic regression, independent predictors of CAD were older age (OR 1.04, 95% CI 1.03-1.05, $P < .001$), male sex (OR 0.39, 95% CI 0.33-0.46, $P < .001$), current smoking (OR 1.37, 95% CI 1.12-1.66, $P = .002$), hypertension (OR 2.00, 95% CI 1.68-2.38, $P < .001$), microvascular complications (OR 1.48, 95% CI 1.26-1.74, $P < .001$), higher HbA1c (OR 1.12 per %, 95% CI 1.07-1.17, $P < .001$), longer diabetes duration (OR 1.04 per year, 95% CI 1.02-1.05, $P < .001$), and lower income (OR 0.74, 95% CI 0.62-0.88, $P = .001$). Exercise, diet, hypoglycemia, education, and body mass index were not independently associated with CAD (all $P > .05$).

Conclusion: In this large national cohort of T2DM patients, CAD was independently associated with classical cardiometabolic risk factors, microvascular complications, and lower income, whereas lifestyle factors were not independently associated after adjustment. These findings highlight dominant role of cumulative metabolic burden and vascular damage in determining CAD risk and emphasize the importance of early, sustained, risk factor–targeted management.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1800

EP1744 - LBA_ECE_1037 - Adrenocortical carcinoma: a case series highlighting diagnostic challenges, hormonal heterogeneity and therapeutic complexity

Mara Patricia Rotaru-Wagner[1,2], Oana Stanoiu-Pinzariu[1,2] and Carmen Emanuela Georgescu[1,2]
[1]*Department of Endocrinology, Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania;* [2]*Department of Endocrinology, Clinical County Emergency Clinical Hospital, Cluj-Napoca, Romania*

Introduction: Adrenocortical carcinoma (ACC) is a rare malignancy (0.5-2 cases/million/year), characterised by heterogeneous clinical presentation, variable hormonal secretion and poor prognosis in advanced stages. Multidisciplinary management combining surgery, mitotane and cytotoxic chemotherapy remains the gold standard of treatment. We report three cases illustrating distinct clinical phenotypes of ACC managed at a tertiary endocrine centre.

Case Presentations: Case 1: A 39-year-old woman presented with hypertension, hirsutism and generalised oedema. Hormonal evaluation demonstrated cortisol and androgen secretion (suppressed adrenocorticotropic hormone, elevated dehydroepiandrosterone sulfate, testosterone, urinary free cortisol and no suppression of cortisol with 1 mg dexamethasone). Computed tomography (CT) identified a right retroperitoneal mass of 98 × 94 × 98 mm. Laparoscopic right adrenalectomy confirmed high-grade ACC (pT2NxMxL1V1, Ki67 15%-20%). Post-operative corticotropic insufficiency required glucocorticoid substitution. Adjuvant mitotane was initiated and therapeutic levels were achieved slowly. Serial imaging showed no recurrence, though mitotane side effects required dose adjustments.

Case 2: A 52-year-old man presented with left lumbar pain. CT identified a left retroperitoneal mass of 133 × 90 × 136 mm, bilateral pulmonary nodules, locoregional adenopathy and a right adrenal nodule. Extended surgery included tumour resection with left nephrectomy, splenectomy, body and tail pancreatectomy and periaortic lymph node dissection. Histopathology confirmed non-functioning high-grade ACC (Ki67~60%). Post-operative staging revealed multiple hepatic metastases and therapy with mitotane combined with EDP (etoposide, doxorubicin, cisplatin) chemotherapy was initiated.

Case 3: A 50-year-old male patient was incidentally diagnosed with a left adrenal mass of 12 × 7 × 8 cm on a CT performed for suspected disc herniation. Partial left adrenalectomy with splenectomy and distal pancreatectomy confirmed a low-grade oncocytic ACC (pT2L0V0R0M0, Ki67 10%). Subsequent imaging revealed local recurrence and hepatic metastases, requiring reoperation with resection of the pancreatic body and tail, residual left adrenal, atypical hepatic resection (segments II and V), partial gastrectomy and omentectomy. Adjuvant mitotane and EDP chemotherapy were initiated.

Discussion: The present case series illustrates the clinical, hormonal and histological heterogeneity of ACC: a functioning localised tumour with slow mitotane titration, a non-functioning metastatic high-grade ACC requiring systemic chemotherapy and a low-grade oncocytic ACC with metastatic relapse requiring repeated surgical interventions. These cases highlight the challenges of achieving therapeutic mitotane levels, managing adrenocortical insufficiency and coordinating multidisciplinary oncological care.

Conclusion: The cases presented confirm that no two ACC presentations are alike. Histological subtype, functional status and disease stage at diagnosis influence therapeutic strategy and long-term outcomes in this aggressive malignancy.

Abstract citation ID: lvag096.1801

EP1745 - LBA_ECE_1299 - An unusual presentation: panhypopituitarism and central diabetes insipidus revealing small cell lung cancer

Neslihan Koray Fedai, Nagihan Uzun, Revah Cankaya, Murat Calapkulu, Bekir Ucan, Mustafa Ozbek and Erman Cakal
Endocrinology and Metabolism, University of Health Sciences, Ankara Etlik City Hospital, Ankara, Turkey

Pituitary metastasis (PM) is rare, accounting for approximately 1% of surgically resected sellar lesions, and is typically observed in patients with extensive disease. Breast and lung cancers represent the most common primary malignancies. Although PM is often asymptomatic, when present, the most frequent clinical manifestations include panhypopituitarism and central diabetes insipidus (CDI). CDI is uncommon in pituitary adenomas and should raise suspicion for an alternative etiology. The presence of CDI or cranial neuropathy, particularly in patients over 50 years of age, should prompt consideration of pituitary metastasis.

A 65-year-old man with a history of traumatic paraplegia following a fall from height two years earlier was referred to our endocrinology clinic with a two-month history of progressive fatigue, generalized weakness, hypotension, and polydipsia. At initial evaluation, his symptoms were attributed to his underlying neurological condition. However, further laboratory assessment revealed panhypopituitarism, as shown in Table 1. Additionally, hypernatremia, elevated serum osmolality, and inappropriately low urine osmolality were consistent with CDI.

MRI of the pituitary gland revealed a 16 × 25 mm heterogeneously enhancing dumbbell-shaped sellar mass with suprasellar extension and optic chiasm indentation (Figure 1), with imaging features raising strong suspicion for metastatic disease rather than a primary pituitary adenoma. The patient had a 20 pack-year smoking history. Thoracic computed tomography was performed to identify a potential primary malignancy, revealing a 23 × 35 mm pleura-based, irregularly marginated mass lesion in the posterior segment of the right lower lobe, highly suspicious for primary lung malignancy. Endobronchial ultrasound-guided biopsy confirmed small cell lung carcinoma, with tumor cells positive for INSM1 and TTF1. FDG PET-CT demonstrated increased metabolic activity in the pituitary lesion (SUVmax 7.17), supporting metastatic involvement. Additional findings included bilateral adrenal, hepatic, skeletal, and mediastinal lymph node metastases, as well as right-sided pleural effusion.

Hormone replacement therapy was initiated, resulting in rapid clinical improvement. The patient was referred to oncology for systemic treatment.

This case highlights that panhypopituitarism and CDI may represent the initial manifestation of extensive-stage cancer. Pre-existing neurological comorbidities may mask classic

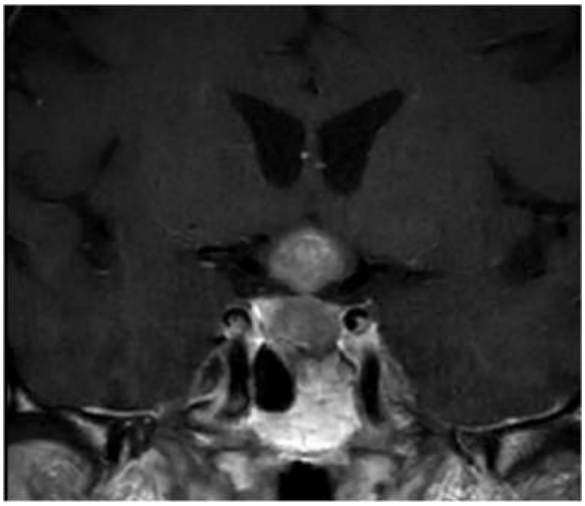
Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

endocrine symptoms, leading to diagnostic delay. In any patient presenting with combined anterior and posterior pituitary failure of unclear etiology, sellar MRI and systematic screening for underlying malignancy are warranted.

Table 1

ACTH (ng/L)	5.5
Cortisol (μg/dl)	2.7
TSH (mIU/L)	0.2
T4 (ng/dl)	0.5
Prolactin (μg/L)	14.7
FSH (IU/L)	1.1
LH (IU/L)	0.3
Total testosterone (ng/dL)	<2.5
IGF-1 (ng/mL)	44

Figure 1



Abstract citation ID: lvag096.1802

EP1746 - LBA_ECE_1378 - When a sellar mass is not what it seems: hypopituitarism caused by a suprasellar tuberculoma

Paulo Perez Damasco, Liseth Gabriela Delgado Castro and Jose Edmond Esquivel Vargas
Caja Costarricense de Seguro Social, San José, Costa Rica

Background: Although pituitary adenomas account for the majority of sellar region lesions, a small proportion correspond to less common entities such as infections, cysts, or malignancies. Involvement of the hypothalamus-pituitary axis by tuberculosis is exceedingly rare, and isolated sellar tuberculoma represents an exceptional presentation. Its clinical, radiological, and endocrine features are often indistinguishable from more frequent sellar pathologies, making diagnosis challenging. Recognizing this entity is crucial, as therapeutic strategies and outcomes differ significantly from those of neoplastic lesions.

Case Presentation: A 43-year-old woman with a history of diabetes mellitus presented with a one-year history of progressive headaches, nausea, vomiting, and dizziness, accompanied by decreased visual acuity, generalized weakness, and malaise. Cranial CT revealed a well-delimited, homogeneous, isodense solid mass in the suprasellar region with sellar extension, associated vasogenic edema, and marked contrast enhancement (>90%), measuring approximately 28 × 27 × 29 mm. MRI demonstrated a well-defined lesion located at the floor of the third ventricle, isointense on T1- and T2-weighted sequences, with intense and homogeneous contrast enhancement.

Given the radiologic appearance, germinoma or meningioma was initially suspected. Hormonal evaluation revealed hypopituitarism, including central adrenal insufficiency (low morning cortisol with inappropriately low ACTH), hypogonadotropic hypogonadism, central hypothyroidism, hyperprolactinemia, and low IGF-1. Hydrocortisone and levothyroxine replacement therapy was initiated.

The patient underwent transcranial biopsy, which revealed a midline suprasellar mass infiltrating both optic nerves without a clear surgical plane. Frozen sections suggested inflammatory tissue. Definitive histopathology showed fibroconnective tissue with mononuclear inflammatory infiltrates composed of lymphocytes and macrophages, poorly formed granulomas, CD3+ and CD20+ lymphocytes, and isolated acid-fast bacilli on special staining, with no fungal organisms identified. A diagnosis of sellar tuberculosis was made, and antifimic therapy was administered for one year.

Despite completion of treatment, the patient discontinued endocrine follow-up and hormone replacement. One year later, she presented with progressive neuropsychiatric deterioration, polydipsia, polyuria, weight loss, and persistent gastrointestinal symptoms. Evaluation revealed persistent panhypopituitarism and new central diabetes insipidus with hypernatremia and low urine osmolality. Hormone replacement with hydrocortisone, levothyroxine and desmopressin was restarted.

Conclusions: This case underscores the importance of including sellar tuberculoma in the differential diagnosis of sellar masses associated with hypopituitarism. Definitive diagnosis relies on histopathological evaluation. Early surgical sampling, prompt initiation of antitubercular therapy, and adequate hormonal replacement are key to optimizing clinical outcomes. Greater awareness of this rare condition may help reduce diagnostic delays and improve long-term prognosis.

Abstract citation ID: lvag096.1803

EP1747 - LBA_ECE_1003 - TMC from *Glycyrrhiza uralensis* suppresses hypoxic tumor microenvironment by co-targeting the HIF-1α–neuroendocrine axis and angiogenic signaling in colorectal cancer

Su Jung Hwang[1], Hye Jung Bang[1], Se Yun Jeong[1], Hye In An[1], Bowon Jung[2], Eon Chung Park[1], Seulah Lee[2], Ki Hyun Kim[1] and Hyo-Jong Lee[1]
[1]*School of Pharmacy, Sungkyunkwan University, Suwon, South Korea;* [2]*College of Life Science, Kyung Hee University, Yongin, South Korea*

Hypoxia is a key feature of the tumor microenvironment that activates hypoxia-inducible factor-1α (HIF-1α), leading to enhanced angiogenesis and dysregulation of neuroendocrine signaling pathways. In this study, we investigated the effects of 3,3′,4,4′-tetrahydroxy-2-methoxychalcone (TMC), a bioactive chalcone isolated from *Glycyrrhiza uralensis*, on hypoxia-induced

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

angiogenic signaling and neuroendocrine mediator expression.

In human colorectal cancer HCT-116 cells, hypoxic exposure markedly increased HIF-1α protein expression, accompanied by elevated vascular endothelial growth factor (VEGF) levels. TMC treatment significantly suppressed hypoxia-induced HIF-1α protein accumulation through a post-translational mechanism and consequently reduced VEGF expression.

Notably, hypoxia also significantly increased the mRNA expression of neuroendocrine-related mediators, including tyrosine hydroxylase (TH), corticotropin-releasing hormone (CRH), and endothelin-1 (ET-1). Treatment with TMC significantly reduced these hypoxia-induced increases at higher concentrations, suggesting that TMC may modulate neuroendocrine stress responses under hypoxic conditions.

The anti-angiogenic activity of TMC was further evaluated in human umbilical vein endothelial cells (HUVECs), where TMC significantly inhibited VEGF-induced tube formation, wound healing, and invasion. In addition, treatment with TMC in a zebrafish model reduced HIF-1α protein levels without observable developmental or cardiac toxicity.

Collectively, these findings demonstrate that TMC acts as a multitarget inhibitor that suppresses hypoxia-driven angiogenic signaling while simultaneously modulating the neuroendocrine stress axis involving TH, CRH, and ET-1. These results suggest that TMC may serve as a potential therapeutic candidate for targeting hypoxia-associated neuroendocrine signaling and angiogenesis.

Abstract citation ID: lvag096.1804

EP1748 - LBA_ECE_1446 - Association between urinary bisphenol levels and breast cancer: insights from a case–control study and lifestyle assessment

Miodrag Milošević[1], Jelena Tomašević[1], Đurđica Marić[1], Biljana Antonijević[1], Vera Lukić[2], Zoran Mihailovic[2], Mina Hagen[3], Darko Zdravković[4], Simona Petričević[4], Connor Powell[5], Michael Antoniou[5] and Aleksandra Buha[1]

[1]Department of Toxicology, University of Belgrade-Faculty of Pharmacy, Belgrade, Serbia; [2]Faculty of Medicine, University of Belgrade, Institute of Forensic Medicine, Belgrade, Serbia; [3]Department of Psychology, Faculty of Media and Communications, Belgrade, Serbia; [4]University Hospital Medical Center Bezanijska Kosa, Belgrade, Serbia; [5]Department of Medical and Molecular Genetics, Faculty of Life Sciences and Medicine King's College London, London, United Kingdom

Bisphenols are widely distributed endocrine disruptors used in the production of clear plastics such as polycarbonates and resins that are extensively used as food packaging materials. The primary route of human exposure to bisphenols is through leakage into food from packaging, while certain lifestyle habits may contribute to increased internal exposure. Bisphenol exposure has been associated with various pathological conditions. As xenoestrogens, they bind to estrogen receptors and activate signaling pathways that promote cell proliferation and inhibit apoptosis. Their potential to stimulate the proliferation of hormone-dependent breast cancers has been demonstrated. This study aimed to evaluate the correlation between urinary levels of three selected bisphenols (BPA, BPAF, BPS) and breast cancer diagnosis in women in Serbia, by comparing concentrations in urine samples of patients and healthy subjects. Additionally, the influence of lifestyle habits (frequency of canned food consumption, use of plastic packaging, and number of white dental fillings) on urinary bisphenol levels was evaluated.

The study included 72 participants, of which 40 were breast cancer patients, and 32 were healthy subjects who formed the control group. Urine samples were collected at the University Hospital Medical Center "Bežanijska Kosa" in Belgrade, Serbia. Concentrations of BPAF and BPS were measured using GC-MS/MS, while BPA was measured using an ELISA. Lifestyle habits were assessed using a questionnaire developed based on known exposure pathways, obtained from data from the European Chemicals Agency (ECHA) and in accordance with REACH guidelines, as well as relevant scientific literature.

Urinary BPA levels were statistically significantly higher in the patient group compared to the control group, while no statistically significant differences were observed for BPAF and BPS. No statistically significant association was found between self-reported lifestyle habits and urinary bisphenol concentrations. In some cases, higher bisphenol levels were observed in participants reporting fewer risk-related habits.

The results suggest a possible correlation between elevated urinary BPA levels as a marker of BPA exposure and breast cancer development. Based on the current data, no association can be established between BPAF and BPS and breast cancer. The presence of bisphenols in the urine of both study groups indicates their widespread distribution and significant exposure among women in Serbia. The results of the assessment of the impact of lifestyle habits highlight the complexity of bisphenol exposure assessment and the limited reliability of self-reported data as indicators of internal exposure.

Keywords bisphenols, breast cancer, questionnaire, lifestyle habits, urine

Abstract citation ID: lvag096.1805

EP1749 - LBA_ECE_1151 - Associations between short-chain fatty acid profiles and sensory diabetic polyneuropathy in patients with type 2 diabetes and non-alcoholic fatty liver disease: a pilot study

Tulkin Atoev[1], Yuri Khalimov[2], Gulandom Shodikulova[3], Anna Bystrova[4], Gennady Rodionov[5], Vera Kuzmina[6] and Lilya Garifulina[7]

[1]Endocrinology, Samarkand State Medical University, Samarkand Regional Branch of the Republican Specialised Scientific and Clinical Medical Centre for Endocrinology named after Academician Y.H. Turakulov, Samarkand, Uzbekistan; [2]Internal Medicine with a Course in Endocrinology and Cardiology, and the Clinic named after Academician G.F. Lang, First Pavlov State Medical University of St Petersburg, Saint-Petersburg, Russia; [3]Samarkand State Medical University, Samarkand City Medical Association Hospital, Internal diseases #3, Samarkand, Uzbekistan; [4]First Pavlov State Medical University of St Petersburg, Saint-Petersburg, Russia; [5]Research Laboratory for Toxicology and Pharmacovigilance, All-Russian Centre for Emergency and Radiation Medicine named after A.M. Nikiforov, Saint-Petersburg, Russia; [6]6th Year Student of Medical Faculty, First Pavlov State Medical University of St Petersburg, Saint-Petersburg, Russia; [7]Samarkand State Medical University, Multidisciplinary Clinic of Samarkand State Medical University, Samarkand, Uzbekistan

Objective: The gut microbiome is a source of potential non-invasive biomarkers, so we investigated the relationship

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

between serum levels of microbiome-derived short-chain fatty acids (SCFAs) and sensory diabetic polyneuropathy (DPN) in patients with comorbid type 2 diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD).

Methods: We prospectively enrolled 167 patients with T2DM and NAFLD (2023-2025). A matched cohort of 55 patients (37 T2DM +steatosis (ST), 18 T2DM+steatohepatitis (SH)) underwent detailed assessment. SH was diagnosed by transient elastography with elevated ALT and AST (patients with other reasons of high level of this enzymes excluded). Serum SCFAs were quantified by gas chromatography-mass spectrometry (GC-MS) (Agilent Technologies, USA). Sensory neuropathy was evaluated via standardized tests: vibration (128 Hz tuning fork), thermal (TipTherm, at 23 °C), and tactile (10-g monofilament) sensitivity. Statistical analyses used Fisher's exact test and binary logistic regression.

Results: The prevalence of DPN was high (89.2% T2DM+ST vs 88.9% T2DM+SH) and comparable. No significant differences were found in vibration ($P = .382$), tactile or temperature ($P = .713$) impairment. Distinct SCFA profiles predicted each sensory modality: thermal impairment (Nagelkerke $R^2 = 0.582$, 78% sensitivity (Se) and 73.5% specificity (Sp), $P = .039$) was associated with C2, C4, C5; tactile impairment ($R^2 = 0.507$, Se – 78.3% and Sp – 67.9%, $P = .039$) with C3, C5, iC5, C6; and vibration impairment ($R^2 = 0.641$, Se – 70.6% and Sp – 82.6%, $P = .044$) with C2, C3, iC4, C6.

Discussion/Conclusion: This pilot study confirms a high burden of sensory DPN in T2DM-NAFLD patients. The finding that distinct SCFA profiles are associated with thermal, tactile, and vibratory deficits suggests divergent pathophysiological mechanisms and highlights the relevance of branched-chain isomers (iC4, iC5). While these preliminary results indicate a link between SCFAs and specific nerve fiber damage, the cross-sectional design limits causal inference. Further longitudinal and mechanistic studies are needed to validate these associations and explore therapeutic implications.

Abstract citation ID: lvag096.1806

EP1750 - LBA_ECE_1239 - The impact of glycated hemoglobin on rehospitalizations in patients with peripheral arterial disease undergoing surgical intervention

Jennifer Romani, Izabella Zgoda, Beatriz Santos, Julia Ventura Niclewicz, Amanda Araújo MacHado and Giovanna Voigt Pisconti MacHado
Hospital Universitário Cajuru, Curitiba, Brazil

Introduction: Peripheral Arterial Disease (PAD) is a serious manifestation of atherosclerosis, frequently associated with diabetes mellitus (DM). Chronic glycemic control, measured by glycated hemoglobin (HbA1c), is a key parameter for identifying perioperative risks and optimizing clinical outcomes in patients undergoing vascular surgical procedures.

Objective: To investigate the association between HbA1c levels at admission and the 30-day readmission rate in patients with PAD undergoing vascular procedures at a tertiary care hospital.

Methods: A retrospective, analytical study was conducted involving a review of the medical records of 136 patients who underwent vascular surgical procedures between January 2023 and October 2025. The sample was divided into controlled HbA1c (≤7%) and elevated HbA1c (>7%) groups. Chi-square tests, Fisher's exact test, and Student's t-test were used for statistical analysis.

Results: Most patients were male (70.6%) and underwent emergency surgery (66.9%). Prior DM was identified in 67.6% of the sample. There was no statistically significant difference in the readmission rates between the two groups (33.3% for the controlled group and 27.8% for the elevated group, $P = .571$). The mean length of stay also showed no significant difference between the groups ($P = .216$).

Conclusion: HbA1c levels at admission did not act as isolated predictors of readmission within 30 days. In high-severity and critical ischemia scenarios, where emergency interventions predominate, acute clinical status and the extent of vascular disease have a greater impact on short-term outcomes than chronic metabolic control.

Keywords diabetes mellitus, peripheral arterial disease, glycated hemoglobin, hospital rehospitalization, vascular surgery

Abstract citation ID: lvag096.1807

EP1751 - LBA_ECE_1411 - Rare presentation of down syndrome without congenital heart defect complicated by hypothyroidism, dyslipidemia, and ischemic heart disease in a 10-year-old girl—marked improvement after treatment

Uttam Kumar Dey
Birdem Hospital, Dhaka, Bangladesh

Background: Down syndrome (DS, trisomy 21) is frequently associated with congenital heart defects (40%-60% prevalence), hypothyroidism (up to 25% in children), intellectual disability, and dyslipidemia. Acquired ischemic heart disease (IHD) is exceptionally rare in pediatric DS, especially in the absence of septal defects. Untreated hypothyroidism can exacerbate cardiac strain, cognitive impairment, and delayed puberty. We present a rare case of late-diagnosed DS without congenital septal defect, complicated by hypothyroidism-induced features of IHD and dyslipidemia, with remarkable recovery after targeted therapy.

Case Presentation: A 10-year-old girl presented with low IQ and developmental delay. Karyotyping confirmed DS (47,XX,+21). Echocardiography revealed no septal defect or major congenital heart anomaly. Laboratory evaluation showed overt hypothyroidism (elevated TSH, low free T4), dyslipidemia (elevated total cholesterol and LDL), and clinical/electrocardiographic features consistent with myocardial ischemia (ST-segment changes, exertional symptoms). No coronary anomalies were identified. Multidisciplinary management included levothyroxine replacement (titrated to normalize thyroid function), statin therapy for dyslipidemia, anti-ischemic measures, nutritional support, and developmental interventions.

Results: After 12-18 months of consistent treatment, the patient showed significant improvement: thyroid function normalized, lipid profile improved markedly, ischemic symptoms resolved completely, and repeat cardiac evaluation demonstrated stable ventricular function. Cognitive and memory functions enhanced noticeably (improved school performance and recall). Menarche occurred at age 11, indicating restored pubertal progression. Overall quality of life improved with better daily functioning and reduced fatigue.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Conclusion: This case highlights that late diagnosis of DS can present with reversible multimorbidity, including hypothyroidism-driven IHD and dyslipidemia even without structural heart defects. Early thyroid screening and aggressive multidisciplinary management in DS can reverse cardiac, metabolic, cognitive, and pubertal complications. Routine thyroid function testing and cardiac vigilance are essential in all DS patients, regardless of age or absence of congenital heart disease. Larger prospective studies in resource-limited settings are warranted to optimize protocols.

Abstract citation ID: lvag096.1808

EP1752 - LBA_ECE_1438 - Case study—pseudohypoparathyroidism: albright hereditary osteodystrophy (AHO)

Nazi Tchelidze[1] and Natia Vashakmadze[2]
[1]Endocrinology, LTD"Aversi Clinic"; University of Georgia, Aversi Clinic, Tbilisi, Georgia; [2]Endocrinology, Israeli-Georgian Medical Research Clinic "Healthycore"; Ilia State University, Israeli-Georgian Medical Research Clinic "Healthycore", Tbilisi, Georgia

A patient, 24 y/o female, presented with weakness, fatigue, brittle nails, frequent cramping around her mouth. She had been diagnosed with epilepsy from 10 years of age. The main trigger for the seizures—increased physical activity. She was being treated with carbamazepine and levetiracetam. The June 2024 brain CT scan showed multiple areas of calcification (especially in cerebellar area and basal ganglia), that led to her neurologist checking the levels of PTH which was markedly elevated – 322 ng/l (normal range 11-43). Additional tests: total Ca^{2+} – 1.23 mmol/l (2.15-2.5); albumin – 28 g/l (35-52); corrected Ca^{2+} – 1.02 mmol/l; ionized Ca^{2+} – 0.67 mmol/l (1.12-1.32); Mg^{2+} – 0.64 mmol/l (0.66-1.07); Pi – 2.22 mmol/l (0.81-1.45); 25(OH)D3 – 6.71 ng/mL (30-100). Clinical signs: short stature, short fingers (especially the 4^{th} and 5^{th}), obesity, round face, apparent physical and mental developmental delay.

Based on the patient's history, lab results and physical evaluation the diagnosis of pseudohypoparathyroidism type 1a was made. At the same time she was diagnosed with chronic hypothyroidism (TSH – 7.7 mIU/mL) due to the thyroid gland hypoplasia. The patient was prescribed calcitriol, cholecalciferol, calcium carbonate, magnesium carbonate/oxide, levothyroxine. Within the month PTH levels normalized – 16 ng/l (11-43), total and corrected calcium levels increased – 2.45 mmol/l (2.15-2.5).

After 5 months of treatment, on the patient's next clinic visit all the initial laboratory results had been normalized: PTH – 19 ng/l, 25(OH)D – 29.4 ng/mL, TSH – 6.26 mIU/l, corrected Ca – 2.28 mmol/l, ionized Ca^{2+} – 1.22 mmol/l, Pi – 1.3 mmol/l, Mg^{2+} – 0.79 mmol/l.

Due to continuous treatment and surveillance, the patient's symptoms and overall quality of life has improved. The complete withdrawal of the antiepileptic medications is planned, the doses are being titrated down by the neurologist. The patient has not had any more cramps or seizures.

Abstract citation ID: lvag096.1809

EP1754 - LBA_ECE_1086 - The value of PTH fine needle aspiration washout in the preoperative diagnostic work-up of primary hyperparathyroidism: a retrospective real-life study

Antonino Russo[1], Davide Donner[2], Fabio Magnani[2], Marco Erini[2], Silvia Fasanella[3], Carlo Cosimo Quattrocchi[4] and Vito Racanelli[1]
[1]Internal Medicine Division, Azienda Sanitaria Universitaria Integrata del Trentino (ASUIT), Santa Chiara Hospital, Trento, Italy; [2]Nuclear Medicine Unit, Azienda Sanitaria Universitaria Integrata del Trentino (ASUIT), Santa Chiara Hospital, Trento, Italy; [3]Clinical Pathology Unit, Azienda Sanitaria Universitaria Integrata del Trentino (ASUIT), Santa Chiara Hospital, Trento, Italy; [4]Multizonal Unit of Rovere to and Arco, Radiology, Azienda Sanitaria Universitaria Integrata del Trentino (ASUIT), Rovereto, Italy

Introduction: The success of Minimally Invasive Parathyroidectomy (MIP) is dependent upon the precision of imaging modalities necessary for Parathyroid Adenoma (PA) localization.[1] Parathyroid hormone assay on fine needle aspiration ultrasound-guided biopsy (FNA-US) washout is a promising, simple and safe localization's diagnostic method.[2]

Aim: Evaluate if PTH FNA-US washout, due to its safety and the possibility of combining it with ultrasound examination, could be characterised as a first-level investigation in the diagnostic work-up of primary hyperparathyroidism, and the role of nuclear medicine diagnostic tools to identify PA.

Methods: A single-center retrospective study on 32 patients undergoing parathyroidectomy for primary hyperparathyroidism. Histological data and PTH levels in FNA washout were available for all patients. Biochemical assessment together with nuclear imaging (99mTc-MIBI-SCAN, PET-CT 18F-Choline) were evaluated.

Results: In 20/32 patients (21.8%), PTH FNA-US washout was positive: 7/20 (35%) were referred for surgery based only on PTH FNA-washout, and in all cases, histological examination confirmed the preoperative diagnosis of localization; 13/20 (65%) were referred to surgery based on the results of PTH FNA washout + MIBI; however, only in 7/13 (53.8%) MIBI was diagnostic, while in the remaining 6/13 (46.2%) it was not diagnostic. In 12/32 patients (37%), the PTH FNA-US washout value was negative. In this group, the sensitivity of MIBI was 6/12, or 50%. In the remaining patients, where both PTH FNA washout and MIBI were negative, 18F-Choline PET-CT was performed and allowed parathyroid adenoma to be located in 100% of cases.

Conclusions: Although the limited data and its retrospective nature, this study emphasises the usefulness of the PTH FNA-US washout method in the preoperative diagnosis of primary hyperparathyroidism. This method could be characterised as a first-level investigation in a large proportion of patients and could be a filter for selecting those patients to be sent for a single second-level examination such as 18F-Choline PET-CT for preoperative localization of the incriminated parathyroid gland. In this context, the use of MIBI could be avoided, which would reduce costs, diagnosis times and the degree of radiation exposure for patients.

References

1. Lubitz CC, Stephen AE, Hodin RA, Pandharipande P. Preoperative localization strategies for primary hyperparathyroidism: an economic analysis. *Ann Surg Oncol*. 2012;19(13):4202-4209. https://doi.org/10.1245/s10434-012-2512-2
2. Kuzu F, Arpaci D, Cakmak GK, et al. Focused parathyroidec tomy without intra-operative parathormone monitoring: the value of PTH assay in preoperative ultrasound guided fine nee dle aspiration washout. *Ann Med Surg*. 2016;6:64. https://doi.org/10.1016/j.amsu.2015.12.065

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1810

EP1755 - LBA_ECE_1325 - Altered myokine profile and reduced muscle strength in primary hyperparathyroidism: reversal after parathyroidectomy

Seren Aksun[1], Banu Ertürk[1], Incilay Lay[2], Ahmet Bülent Doğrul[3], Ömer Cennet[3], Didem Karaduman[4], Murat Pehlivan[4], Meltem Gülhan Halil[4] and Alper Gurlek[1]
[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey; [2]Department of Biochemistry, Hacettepe University Faculty of Medicine, Ankara, Turkey; [3]Department of General Surgery, Hacettepe University Faculty of Medicine, Ankara, Turkey; [4]Division of Geriatrics, Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey

Background and Aim: Primary hyperparathyroidism (PHPT) is associated with skeletal and neuromuscular manifestations; however, the potential role of myokines in PHPT-related muscle dysfunction remains poorly understood. We aimed to evaluate circulating myokine levels and muscle strength in patients with PHPT and to assess their changes after parathyroidectomy.

Methods: Fifty-seven patients with primary hyperparathyroidism (PHPT) and 50 age-, sex-, and body mass index (BMI)-matched healthy controls were included. Circulating levels of myostatin, follistatin, decorin, irisin, adiponectin, rantes, and resistin were measured. Muscle strength was assessed using handgrip dynamometry. A subgroup of 30 patients were reassessed after parathyroidectomy with a median follow-up of 134 days. Correlation analyses and adjusted group comparisons were performed.

Results: Patients with PHPT exhibited significantly higher circulating myostatin levels (30.3 ± 7.2 vs 23.7 ± 8.0 ng/mL, $P < .001$) and decorin levels (1081.3 vs 852.0 pg/mL, $P = .003$), **accompanied by lower circulating follistatin levels** ($P = .048$). Handgrip strength was also reduced in the PHPT group (24.1 vs 26.6 kgf, $P = .03$). Circulating myostatin levels showed positive correlations with both PTH ($r = 0.346$, $P < .001$) and serum calcium levels ($r = 0.373$, $P < .001$). After adjustment for age, sex, and BMI, PHPT status remained a significant determinant of circulating myostatin levels (ANCOVA $F = 9.57$, $P = .003$).

Parathyroidectomy was associated with significant changes in circulating myokines and muscle strength, marked by a reduction in myostatin levels (30.7 ± 7.7 to 22.7 ± 9.9 ng/mL, $P < .001$) and concomitant increases in follistatin ($P < .001$), irisin ($P = .003$), and handgrip strength ($P = .007$).

Conclusion: PHPT is characterized by a distinct circulating myokine profile marked by increased myostatin and reduced follistatin levels, accompanied by impaired muscle strength. The reversal of these alterations after parathyroidectomy suggests a potentially reversible myokine-mediated mechanism underlying muscle dysfunction in PHPT and supports a role for the myostatin–follistatin axis in the neuromuscular manifestations of this disease.

Abstract citation ID: lvag096.1811

EP1756 - LBA_ECE_1192 - Clinical and hormonal profile of adult-onset growth hormone deficiency: real-world evidence from a UK Tertiary Endocrine Centre

Thanikai Sasikanth[1], Pratibha Natesh[1], Christina Millou[1], Asma Belheddad[1], Elizabeth Varghese[1] and Harpal S. Randeva[1]
[1]Diabetes and Endocrine, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, United Kingdom

Background: Adult-onset growth hormone deficiency (AO-GHD), most commonly secondary to pituitary or hypothalamic pathology, is associated with impaired quality of life (QoL) and adverse metabolic outcomes. NICE TA64 recommends GH therapy only in severe cases with documented QoL impairment and continuation only if benefit is demonstrated. Contemporary UK real-world data on AO-GHD remain limited.

Methods: We retrospectively analysed adults diagnosed with GHD at ≥18 years and currently receiving GH therapy at a tertiary endocrine centre. Extracted variables included demographics, aetiology, diagnostic modality, pituitary hormone deficits, IGF-1 values, and Adult Hypopituitarism and Growth Hormone Deficiency Assessment (AGHDA) scores. Pre- and post-treatment AGHDA scores were compared.

Results: Of the 50 patients receiving GH therapy, 29 met criteria for AO-GHD. The mean age at diagnosis was 51.0 ± 15.7 years (range 24-75), with most patients aged 60-75 years. The current mean age is 62.1 ± 12.7 years (range 44-84). The cohort was predominantly Caucasian (93%) and female (18/29).

Non-functioning pituitary adenoma (NFPA) was the leading aetiology (52%), followed by craniopharyngioma (10%), prolactinoma (7%), acromegaly (7%), and rarer causes including autoimmune hypophysitis, Sheehan's syndrome, and chemotherapy-associated GHD.

Diagnosis was confirmed by GH stimulation testing in 25/29 (86%), predominantly via Glucagon stimulation test. Four patients were diagnosed based on low IGF-1 with ≥3 additional pituitary deficits (2/29) or historical documentation (2/29).

Multi-axis pituitary failure was common: central hypothyroidism (97%), ACTH deficiency (69%), ADH deficiency (28%), and hypogonadism in all males. Six patients had four additional hormonal deficits and eleven had three.

AGHDA scores improved significantly from baseline (median 17, range 12-22) to follow-up (median 10, range 7-15). Current GH doses ranged from 0.2-0.5 mg/day.

Limitations included missing baseline AGHDA scores in long-standing patients and incomplete diagnostic documentation in transferred cases.

Conclusion: AO-GHD in this UK cohort was predominantly secondary to NFPA and characterised by a high burden of multi-axis pituitary hormone deficiency. GH therapy was associated with clinically meaningful improvement in QoL scores. These findings emphasise the importance of systematic pituitary assessment, adherence to NICE TA64, and structured long-term follow-up in adults with suspected GHD.

Abstract citation ID: lvag096.1812

EP1759 - LBA_ECE_1376 - Higher order serum–adipose coordination defines functional markers of glucocorticoid action

Kate Bennett[1], Dimitrios Chantzichristos[2], Anja Meyer[1], Eleanor Doman[1], Terence Garner[1], Per-Anders Jansson[2], Gudmundur Johannsson[2] and Adam Stevens[1]
[1]Developmental Biology and Medicine, University of Manchester, Manchester, United Kingdom; [2]Sahlgrenska University Hospital, Gothenburg, Sweden

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Glucocorticoids (GCs) regulate metabolism across tissues, yet systems-level mechanisms linking adipose and circulating metabolites remain unclear. Analyses often track pathways or pairwise correlations and miss *higher-order interactions*—coordinated relationships among ≥3 molecular features that reveal emergent organisation. We asked how GCs reorganise this higher-order, adipose–serum multi-omic structure in humans.

Methods: In a randomised, cross-over trial ($n = 10$) with near-physiological hydrocortisone exposure versus withdrawal (26 h), we profiled transcriptomics and microdialysis metabolomics in adipose tissue, and serum metabolomics. We quantified:

transcriptomic entropy (pathway-level specialisation);

) hypergraph modelling of higher-order associations (hyperedges linking multiple nodes);

topological data analysis (TDA) to characterise global omic architecture (connected components H0, loops H1, voids H2).

Group differences (GC exposure vs withdrawal) were assessed using Δ total co-degree and Wasserstein distance, with bootstrapping and permutation testing to confirm that differences reflected genuine GC-driven network reorganisation.

Results: GC exposure in adipose tissue increased lipid mobilisation and amino-acid catabolism. Entropy analysis revealed consistent pathway-level reorganisation across nine metabolic pathways, distinct from random controls. Adipose entropy was generally lower during GC exposure—indicating more specialised networks—while amino-acid, carbohydrate and lipid catabolism showed the strongest changes.

Cross-tissue hypergraphs revealed that serum metabolites formed more higher-order connections to both adipose transcripts and adipose metabolites during exposure. This produced a right-shift in Δ total co-degree (mean $\Delta = 0.167$ exposure vs −0.003 withdrawal), demonstrating increased serum–adipose higher-order coordination beyond pairwise relationships.

TDA confirmed robust topological separation between GC states: inter-state Wasserstein distances exceeded intra-state across dimensions ($H1 = 1.36$, $H0 = 1.22$, $H2 = 0.74$; permutation $P = .0005$). GC exposure also generated longer-persistence H1 features, indicating a more ordered integrated serum–adipose network structure. Independent TDA testing across homology dimensions yielded $P < .05$.

Conclusion/Clinical Application: GCs remodel not only adipose-intrinsic pathways but also the higher-order architecture linking adipose molecular networks to circulating metabolites. This distinguishes changes arising in adipose tissue (lipid and amino-acid metabolism, pathway specialisation) from those detected in serum (cross-tissue higher-order coordination and topological restructuring). Circulating metabolites embedded in these multi-molecule features represent mechanistically anchored serum markers of adipose GC action. Such markers could support personalised glucocorticoid dosing in adrenal insufficiency by more accurately capturing tissue-level GC effects.

Abstract citation ID: lvag096.1813

EP1760 - LBA_ECE_1404 - Enhanced selectivity and reduced off-target effects of seviteronel as a CYP17A1 inhibitor targeting castration-resistant prostate cancer

Jibira Yakubu, Therina Du Toit and Amit Pandey
University of Bern, Bern, Switzerland

Background: Androgen Receptor (AR) signaling remains a key driver in castration-resistant prostate cancer (CRPC), necessitating agents that effectively suppress it. While abiraterone is a foundational therapy that inhibits the CYP17A1 enzyme, its lack of selectivity leads to off-target endocrine effects requiring concomitant corticosteroid administration. Recent studies also connect AR signaling to ferroptosis, a form of programmed cell death, suggesting that AR inhibition may sensitize cells to this pathway.

Aims: To compare the next-generation CYP17A1 inhibitor seviteronel against abiraterone. The analysis aims to delineate seviteronel's mechanistic and selectivity profiles and to explore its potential to induce ferroptosis by targeting the AR axis.

Methods: We synthesized preclinical data from in vitro and in vivo studies. In vitro assays included proliferation studies in prostate cancer cell lines (LNCaP) and steroidogenic cell lines (NCI-H295R), as well as radioactive substrate and LC-MS analyses to measure androgen biosynthesis inhibition and selectivity. An AR ligand binding assay was used to characterize direct AR antagonism.

Results: Seviteronel demonstrated potent and highly selective inhibition of the CYP17A1 17,20-lyase activity (IC_{50} 69 nM), with a 10-fold selectivity over its 17α-hydroxylase activity (IC_{50} 670 nM). In contrast, abiraterone was found to be hydroxylase-selective, with an IC_{50}

of 2.5 nM for hydroxylase activity versus 15 nM for lyase activity. Seviteronel also showed no significant inhibition of the CYP21A2 enzyme, a key enzyme in cortisol synthesis, preventing the mineralocorticoid excess syndrome associated with abiraterone and allowing for a prednisone-free regimen. Though mechanistic studies on AR modulation and ferroptosis induction are ongoing, existing evidence suggests that AR axis disruption may enhance sensitivity to ferroptosis cell death. This dual mechanism may confer efficacy against mutated AR forms that drive resistance to abiraterone and other antiandrogens.

Conclusions: Seviteronel's superior selectivity and unique dual-action mechanism, combining potent androgen synthesis inhibition with direct AR antagonism, positions it as a promising next-generation therapeutic for CRPC. This profile not only addresses abiraterone's primary clinical limitations but also presents a novel strategy to overcome treatment resistance by potentially sensitizing tumors to ferroptosis. Further studies are warranted to fully explore this synergistic effect.

Abstract citation ID: lvag096.1814

EP1764 - LBA_ECE_1033 - A decade-long diagnostic journey: central diabetes insipidus as the first manifestation of multisystem langerhans cell histiocytosis

Melinda Kolcsar[1] and Krisztina Lázár[2]
[1]*Pharmacy, Sciences and Technology of Targu Mures, Pharmacology and Clinical Pharmacy, George Emil Palade University of Medicine, Tg Mures, Romania;* [2]*Endocrinology, Mures County Clinical Hospital, Tg Mures, Romania*

Introduction: Langerhans cell histiocytosis (LCH) is a rare disorder characterized by clonal proliferation and tissue infiltration of CD1a/CD207-positive dendritic cells. Although bone and skin are the most commonly affected sites, the hypothalamic–pituitary axis may also be involved. Arginine vasopressin (AVP)

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

deficiency, presenting as central diabetes insipidus, may represent the first manifestation of the disease, often preceding the diagnosis of LCH.

Case Presentation: A previously healthy 31-year-old woman presented in December 2009 with severe polyuria and polydipsia, consuming approximately 16 liters of fluid daily. A positive water deprivation test confirmed central diabetes insipidus, while other pituitary hormones were initially within the normal range. Sellar MRI demonstrated the absence of the posterior pituitary bright spot, a thickened pituitary stalk (4.5 mm), and a small suprasellar lesion, initially interpreted as lymphocytic hypophysitis. Desmopressin therapy successfully controlled symptoms. During follow-up, the patient developed central hypogonadism and central hypothyroidism requiring hormone replacement. Serial MRI examinations showed progressive enlargement of the pituitary stalk lesion, which grew until 2021 (measuring $10 \times 7 \times 8$ mm), after which it stabilized. In 2022, a fracture of the left eighth rib prompted further investigation, revealing an osteolytic lesion. Histopathological examination following partial rib resection confirmed Langerhans cell histiocytosis (positive for CD1a, CD68, and S100). Retrospective evaluation also identified a previously excised vulvar lesion as LCH. Genetic analysis revealed the presence of wild-type BRAF-V600E. Follow-up PET-CT scans demonstrated decreasing metabolic activity of residual lesions under bisphosphonate therapy.

Discussion and Conclusion: The multisystem nature of the disease suggests that AVP deficiency and progressive multiple pituitary hormone deficiencies result from hypothalamic–pituitary infiltration by LCH. This case highlights AVP deficiency as a potential sentinel manifestation of infiltrative disorders, particularly when associated with thickening of the pituitary stalk.

Abstract citation ID: lvag096.1815

EP1766 - LBA_ECE_1328 - Thoracic paraganglioma with SDHB germline mutation

Constantina Philippidou, Chrysanthi Balodimou, Georgios Christantoniou, Charalampos Papadopoulos, Eleana Zisimopoulou, Maria Boudina and Alexandra Chrisoulidou
Department of Endocrinology, Theagenio Cancer Hospital, National Center of Oncology, Thessaloniki, Greece

Thoracic paragnagliomas (PPGLs) are rare neuroendocrine tumors arising from extra-adrenal chromaffin tissue and are frequently associated with hereditary syndromes, such as mutations in the succinate dehydrogenase subunit B (SDHB) gene. These tumors often present diagnostic and therapeutic challenges due to their location and potential for multifocal and progressive disease.**Objective:** To present a case of intrathoracic paraganglioma located behind the inferior vena cava in a young patient harboring an SDHB germline mutation.

Methods: A 21-year-old woman presented with long-standing hypertension, palpitations, vomiting and intermittent febrile episodes, for approximately two years. Cardiac magnetic resonance imaging identified a 35×35 mm mass posterior to vena cave without evidence of vascular invasion. Biochemical assessment demonstrated elevated 24-hour urinary metanephrines and normetaphrines. Histopathological evaluation following unsuccessful surgical intervention due to extensive hemorrhage, confirmed paraganglioma, with Ki-67 index 2%, 10 mitotic figures, absence of necrosis, and positive synaptophysin immunostaining and CgA. Fuctional imaging included MIBG scintigraphy, Ga-PET, FDG-PET.

Results: Ga-PET demonstrated uptake in the main lesion (SUVmax 4,6), while FDG-PET revealed intense metabolic activity (SUVmax 44,6) and two additional nodular lesions, suggestive of multifocal disease involvement. The patient underwent embolization followed by three therapeutic doses of 131-MIBG, confirming uptake in the known lesions. Follow-up computed tomography scans indicated further progressive enlargement of the lesion to 5 cm despite medical treatment with alpha-adrenergic blockade, beta-blockers, and calcium channel antagonists.

Conclusion: Thoracic paragangliomas associated with SDBH mutations represent rare but clinically significant entities with potential for multifocal progression. Management often requires a multimodal approach, including embolization, radionuclide therapy and systemic or targeted treatments such as peptide receptor radionuclide therapy (PRRTs), chemotherapy, tyrosine kinase inhibitors and local therapies. Multidsciplinary evaluation is essential for optimizing patient outcomes.

Abstract citation ID: lvag096.1816

EP1767 - LBA_ECE_1133 - Self-management education in type 2 diabetes: a path to better glycemic control and patient outcomes

Daria Lahoda, Valentyna Velychko and Yelyzaveta Tuliantseva
Odessa National Medical University, Odesa, Ukraine

Background: Type 2 diabetes remains a major global health challenge, particularly in patients with obesity, where glycemic control is often suboptimal. Patient education and self-management are ключові components of effective care. However, real-world evidence on their clinical impact is limited, highlighting the need to evaluate their role in improving metabolic outcomes and quality of life.

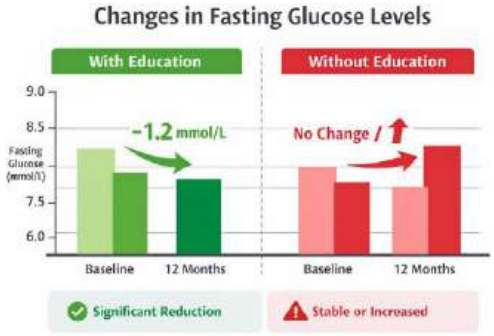
Materials and methods: A prospective observational study included patients with type 2 diabetes and obesity or overweight, divided into groups with and without self-management education. Clinical, metabolic, and behavioral parameters were assessed at baseline and after 3, 6, and 12 months. Statistical analysis was performed to evaluate changes and between-group differences.

Aim: To evaluate the impact of self-management education on glycemic control and clinical outcomes in patients with type 2 diabetes, with a focus on metabolic parameters, behavioral changes, and overall patient-related outcomes.

Results: Self-management education significantly improved glycemic control, with a sustained reduction in HbA1c over 12 months.

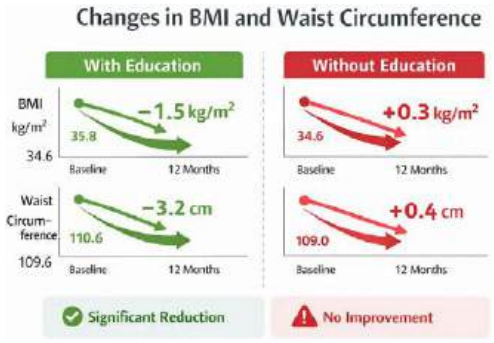
Fasting glucose levels decreased significantly in trained patients, while remaining stable or worsening without education.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

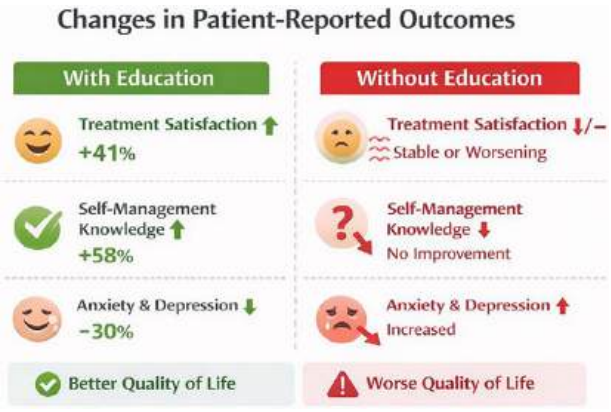


Timepoint	With Education	Without Education
Baseline	~7.6%-7.9%	~7.3%-7.5%
3 months	↓ significant	~no change
6 months	↓ further	slight increase
12 months	~6.8%-7.0%	~7.6%-7.9%

Patients who received education showed significant reductions in BMI and waist circumference, indicating improved metabolic status.



Education was associated with improved treatment satisfaction, reduced anxiety and depressive symptoms, and better self-management knowledge.



Conclusions:

1. Self-management education is a key driver of improved glycemic control in type 2 diabetes.
2. Educational interventions positively influence metabolic, behavioral, and psychological outcomes.
3. Integrating patient education into routine care can significantly enhance long-term diabetes management.

Abstract citation ID: lvag096.1817

EP1769 - LBA_ECE_1076 - Severe hyponatremia (104 mmol/L) and SIADH-like syndrome associated with tirzepatide: a novel safety signal

Nithin Tumkur Prasad[1,2]
[1]Bengaluru, India; [2]Department of Internal Medicine, Apollo Speciality Hospital | Best Hospital in Jayanagar, Bengaluru, India

Introduction: Tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, is increasingly used for the management of type 2 diabetes and obesity. While gastrointestinal adverse effects are well recognised, its impact on water homeostasis remains poorly characterised.

Aim: To report a case of severe symptomatic hyponatremia with syndrome of inappropriate antidiuretic hormone secretion (SIADH)-compatible biochemical features temporally associated with tirzepatide therapy.

Case Report: In early February 2026, a 46-year-old woman with type 2 diabetes and obesity (BMI 45.4 kg/m^2) developed severe symptomatic hyponatremia two weeks after initiation of tirzepatide. At presentation, serum sodium was 104 mmol/L (baseline within normal limits) with a calculated serum osmolality of 224 mOsm/kg. Clinical examination was consistent with euvolemia.

Investigations: Biochemical evaluation demonstrated hypoosmolar hyponatremia with inappropriately elevated urine osmolality and urine sodium (assessed following appropriate diuretic washout), consistent with SIADH physiology. Adrenal insufficiency and hypothyroidism were excluded with normal morning cortisol and thyroid function tests. No alternative etiology was identified.

Management: The patient was managed in the intensive care unit with hypertonic saline and fluid restriction. Sodium correction was carefully controlled (<10 mmol/L per 24 h) to minimise the risk of osmotic demyelination syndrome. Tirzepatide was discontinued. Serum sodium normalised gradually with complete clinical recovery and no neurological sequelae.

Conclusion: The case suggests a probable association between tirzepatide and SIADH-compatible hyponatremia. Potential mechanisms include non-osmotic vasopressin release due to gastrointestinal symptoms or direct pharmacological effects on water regulation. The profound hyponatremia (Na 104 mmol/L) may reflect a synergistic 'triple-hit' mechanism: GLP-1/GIP-mediated inhibition of the renal sodium-hydrogen exchanger 3 (NHE3), increased atrial natriuretic peptide (ANP) release, and reduced oral solute intake. This is consistent with emerging pharmacovigilance signals suggesting dual-incretin agonists may contribute to SIADH-like presentations.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Impact: This case highlights a clinically significant and potentially under-recognised association between tirzepatide and severe hyponatremia. Given the frequency of gastrointestinal adverse effects during treatment initiation, heightened clinical vigilance may facilitate early identification and management of drug-associated hyponatremia. A low threshold for serum sodium monitoring should be considered in patients with significant gastrointestinal symptoms or concomitant diuretic use. Given its direct clinical implications, this case may inform practice and stimulate discussion in a broad cardiometabolic audience.

Abstract citation ID: lvag096.1818

EP1772 - LBA_ECE_1314 - Not All SIADH Is SIADH": chronic hyponatraemia revealing radiation-induced isolated secondary adrenal insufficiency despite preserved pituitary function

Paul Chatee, Muhammad Waqar Khan, Nur Fatin Aqilah Binti Suharinizam and Paul Pravin
Endocrinology, Univeristy Hospital Limerick, Limerick, Ireland

Background: Hyponatraemia is frequently attributed to Syndrome of Inappropriate Antidiuretic Hormone Secretion, particularly in patients with intracranial pathology. However, SIADH remains a diagnosis of exclusion, and adrenal insufficiency must be excluded prior to confirmation.[1] Secondary adrenal insufficiency is an important mimic, particularly following cranial radiotherapy.[2]

Case Presentation: We report a patient with a history of astrocytoma treated with cranial radiotherapy, presenting with chronic hypotonic hyponatraemia. Initial evaluation demonstrated low serum osmolality with inappropriately elevated urine osmolality and sodium, consistent with euvolaemic hyponatraemia, leading to a presumptive diagnosis of SIADH. Fluid restriction resulted in minimal improvement.

Further evaluation revealed a low morning cortisol. Plasma ACTH was within the reference range but inappropriately normal in the context of cortisol deficiency. A Synacthen test demonstrated a borderline cortisol response. Given persistent clinical suspicion, and as insulin tolerance testing was contraindicated due to intracranial pathology and seizure risk, a Glucagon stimulation test was performed, demonstrating an inadequate cortisol response and confirming secondary adrenal insufficiency.

Other pituitary axes were preserved, consistent with isolated corticotroph deficiency. In the context of prior cranial radiotherapy, this was attributed to hypothalamic–pituitary dysfunction. Glucocorticoid replacement resulted in rapid normalisation of serum sodium.

Discussion: Secondary adrenal insufficiency can mimic SIADH both clinically and biochemically. Cortisol deficiency increases vasopressin secretion and impairs free water clearance, producing an indistinguishable biochemical profile. In early disease, adrenal responsiveness to exogenous ACTH may be preserved, resulting in a borderline Synacthen response, while dynamic testing reveals impaired ACTH reserve. This highlights the importance of interpreting results in clinical context and pursuing further testing where suspicion persists.[3]

Conclusion: Adrenal insufficiency must be excluded in all cases of hyponatraemia prior to diagnosing SIADH. This case highlights the limitations of the Synacthen test and the importance of second-line dynamic testing, as failure to recognise this may delay treatment and worsen outcomes.

References

1. Spasovski G, et al. *Eur J Endocrinol*. 2014.
2. Higham CE, et al. *Endocr Dev*. 2013.
3. Crowley RK, et al. *Clin Endocrinol*. 2014.

Abstract citation ID: lvag096.1819

EP1773 - LBA_ECE_1350 - Coital cramps as a highly specific sentinel manifestation of subclinical hypokalemia in primary hyperaldosteronism: a striking case of refractory hypertension in a young woman

Claudia Arnas-Leon[1,2], Asuncion Acosta-Merida[3], Inmaculada Molinero-Marcos[1], Borja Santana-Ojeda[1], Ricardo Jose de Leon-Durango[1], Alba Hernandez-Lazaro[4], Carmen Acosta-Calero[5], Agnieszka Kuzior[2], Fabianna Genesi[6] and Francisco Javier Martinez-Martin[1,2]
[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain; [3]Digestive and General Surgery, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [4]Servei d'Endocrinologia i Nutricio, Parc Taulí Hospital Universitari, Sabadell, Barcelona, Spain; [5]Cardiology, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [6]Centro de Salud de Arucas, Arucas, Las Palmas, Spain

Background: Primary aldosteronism (PA) is the most common cause of secondary hypertension. However, it remains substantially underdiagnosed, often with prolonged diagnostic delay. Although classically characterized by hypertension and hypokalemia, fewer than one-third of patients present with overt hypokalemia, limiting clinical recognition.

In young, lean women, PA may present predominantly with hypokalemia-related neuromuscular symptoms, even in the absence of overt hypertension. Atypical presentations may further obscure diagnosis. We report a case of PA presenting with a previously undescribed symptom.

Case Presentation: A 30-year-old lean woman was referred to Endocrinology for refractory hypertension, maintained for the last three years. She did not use oral contraceptives. Over approximately the same timeframe she was experiencing recurrent intense bilateral lower limb cramps which were triggered only during sexual intercourse, resolving promptly with rest. She had undergone a thorough dyspareunia workup in a Gynecology Clinic with negative results. Serum potassium was borderline low (3.64 mEq/L) in multiple determinations, without overt hypokalemia. The renal angio-MRI showed normal renal arteries but also revealed a 1.2 cm left adrenal adenoma with signal drop on opposed-phase T1 imaging, suggestive of lipid-rich adenoma. After washout of the antihypertensive treatment, adrenal function testing was performed in the follicular phase, showing adequate cortisol suppression and normal plasma metanephrines, but borderline results for primary aldosteronism (aldosterone 151 pg/mL, renin 5.63 mIU/L, aldosterone-to-renin ratio 2.68). Confirmatory testing with captopril challenge showed

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

non-suppressible aldosterone (227-214 pg/mL) and persistently suppressed renin (1.61-1.57 mIU/) confirming PA (Litinsky-Conn syndrome). Adrenal venous sampling was not performed due to the patient's age. Laparoscopic left adrenalectomy was successfully performed. Postoperatively, serum potassium normalized rapidly, hypertension improved allowing drug withdrawal, and coital cramps resolved completely.

Discussion: This case illustrates a remarkably specific "stress test" unmasking relative hypokalemia: the autonomic activation, sustained isometric muscle contraction, and metabolic demand during coitus lowered the threshold for neuromuscular irritability due to aldosterone-driven potassium wasting. Literature on situation-specific neuromuscular symptoms in PA is virtually absent; generalized cramps or weakness predominate when hypokalemia is overt. The rapid and complete resolution of this sentinel symptom post-adrenalectomy underscores the causal link and highlights the value of detailed, unbiased history-taking in young patients with resistant hypertension.

Conclusions: Coital cramps can serve as a unique sign of underlying PA-associated hypokalemia. Systematic screening for PA should be pursued in refractory hypertension irrespective of potassium levels or classic features, as subtle or unexpected symptoms may hold the diagnostic key.

Abstract citation ID: lvag096.1820

EP1774 - LBA_ECE_1371 - Arginine vasopressin deficiency as the initial presentation of suspected multisystem Langerhans cell histiocytosis

Nisa Babacanlar, Kadircan Karatoprak, Can Özgü, Alper Batu, Rümeysa Kantar, Ozen Oz Gul, Soner Cander, Canan Ersoy and Erdinc Erturk
Department of Endocrinology and Metabolism, Bursa Uludag University, Bursa, Turkey

Background: Arginine vasopressin deficiency (AVP-D) is a rare disorder characterized by impaired vasopressin secretion, resulting in polyuria and polydipsia. Although many cases are idiopathic, infiltrative and neoplastic disorders should be considered, particularly in patients with pituitary stalk abnormalities. Langerhans cell histiocytosis (LCH) is a rare inflammatory myeloid neoplasm that may involve multiple organs, including the lungs and hypothalamic-pituitary axis. AVP-D may rarely be the first manifestation of multisystem disease.

Case Presentation: A 24-year-old man presented with progressive polydipsia and polyuria. His daily fluid intake had increased from 5-6 L to approximately 15 L. He had no history of head trauma, malignancy, cranial surgery, or medication use, and reported smoking one pack every three days. Initial evaluation revealed a urine density of 1.004 and serum sodium of 147 mmol/L. The patient was diagnosed with AVP-D and started on desmopressin therapy. Following treatment, urine osmolality increased and urine output decreased, supporting the diagnosis. Pituitary magnetic resonance imaging demonstrated loss of the posterior pituitary bright spot and thickening of the infundibular stalk (3.5 mm), suggesting an infiltrative process. Seven months after the diagnosis of AVP-D, thoracic computed tomography performed for an unrelated indication revealed bilateral upper lobe–predominant cystic changes and multiple centrilobular ground-glass nodules, raising suspicion for pulmonary Langerhans cell histiocytosis; miliary tuberculosis was also considered in the differential diagnosis but was subsequently excluded based on clinical and microbiological evaluation. Positron emission tomography showed diffuse reticulonodular changes with mild heterogeneous hypermetabolic activity, consistent with interstitial lung involvement. Bronchoalveolar lavage cytology was benign, immunohistochemical staining was negative for CD1a and Langerin, and BRAF V600 mutation analysis was negative. Given the characteristic radiological findings and clinical context, thoracic imaging was considered highly compatible with pulmonary LCH, and invasive biopsy was not pursued. Considering the coexistence of AVP-D, pituitary stalk thickening, pulmonary involvement, and smoking history, multisystem LCH was considered the most likely diagnosis.

Conclusion: AVP-D may be the initial manifestation of multisystem LCH. In patients presenting with AVP-D and pituitary stalk thickening, LCH should be considered in the differential diagnosis even in the absence of histopathological confirmation, particularly when characteristic pulmonary findings emerge during follow-up. Although BRAF mutations are detected in more than half of cases, their absence does not exclude the diagnosis. Early recognition of this association is important for timely evaluation of systemic involvement and long-term endocrine follow-up.

Abstract citation ID: lvag096.1821

EP1776 - LBA_ECE_1240 - Targeting prediabetes and MASLD: effects of a nutraceutical based on white mulberry, fenugreek, inulin, niacin, chromium and zinc on FIB-4 score and C-reactive protein in subjects with prediabetes

Inmaculada Molinero-Marcos[1], Sara Andrada-Diaz[2], Agnieszka Kuzior[3], Ana Maria Sanchez Garcia[3], Juan Fernandez-Jimenez[3], Irene Hernandez-Hernandez[1,3], Facundo Marcelo Guerrero-Kesselman[3], Borja Santana-Ojeda[1], Claudia Arnas-Leon[1,3] and Francisco Javier Martinez-Martin[1,3]
[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Medical Advisory, Bioksan Naturalmente Juntos, Las Palmas de Gran Canaria, Spain; [3]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain

Background and Objectives: Prediabetes is frequently associated with overweight or obesity, low-grade chronic inflammation, and metabolic dysfunction-associated steatotic liver disease (MASLD). We conducted a trial in patients with prediabetes to evaluate a novel nutraceutical. This formulation includes several key components:

- White mulberry (*Morus alba*) leaf extract, containing the α-glucosidase inhibitor 1-deoxynojirimycin;
- Fenugreek (*Trigonella foenum-graecum*) extract, an AMPK activator;
- Inulin (a soluble fiber) and *Lactiplantibacillus plantarum* A7 (a probiotic);
- Niacin (vitamin B_3), chromium, and zinc.

The primary endpoint was the change in insulin resistance, estimated by HOMA2-IR index, a predictor for the development of type 2 diabetes (T2DM).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

In this substudy, we aimed to assess changes in liver enzymes and the FIB-4 score. We also examined related changes in body mass index (BMI) and C-reactive protein (CRP), while monitoring the overall tolerability.

Methods: Adult participants with prediabetes were enrolled in this open-label trial to receive a daily dose of the nutraceutical over a 6-month period, including a 3-month interim assessment.

The clinical evaluations at each visit included BMI, HOMA2-IR index, FIB-4 score, liver enzymes (ALT, AST, GGT) and CRP. Additionally, a questionnaire was used to record adverse effects.

Results: Out of the 144 individuals enrolled, 113 finished the trial (71 female, age 56.4 ± 6.7 years).

The HOMA2-IR index decreased from 1.659 ± 0.721 to 1.269 ± 0.581, (−23.5%, $P < .001$). 33 participants (29.2%, $P < .001$) achieved normoglycemia, whereas 3 (2.65%, p NS) progressed to T2DM. Notably, there were no significant alterations in body weight during the study period.

The FIB-4 score decreased from 1.42 ± 0.25 to 1.22 ± 0.24 ($P = .003$). The number of patients with FIB-4 <1.45 (cutoff point for low risk of liver fibrosis) increased significantly ($P = .028$) from 61 (54%) to 78 (69%). Plasma CRP decreased from 3.66 ± 1.97 to 2.89 ± 1.27 (−21%; $P < .001$).

Although a few patients (9, 8%) reported mild gastrointestinal side effects, the treatment was well-tolerated overall, with no serious issues or related study withdrawals.

Conclusions: The nutraceutical was well-tolerated and yielded significant improvements in insulin resistance among patients with prediabetes, occurring independently of alterations in body mass index.

Treatment was further associated with a marked attenuation of systemic inflammation and a reduction in liver fibrosis risk, as characterized by significant decreases in CRP levels and FIB-4 scores, alongside an increased proportion of patients achieving low-risk status. These findings suggest a potential therapeutic role in mitigating the metabolic and hepatic dysfunctions associated with prediabetes, warranting further validation in controlled clinical trials.

Abstract citation ID: lvag096.1822

EP1777 - LBA_ECE_1242 - Reversing early metabolic damage with white mulberry leaf extract: nutraceutical-driven improvements in insulin resistance and renal risk in subjects with prediabetes

Borja Santana-Ojeda[1], Sara Andrada-Diaz[2], Agnieszka Kuzior[3], Ana Maria Sanchez Garcia[3], Juan Fernandez-Jimenez[3], Irene Hernandez-Hernandez[3], Facundo Marcelo Guerrero-Kesselman[3], Inmaculada Molinero-Marcos[1], Claudia Arnas-Leon[1,3] and Francisco Javier Martinez-Martin[1,3]

[1]*Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain;* [2]*Medical Advisory, Bioksan Naturalmente Juntos, Las Palmas de Gran Canaria, Spain;* [3]*Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain*

Background and Objective: Globally, diabetic nephropathy represents a major concern for public health. Prediabetes is associated with insulin resistance, low-grade inflammation, endothelial dysfunction, and activation of the renin–angiotensin system. These mechanisms can lead to subtle glomerular damage and increased urinary albumin excretion even before the onset of overt hyperglycemia.

We investigated the effects of a novel nutraceutical in individuals with prediabetes. This formulation combined white mulberry leaves (containing the potent competitive α-glucosidase inhibitor 1-deoxynojirimycin), fenugreek (an AMPK activator), inulin (soluble fiber), the probiotic *Lactiplantibacillus plantarum* A7, niacin, chromium, and zinc. While the primary endpoint focused on changes in the HOMA2-IR insulin resistance index (a key indicator for the risk of developing T2DM) this specific substudy evaluates alterations in renal function.

The objective was to examine changes in the albumin/creatinine ratio (ACR) and estimated glomerular filtration rate (eGFR), and to determine how these relate to changes in HOMA2-IR.

Methods: This open-label study enrolled adults with prediabetes who were administered the nutraceutical once daily over a 6-month period. Assessments for eGFR, ACR, and HOMA2-IR were conducted at baseline, at a 3-month interim visit, and at the 6-month conclusion. Furthermore, any issues regarding tolerability were documented using a participant questionnaire.

Results: The study was completed by 113 of the 144 enrolled patients (78.5%), including 71 women, with a mean age of 56.4 ± 6.7 years. A significant reduction in HOMA2-IR was observed, falling from 1.659 ± 0.721 to 1.269 ± 0.581 (−23.5%, $P < .001$). While 3 patients (2.65%, p NS) progressed to T2DM, 33 individuals (29.2%, $P < .001$) successfully reached normoglycemia.

Regarding renal markers, eGFR showed no significant variation, moving from 86.5 ± 11.9 to 88.3 ± 11.6 ($P = .251$, paired t-test). However, albuminuria experienced a significant decline from 28.4 ± 15.2 to 21.5 ± 14.3 mL/min/1.73 m^2 (−24.3%, $P = .036$, Mann-Whitney´s U).

A backwards stepwise multiple regression analysis identified the change in HOMA2-IR as a significant independent predictor of eGFR alterations (p-value 0.012). In contrast, changes in HbA1C, body weight, or mean blood pressure did not function as independent predictors.

Conclusions: This study shows that the nutraceutical significantly improves insulin resistance in prediabetes, with nearly 30% of participants reverting to normoglycemia. Kidney filtration (eGFR) remained stable, while albuminuria decreased significantly, indicating reduced early renal damage. Changes in insulin resistance independently predicted renal function changes, unlike HbA1c, weight, or blood pressure. These findings suggest that improving insulin sensitivity may play a key role in protecting renal health, supporting this nutraceutical as a promising strategy for early metabolic and renal risk reduction.

Abstract citation ID: lvag096.1823

EP1778 - LBA_ECE_1292 - GLP-1 receptor agonist therapy in "double diabetes": a case demonstrating arked improvement in glycaemic control and insulin requirements in type 1 diabetes

Tabinda Dugal

Endocrinology Unit, Lusail, Qatar

Background: "Double diabetes" describes individuals with type 1 diabetes (T1D) who develop insulin resistance, often associated with overweight or obesity, leading to increased insulin requirements and glycaemic variability. While GLP-1 receptor agonists

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

(GLP-1RA) are established in type 2 diabetes, their use in T1D remains off-label. Randomised trials (ADJUNCT ONE and TWO) and recent meta-analyses demonstrate modest HbA1c reductions (~0.2%-0.4%), weight loss (~3-5 kg), and reductions in insulin dose (10%-20%), albeit with an increased risk of ketosis and hyperglycaemia with reduced insulin dosing.[1-4]

Case Presentation: A 38-year-old Danish male with a 12-year history of T1D and 10-year history of hypertension was reviewed in October 2025. He was treated with basal-bolus insulin (faster aspart 10-15 units per meal; insulin degludec 46 units daily) and atorvastatin. BMI was 28 kg/m^2 (102 kg, 191 cm). There was no evidence of microvascular or macrovascular complications.

Continuous glucose monitoring (Libre) showed suboptimal control:

- Time in range (3.9-10 mmol/L): 55%
- Time >13 mmol/L: 16%
- Recurrent nocturnal hypoglycaemia

GLP-1RA therapy was initiated off-label in January 2026 following structured counselling regarding risks, ketone monitoring, and conservative insulin dose adjustment.

At 2-month follow-up:

- Mealtime insulin reduced to ~6 units/meal
- Basal insulin reduced from 46 to 38 units
- Time in range improved to 80% (HbA1c improved from 7.2% to 6.5%
- Marked reduction in hypoglycaemia
- Significant improvement in patient-reported quality of life

Discussion: This case demonstrates clinically meaningful improvements exceeding those typically reported in trials. GLP-1RA effects include delayed gastric emptying, appetite suppression, and reduced postprandial glycaemic excursions. However, safety is critical; trials report increased risk of ketosis, particularly with rapid insulin reduction.[1,2]

Contraindications include prior pancreatitis, medullary thyroid carcinoma or MEN2, severe gastroparesis, and high risk of insulin omission.

Conclusion: GLP-1RA therapy may offer substantial benefit in selected patients with T1D and insulin resistance. Careful patient selection, education, and monitoring are essential. This case supports a personalised adjunctive role of GLP-1RA in “double diabetes.”

References

1. Mathieu C, et al. *Lancet Diabetes Endocrinol*. 2016.
2. Ahrén B, et al. *Lancet Diabetes Endocrinol*. 2016.
3. Park J, et al. *Diabetes Obes Metab*. 2020.
4. Dicembrini I, et al. *Acta Diabetol*. 2021.
5. ADA Standards of Care 2024 – Pharmacologic Approaches.

Abstract citation ID: lvag096.1824

EP1779 - LBA_ECE_1459 - Beyond idiopathic diabetes insipidus: dynamic pituitary stalk changes and progressive hormonal deficits in children—case series

Diandra Carmen Cosma[1], Bianca Andreea Balint[1], Radomir Lidia[1], Aura Madalina Boboc[1,2], Andreea Cristiana Brehar[1], Elena Braha[1] and Iuliana Gherlan[1,2]

[1]Pediatric Endocrinology, CI Parhon National Institute of Endocrinology, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Introduction: Pituitary stalk lesions are rare hypothalamic–pituitary disorders, most often identified during the diagnostic work-up of patients presenting with diabetes insipidus.

Aim: To describe the clinical and imaging findings in a series of pediatric patients presenting with diabetes insipidus evaluated in a pediatric endocrinology department between 2011 and 2025.

Results: We included 10 patients (6 boys, 4 girls), aged 3.1-13.3 years at diagnosis; 9 presented with complete and 1 with partial diabetes insipidus. Eight patients were diagnosed in our department, while 2 were already under treatment.

Anterior pituitary function. At diagnosis, one patient had associated pituitary deficiency—central hypothyroidism (case_9). During a median follow-up of 3.9 years, 5 patients (50%) developed growth hormone (GH) deficiency; 3 received somatropin for short stature, while 2 maintained normal height. Three patients developed central adrenal insufficiency during follow-up (at 10.2 and 13.8 years in two cases; missing data in one case). One patient presented panhypopituitarism and hyperprolactinemia (case_10) during follow-up.

Imaging findings. At diagnosis, 8 patients had a normal anterior pituitary on MRI, one had a non-functioning microadenoma and one had an infundibular tumor. The posterior pituitary bright spot was absent in 9 patients. Pituitary stalk thickening was identified in 5 patients at diagnosis (4 by MRI, 1 by CT) and in 2 additional patients during follow-up. Five patients had an undulating evolution of the stalk thickening, but eventually showed partial regression.

Pituitary stalk and hormonal deficiencies. Among the 7 patients with stalk thickening, 3 developed pituitary deficiencies during follow-up (GH deficiency in 3, adrenal insufficiency in 1). Notably, one of the two patients with initially normal stalk developed both GH deficiency and central adrenal insufficiency.

Etiological screening. Serum β-human chorionic gonadotropin and alpha-fetoprotein were normal in all patients, making germinoma unlikely. In one patient (case_7) the suspicion was high, so cerebrospinal fluid evaluation was proposed. Langerhans cell histiocytosis was excluded in 3 cases (case_3, case_6, case_9). One patient is under evaluation for hypophysitis (case_4). One patient (case_6) had a cranial trauma before the onset of polyuria and polydipsia. Syndromic diabetes insipidus was suspected in one case (case_10), with negative array-CGH and NGS; whole exome sequencing is ongoing.

Conclusion: Idiopathic diabetes insipidus in children may mask a dynamic hypothalamic–pituitary process, characterized by evolving pituitary stalk abnormalities and progressive hormonal deficiencies. In our series, imaging changes did not consistently predict endocrine outcome. Larger registries are needed to better define long-term outcomes.

Abstract citation ID: lvag096.1825

EP1780 - LBA_ECE_1440 - Virilization in a female child: taking clues from antenatal history

Sai Subrahmanyam Pappu, Bhanu Nalluri, Neelaveni Kudugunti and Rakesh Sahay

Osmania General Hospital, Hyderabad, India

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Virilization in a female child is due to androgen exposure during 10-12 weeks of gestation. The most common cause is CAH due to 21 OH deficiency. Placental Aromatase deficiency is a rare disorder that leads to defective conversion of androgens into estrogens by the placenta, thus causing maternal and fetal virilization. The effected infants present with atypical genitalia and no features of CAH like salt wasting crisis or hyperpigmentation and the virilization is characteristically non progressive in the immediate postnatal period.

Case Presentation: A 2 months old child, reared as a female was brought with history of enlarged phallic structure noted at birth. There was no history of pigmentation or crisis.

Antenatally, mother had a severe form of cystic acne.

On examination, Genitalia were female looking with an enlarged phallic structure of 15 mm in length.

There were no palpable gonads, labioscrotal swellings or inguinal hernias.

There was a single urogenital opening, Prader stage 3, with evidence of posterior fusion of labioscrotal folds.

No hyperpigmentation or rugosity was seen.

EGS was 2.5 with an anogenital ratio of 0.7.

Serum potassium- 4.9 meq/l.

Stimulated 17 OHP-75 ng/dl, Cortisol-41.8 microgram/dl-Normal.

Androstenedione was elevated at 392 ng/dl and testosterone was also elevated, 70 ng/dl.

FSH was elevated at 25.34 mIU/mL.

MRI pelvis identified the presence of Uterus and Ovaries.

In view of elevated androgens, no biochemical features of CAH and history of maternal virilization, Aromatase deficiency was suspected and whole exome sequencing was sent A Homozygous mutation in CYP19A1 gene with a novel c.[1369C>T] variant on exon 10 was identified.

The latest follow up was at 12 months of age where the child was well and maternal acne was spontaneously resolving.

Treatment: The proposed management is usually estrogen supplementation at puberty for development of secondary sexual characters and preserving bone mineral density. Monitoring for Rupture of ovarian cysts. The child was not started on any estrogen.

Follow-up: The child was last seen at 12 months of age, was thriving well.

Acne almost completely resolved in the mother.

The child is planned for feminizing genitoplasty.

Conslusion: We hereby present a case of virilization in mother and neonate due to placental aromatase deficiency. This is a rare disorder can be suspected when there is history of antenatal maternal virilization. The genetic variant in our case is a novel mutation. The identification of this disease has important therapeutic implications for treatment and followup.

Abstract citation ID: lvag096.1826

EP1782 - LBA_ECE_1381 - Short- and long-term effects of hormonal replacement on body composition and metabolism in congenital hypogonadotropic hypogonadism—a study combining longitudinal and cross-sectional cohorts

Rui Zhang[1], Wenzhen Hao[2], Songbai Lin[2] and Xueyan Wu[2]

[1]Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [2]Peking Union Medical College Hospital, Beijing, China

Background & Aim: Congenital hypogonadotropic hypogonadism (CHH) is characterized by testosterone deficiency and is associated with adverse body composition and metabolic abnormalities. However, the temporal dynamics of treatment-induced changes and the extent of metabolic normalization remain unclear. This study aimed to evaluate both short- and long-term effects of hormonal replacement on body composition, adipokines, and metabolic parameters in male CHH patients.

Methods: For the short-term analysis, a **longitudinal cohort** of 15 untreated CHH patients was prospectively followed for 3-10 months during testosterone-based therapy. For the long-term analysis, a **cross-sectional study** was conducted, comparing 33 treated CHH patients (mean therapy duration 4.8 ± 2.3 years) with 33 untreated patients and 21 age-matched healthy controls. Body composition was assessed by dual-energy X-ray absorptiometry (DXA). Serum biochemical parameters, adipokines (leptin, adiponectin), and insulin sensitivity indices were measured.

Results: After short-term treatment (median 6 months), serum testosterone increased significantly (0.36-2.80 ng/mL, $P < .001$). Total fat percentage decreased (0.40-0.39, $P = .008$), lean mass (39.3-45.0 kg, $P < .001$) and basal metabolic rate increased, with parallel improvements in ALT, fasting glucose, and total cholesterol. After long-term treatment, treated patients showed significantly lower body fat percentage (32.0% vs 39.4%, $P < .001$) and visceral adipose tissue volume (741 vs 1015 cm^3, $P = .036$) compared with untreated patients, reaching healthy control levels for visceral fat, lean mass, bone mineral content, and insulin sensitivity indices. Serum leptin decreased significantly (9.62-1.81 ng/mL, $P < .001$), and testosterone was identified as an independent negative predictor of leptin ($\beta = -0.277$, $P = .004$) after adjusting for fat mass.

Conclusion: Hormonal replacement in CHH induces early favorable changes in body composition and metabolism within months. Long-term treatment achieves normalization of visceral fat, lean mass, and insulin sensitivity, though total adiposity remains incompletely reversed. DXA sensitively captures these treatment responses, and testosterone is independently associated with lower leptin levels, independent of fat mass.

Abstract citation ID: lvag096.1827

EP1787 - LBA_ECE_1348 - Real-world treatment persistence and metabolic outcomes with a GLP-1 receptor agonist (tirzepatide) in adults with obesity: an observational cohort study

Mirjeta Guni, Juliana Karanxha, Monika Dede and Florian Toti

Spitali Amerikan 3—American Hospital 3, Tirana, Albania

Background: Obesity is a chronic, relapsing disease associated with increased cardiovascular and metabolic risk. Tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, has demonstrated substantial weight reduction in randomized trials. However, real-world data on treatment persistence and early metabolic outcomes remain limited.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Objective: To evaluate treatment persistence, dose escalation, and changes in weight and metabolic parameters over six months following tirzepatide initiation in routine clinical practice.

Methods: This single-center observational cohort study included 50 adults with obesity (BMI ≥30 kg/m^2) who initiated tirzepatide between March and September 2025. All patients started at 2.5 mg weekly, with dose escalation every ~4 weeks based on tolerability and clinical response. Patients were followed for six months under standard care.

Primary outcomes were treatment persistence and changes in weight and BMI. Secondary outcomes included changes in HbA1c, systolic blood pressure (SBP), LDL cholesterol, dose achieved, and gastrointestinal adverse events. Analyses were descriptive.

Results: Treatment persistence at six months was 100%. Most patients (98%) reached ≥10 mg weekly. Final doses were 5 mg (2%), 10 mg (60%), 12.5 mg (12%), and 15 mg (26%).

Mean weight decreased from 111.4 ± 19.1 kg to 95.3 ± 19.3 kg (−16.1 ± 6.2 kg), corresponding to −14.7 ± 6.0%. BMI decreased from 38.6 ± 5.3 to 32.9 ± 5.8 kg/m^2 (−5.8 ± 1.8). Weight-loss thresholds achieved were ≥5% (94%), ≥10% (82%), ≥15% (50%), and ≥20% (16%).

HbA1c improved from 9.48 ± 1.10% to 6.52 ± 0.88% (−2.96 ± 0.73%). SBP decreased by −7.2 ± 4.9 mmHg, and LDL cholesterol by −12.1 ± 14.8 mg/dL.

Gastrointestinal adverse events were common but manageable: loss of appetite (80%), nausea (76%), vomiting (28%), diarrhea (24%), and constipation (20%). No treatment discontinuations due to adverse events were reported.

Conclusions: In this real-world cohort, tirzepatide was associated with high treatment persistence, substantial weight loss, and significant improvements in glycemic and cardiometabolic parameters over six months. These findings support its effectiveness in routine clinical practice when appropriate titration and follow-up are implemented. Longer-term studies are needed to assess sustainability and cardiovascular outcomes.

Keywords obesity, tirzepatide, GLP-1 receptor agonist, real-world evidence, weight loss, metabolic outcomes

Abstract citation ID: lvag096.1828

EP1789 - LBA_ECE_1152 - Short stature in a Tall syndrome: a rare Xq isochromosome Klinefelter variant in monozygotic twins

Leire Perez Garcia
Hospital Universitario Araba, Vitoria-Gasteiz, Spain

Background: Klinefelter syndrome (KS) is the most common sex chromosome aneuploidy in males (1:500-1000), typically characterized by tall stature. However, the isochromosome Xq variant is exceptionally rare, representing less than 0.3% of cases. Unlike classic 47,XXY KS, this specific variant lacks an extra copy of the *SHOX* gene (located on the short arm of the X chromosome, Xp), which often results in normal or short stature due to *SHOX* gene haploinsufficiency. We report a unique case of monozygotic twins with this rare variant and discordant growth patterns.

Case Presentation: A 14-year-old male was referred for evaluation of short stature (150 cm, −2.33 SDS, 1st percentile), with a mid-parental height of 179 ± 5 cm. The patient and his monozygotic twin were born preterm (30 weeks), appropriate for gestational age. Physical examination revealed prepubertal testes (<3 mL) and a 1-year bone age delay. Laboratory tests showed borderline low IGF-1; while a clonidine stimulation test ruled out GH deficiency, an IGF-1 generation test showed a 62% increase, suggesting bioinactive GH. Karyotype analysis identified the rare 47,XY,i(X)(q10) variant.

Subsequent evaluation of the monozygotic twin revealed the same karyotype despite less severe growth impairment (5th percentile). The second twin failed the clonidine test but passed an insulin tolerance test (ITT), with a 112% IGF-1 increase in the generation test. Both twins developed progressive hypergonadotropic hypogonadism. Semen analysis confirmed azoospermia, and no spermatozoa were identified via testicular biopsy for cryopreservation. Both siblings commenced testosterone replacement at age 17. Growth hormone therapy was denied by the advisory committee due to advanced bone maturity at the time of the request.

Conclusion: This case highlights the remarkable clinical heterogeneity of Klinefelter variants, even in monozygotic twins. The 47,XY,i(X)(q10) variant represents a significant diagnostic pitfall because it lacks the “tall stature” hallmark of classic KS. Clinicians should maintain a high index of suspicion for rare cytogenetic KS variants in adolescents presenting with unexplained short stature and microorchidism to ensure timely management of the GH-IGF-1 axis and appropriate fertility counseling.

Abstract citation ID: lvag096.1829

EP1790 - LBA_ECE_1129 - Clinical presentation of cystic or necrotic paragangliomas: insights from a single-center study and meta-analysis

Anna Maria Wiejak[1], Andreea Georgiana Constantinescu[1], Gintare Žygienė[2], Mercedes Robledo[3,4], Christian G. Ziegler[1], Jens-Peter Kühn[5], Ronald de Krijger[6,7], Christina Pamporaki[1], Matthias Meinhardt[8] and Nicole Bechmann[2,9]
[1]*Department of Medicine III, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany;* [2]*University Hospital Carl Gustav Carus, Technical University Dresden, Institute for Clinical Chemistry and Laboratory Medicine, Dresden, Germany;* [3]*Spanish National Cancer Research Centre (CNIO), Hereditary Endocrine Cancer Group, Human Cancer Genetics Program, Madrid, Spain;* [4]*Institute of Health Carlos III (ISCIII), Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), Madrid, Spain;* [5]*Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Institute and Policlinic for Diagnostic and Interventional Radiology, Dresden, Germany;* [6]*Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands;* [7]*Department of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands;* [8]*Department of Pathology, Faculty of Medicine Carl Gustav Carus, Technical University Dresden, Dresden, Germany;* [9]*Bielefeld, Germany*

(PGLs) are rare neural crest–derived tumors characterized by considerable morphological heterogeneity and variable clinical behavior. Some PGLs exhibit cystic or necrotic alterations, which may influence the clinical presentation and disease course; however, their prevalence and clinical relevance remain insufficiently defined. In this retrospective single-center study (2011-2021), 103 patients with confirmed PGLs were evaluated for cystic and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

necrotic alterations based on imaging findings, pathological reports, and pathological re-evaluation. Cystic alterations, including microscopic, macroscopic, and pseudocystic changes, were identified in 61.8% of tumors. Regardless of their morphological subtype, cystic alterations were not associated with differences in clinical presentation. In contrast, necrotic alterations were observed in 3.9% of PGLs and were associated with a significantly higher rate of metastasis (75% vs 10%, $P = .0124$), larger tumor volume (53.6 cm^3 vs 6.6 cm^3, $P = .0339$), and more pronounced clinical symptoms, including hypertension, palpitations, and weakness, compared with patients without cystic or necrotic lesions. Both cystic and necrotic alterations were more frequently observed in adrenal than in extra-adrenal PGLs. A complementary meta-analysis including 235 patients with PGLs confirmed the higher metastatic rate in necrotic tumors (16% vs 4.5%, $P = .0369$), which were also significantly more often associated with cardiovascular complications ($P < .0001$) compared with cystic PGLs. These findings suggest that pathological alterations, particularly necrosis, may have important implications for the clinical management of PGLs. Incorporating these features into preoperative assessment and follow-up strategies may improve risk stratification, given the increased metastatic potential and cardiovascular risk associated with necrotic PGLs.

Abstract citation ID: lvag096.1830

EP1791 - LBA_ECE_1162 - Relentless recurrence: multimodal treatment-refractory Cushing's disease with aggressive tumour progression, cranial nerve palsy, and neurovascular encasement

Mohammed Mohammed[1], Fresht Naomi[2], Anouk Borg[2], Ahmed Yousseif[1], Efthimia Karra[1], Eleni Armeni[1,2,3], Peirre Bouloux[2], Gayathri Bhaskaran[1], Nasreldin Gifoon[1] and Quazi Tamjidul Islam[1]

[1]*Endocrinology and Diabetes, Royal Free Hospital, London, United Kingdom;* [2]*University College Hospital, London, United Kingdom;* [3]*National and Kapodistrian University of Athens, Aretaieio Hospital, Athens, Greece*

Introduction: Aggressive ACTH-secreting pituitary adenomas causing refractory Cushing's disease is a formidable management challenge on its' own. We present a 50-year-old male with a three-decade history of recurrent disease resistant to successive surgical, radiotherapeutic, and pharmacological interventions, ultimately developing complex neurovascular involvement.

Case History: The patient underwent Le Fort maxillotomy with hypophysectomy (1995) and frontal craniotomy with external beam radiotherapy (1996) in Iran. Following relocation to the UK, transsphenoidal hypophysectomy in 2002 (NHNN) achieved remission until 2016. Relapse prompted metyrapone 500 mg TDS, repeat transsphenoidal surgery (November 2016), and Gamma Knife radiosurgery (2017). Histology confirmed an ACTH-expressing adenoma without atypical features. Block-and-replace therapy was commenced post-radiosurgery, and temozolomide was administered from 2021 to 2022. He has a background of hypertension and a right-sided ischaemic stroke in 2019 without residual deficit. Current treatment includes dexamethasone 0.5 mg, metyrapone (escalated to 500 mg three times daily), levothyroxine, desmopressin, testosterone, and atorvastatin.

Clinical Presentation and Investigations: Recurrence presented with new left sixth cranial nerve palsy causing diplopia, requiring strabismus surgery in 2025. Plasma ACTH increased progressively from 141 pmol/L (1280 pg/mL) in October 2024 to 387 pmol/L (3513 pg/mL) by December 2025 despite escalating blockade with Metyrapone and Dexamethasone as replacement, with variable serum cortisol (81-462 nmol/L; 2.9-16.7 µg/dL) indicating inadequate biochemical control. Panhypopituitarism was confirmed: suppressed TSH (<0.01 mU/L), low FSH/LH (<0.3 IU/L), low testosterone (<4.6 nmol/L; <1.3 ng/mL), undetectable prolactin and low IGF-1 (11.9 nmol/L).

Radiology: Pituitary MRI (February 2023) showed stable residual enhancing tissue in the right sella. Repeat MRI (March 2025) confirmed significant tumour growth with retroclival extension, partial effacement of the pre-pontine cistern, new contact with the basilar artery and right pons, and progressive right cavernous sinus invasion with encasement of the right internal carotid artery. The vessel remained patent. This was flagged as a significant finding likely to alter clinical management.

Management and Conclusion: Pituitary MDT deemed the tumour unsuitable for repeat Gamma Knife or surgery given prior irradiation and neurovascular encasement. Temozolomide rechallenge was recommended. This case highlights the relentless natural history of treatment-refractory Cushing's disease and the role of temozolomide rechallenge in aggressive pituitary tumours when surgical and radiosurgical options are exhausted.

Keywords Cushing's disease, ACTH-secreting adenoma, pituitary tumour, temozolomide, cavernous sinus invasion, cranial nerve palsy, refractory hypercortisolism

Abstract citation ID: lvag096.1831

EP1793 - LBA_ECE_1203 - The TENIS syndrome challenge: empiric RAI may be considered when chronic TSH suppression harms quality of life

Tatia Kutchava[1] and Natalia Jojua[2]

[1]*LTD Diacor, Tbilisi, Georgia;* [2]*Medison Holding, Tbilisi, Georgia*

Background: TENIS syndrome (TG positive, scan negative) can be a challenge for DTC, which mostly has an excellent long-term prognosis. Guidelines recommend avoiding RAI overtreatment, and dynamic risk stratification is used, but TENIS syndrome raises a clinical question whether empiric RAI may still be considered, especially when the TSH target cannot be relaxed.

Aim: To demonstrate that empiric RAI might still be relevant in managing TENIS syndrome and can be an option.

Method: Observational clinical case study: we followed a patient with confirmed TENIS syndrome for 3 years.

Clinical Case: A 17-year-old girl was diagnosed with DTC in 2023, when she underwent total thyroidectomy and RAI therapy (50 mCi). The histopathology result confirmed PTC, with 3 out of 8 lymph nodes showing metastasis (TNM: pT1bN1aMx, pN1a >2 mm). It was considered to have a low-intermediate risk (10%-15%) of recurrence, but pre-RAI TG (151.8 ng/mL) was a significant factor in deciding to perform RAI therapy, and the RAI scan showed pathological uptake in the neck. During LT4 suppression, TG tests remained above 6 ng/mL. A follow-up diagnostic RAI scan (10 mCi) with stimulated TG (139 ng/mL) was performed 6 months later and showed no pathological uptake.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Ultrasounds, neck and chest CT with and without contrast and FDG PET-CT revealed no structural pathology. Therefore, TENIS syndrome was confirmed. The TSH goal was set below the normal reference range because non-stimulated TG consistently remained above 4 ng/mL (>1 ng/mL indicates an incomplete biochemical response), and stimulated TG was over 100 ng/mL (>10 ng/mL indicates an incomplete response). The patient experiences weight loss and heart palpitations. Bone health is also a concern, as the patient already has confirmed permanent hypoparathyroidism. TG levels are highly TSH-dependent, with even a 12.5 mcg change in LT4 raising TG levels. Because of a low quality of life, we began to wonder whether the potential health risks and further decline in QoL might outweigh the benefits of avoiding additional RAI.

Results: Empiric RAI may have an advantage compared to prolonged TSH suppression in individualized cases when QoL is a concern.

Conclusion: When deciding between empiric RAI and ongoing TSH suppression, personalized management should be prioritized and empiric RAI may still be an option for patients.

Abstract citation ID: lvag096.1832

EP1795 - LBA_ECE_1156 - What beyond height? Quality of life in adults with growth hormone deficiency treated with recombinant human growth hormone

Magdalena Goralska[1,2], Marek Roslon[1], Agnieszka Stanczyk[1] and Urszula Ambroziak[1]

[1]Endocrinology and Internal Medicine Department, Warsaw Medical University, Warsaw, Poland; [2]Endokrynology, Medical University of Warsaw, Warszawa, Poland

Growth hormone (GH), beyond influencing growth processes in childhood, plays a crucial role in regulating metabolic processes throughout all stages of life. Its deficiency leads not only to metabolic consequences but also to reductions in muscle and bone mass, significantly increasing mortality from cardiovascular complications and osteoporotic fractures, while markedly impairing quality of life.

Decreased quality of life (QoL) is a common feature in adults with GH deficiency (GHD) and serves as a key measure of treatment efficacy. Various tools have been used to assess QoL in GHD studies, including the Adult Growth Hormone Deficiency Assessment (AGHDA).

Materials and Methods: In a single-center, observational, retrospective study, we evaluated 72 patients with growth hormone deficiency over 24 months of observations (2023-2025), all qualified for recombinant human growth hormone (rhGH) therapy. Patients with GHD requiring GH therapy were classified into two groups: childhood-onset GHD (CO-GHD) which also included patients with Prader-Willi syndrome and adult-onset GHD (AO-GHD).

The Quality of Life questionnaire (QoL-AGHDA) was administered. Biochemical and hormonal assessments were performed, including IGF-1 levels.

Results: Assessment of quality of life (QoL) using the Adult Growth Hormone Deficiency Assessment (AGHDA) scale demonstrated that pre-treatment QoL in adults with GHD is significantly lower than in the general population. However, rhGH replacement therapy leads to QoL improvements that can persist long-term for several years. In patients with multiple pituitary hormone deficiencies, adequate replacement of other pituitary axes was also critical.

Conclusions: Growth hormone deficiency in adults requires precise diagnostics and appropriately managed substitution therapy. Effective GH treatment positively impacts both the quality and longevity of life in patients with somatotropic pituitary insufficiency

Abstract citation ID: lvag096.1833

EP1796 - LBA_ECE_1318 - Two cases of familial partial lipodystrophy associated with a novel LMNA variant

Artemis Kyriakidou[1], Eirini Melidou[1], Georgios Karaliolios[1], Charilaos Kostoulas[2], Ioanna Bouba[2], Hlianna Korosidou[1], Maria Resta[3], Maria Zikopoulou[1], Anastasia Gkounta[1], Litsa Rakitzi[1], Maria Grammatiki[1], Ioannis Georgiou[2], Camille Vatier[4,5,6] and Kalliopi Kotsa[1]

[1]Division of Endocrinology and Metabolism—Diabetes Center, 1st Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA University Hospital, Thessaloniki, Greece; [2]Department of Medical Genetics in Clinical Practice, School of Health Sciences, University of Ioannina, Ioannina, Greece; [3]Department of Paediatric Endocrinology, University Hospital of Nice, Nice, France[4]Department of Endocrinology, National Reference Center for Rare Diseases of Insulin Secretion and Insulin Sensitivity (PRISIS), Sorbonne University, Inserm U938, AP-HP, Saint-Antoine University Hospital, Paris, France; [5]Department of Diabetology and Reproductive Endocrinology, National Reference Center for Rare Diseases of Insulin Secretion and Insulin Sensitivity (PRISIS), Sorbonne University, Inserm U938, AP-HP, Saint-Antoine University Hospital, Paris, France; [6]Department of Molecular Biology and Genetics, National Reference Center for Rare Diseases of Insulin Secretion and Insulin Sensitivity (PRISIS), Sorbonne University, Inserm U938, AP-HP, Saint-Antoine University Hospital, Paris, France

Background: Lipodystrophies comprise a rare and heterogeneous group of congenital or acquired disorders, classified as generalized or partial based on the pattern of adipose tissue loss. Fat atrophy and redistribution are associated with metabolic complications, including insulin resistance, hypertriglyceridaemia, hepatic steatosis, and albuminuria, as well as increased cardiovascular risk. Familial partial lipodystrophy type 2 (FPLD2) is the most common form of congenital partial lipodystrophy and is caused by variants in the *LMNA* gene, encoding nuclear lamins A/C, with autosomal dominant inheritance.

Methods: Two unrelated female patients of Greek origin with clinical features suggestive of partial lipodystrophy were evaluated. Whole exome sequencing (WES) was performed using next-generation sequencing technology.

Results: The first case concerns an 87-year-old woman with a body mass index (BMI) of 19.6 kg/m^2, without metabolic comorbidities, presenting with loss of adipose tissue in both upper and lower limbs and central fat distribution.

The second case concerns a 66-year-old woman with a BMI of 28 kg/m^2, characterized by absence of adipose tissue in the lower limbs, prominent musculature in the thighs and gluteal region, central fat accumulation, and preserved facial fat. She also had

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

hypertriglyceridaemia, insulin-treated type 2 diabetes mellitus, arterial hypertension, hypothyroidism, and hepatic steatosis.

In both patients, a heterozygous nucleotide substitution c.571G>T in the *LMNA* gene was identified. This is a missense variant resulting in a valine-to-leucine substitution at position 191 of the protein. The variant has not been previously reported in the literature and is currently classified as a variant of uncertain significance (VUS).

Conclusions: The identification of the same novel *LMNA* variant in two unrelated individuals with different phenotypes underscores the clinical heterogeneity of the disease and supports a potential pathogenic role of this variant. These findings raise the possibility of a population-specific variant and highlight the importance of integrating genetic testing into the diagnostic evaluation of lipodystrophy.

Abstract citation ID: lvag096.1834

EP1797 - LBA_ECE_1017 - The diagnostic dyssey of Cushing syndrome: unmasking an ectopic ACTH source after multiple pituitary surgeries

Sabri Engin Altıntop[1], Yagmur Eken[2], Irem Sonmezoglu Kutuk[1], Altinova Alev[1], Ali Celik[3], Emetullah Cindil[4], Ethem Turgay Cerit[1], Mujde Akturk[1], Ayhan Karakoc[1] and Fusun Toruner[1]

[1]*Department of Internal Medicine, Division of Endocrinology and Metabolism, Gazi University Faculty of Medicine, Ankara, Turkey;* [2]*Department of Internal Medicine, Gazi University Faculty of Medicine, Ankara, Turkey;* [3]*Ankara, Turkey;* [4]*Department of Radiology, Gazi University Faculty of Medicine, Ankara, Turkey*

Introduction: ACTH-dependent Cushing's syndrome most commonly originates from a pituitary adenoma but can also result from an ectopic source. This case illustrates a prolonged diagnostic course in a patient who underwent three pituitary surgeries before the ectopic source was identified.

Clinical Case: A 48-year-old woman was referred to our center with persistent ACTH-dependent Cushing's syndrome despite three prior transsphenoidal pituitary surgeries performed at different institutions over four years. Initial MRI revealed a 14 × 5 mm nodular lesion in the sellar cavity. Baseline ACTH levels ranged between 20 and 40 pg/mL. Histopathology revealed necrosis with pituitary tissue in the first surgery, normal pituitary tissue in the second, and active chronic inflammation in the third. Ga-68 DOTATATE PET/CT after second surgery revealed no evidence of a neuroendocrine tumor. No inferior petrosal sinus sampling had been performed prior to referral. Her symptoms persisted throughout this period.

At presentation, she had typical cushingoid features with a history of pathological fractures, osteoporosis, hypertension, and type 2 diabetes. Baseline hormonal evaluation in our center showed markedly elevated cortisol in serum, urine, and saliva, absence of suppression after low-dose dexamethasone, and elevated ACTH. Histopathology specimens obtained from her earlier pituitary surgeries were re-evaluated at our center, which demonstrated active chronic inflammation and normal pituitary tissue without evidence of an ACTH-positive adenoma. Pituitary MRI at our center demonstrated no adenoma. Given ongoing hypercortisolism and the absence of MRI findings, inferior petrosal sinus sampling (IPSS) was performed, demonstrating results consistent with ectopic ACTH secretion. Subsequent Ga-68 DOTATATE PET/CT identified a 1 cm left lower lobe lung nodule with mild uptake (SUVmax 6.5).

Following multidisciplinary team meeting, the patient underwent wedge resection of the pulmonary lesion. On postoperative day 1, serum cortisol dropped to 2.2 µg/dL, and glucocorticoid replacement was initiated. Histopathology confirmed a typical grade 1 carcinoid tumor (Ki-67 index <%2, ACTH immunostaining diffusely positive). She required glucocorticoid replacement for approximately six months. At one-year follow-up, she remained in biochemical remission with improved blood pressure, glucose control, and a 4 kg weight loss.

Conclusion: Diagnosing ectopic ACTH syndrome and determining its origin can be highly challenging, especially when initial findings suggest a pituitary source. Persistent hypercortisolism after multiple non-diagnostic pituitary surgeries should prompt strong consideration of an ectopic origin. This case underscores the role of the IPSS in differential diagnosis, and the value of functional imaging at regular intervals in identifying small ectopic neuroendocrine tumors.

Abstract citation ID: lvag096.1835

EP1798 - LBA_ECE_1467 - Thyroglossal duct cyst carcinoma

Blertina Dyrmishi

Hygea Hospital, Tirana, Albania

Introduction: Thyroglossal duct cyst has an incidence around 7% of neck masses in adults and around 70% of midline neck masses in children, but incidence of cancer is rare.

Case Presentation: A 33-year-old woman with a midline neck mass was initially diagnosed with thyroglossal duct cyst and underwent surgery. The histopathologic examination was papillary thyroid carcinoma with extra capsular infiltration and metastasis to the regional lymph node pT1N1Mx. A total thyroidectomy and regional lymph node dissection follow by a treatment with radioactive iodine was performed. After thyroidectomy: TSH (off) 60.9 IU/mL; Thyroglobulin <0.2 ng/mL; Anti Thyroglobulin Ab 114.3 U/mL (Normal values <70). Ablation with radioactive iodine 131 was performed. One year after the surgery, the patient was stable, on levothyroxine therapy and free of disease.

Discussion: Thyroglossal duct carcinoma has a rare incidence. Sistrunk procedure and total thyroidectomy are surgical options for patients who need ablation with 131 radioactive iodine.

Comments and Conclusions: We should consider possible malignancy in the thyroglossal duct cyst before a surgery, if we find suspicions data on ultrasound, although the incidence of thyroglossal duct cyst is rare. In some cases, deferential diagnosis between papillary micro carcinoma with distant metastasis is not easy.

Keywords papillary thyroid carcinoma, thyroglossal duct cyst

Abstract citation ID: lvag096.1836

EP1799 - LBA_ECE_1466 - Pituitary plurihormonality in MEN1: a case of concurrent ACTH, prolactin and IGF-1 excess

Gayathri Bhaskaran[1], Beenish Masood[2], Suhail Abdul-Wahab[3], Rishi Iyer[1], Mohammed Mohammed[1], Eleni Armeni[1] and Bernard Khoo[1]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[1]Endocrinology, Royal Free London NHS Foundation Trust, London, United Kingdom; [2]University College London Hospitals NHS Trust, London, United Kingdom; [3]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

Introduction: Multiple Endocrine Neoplasia Type 1 (MEN1) is a rare autosomal dominant syndrome characterised by primary hyperparathyroidism (PHPT), pituitary adenomas, and pancreatic neuroendocrine tumours (pNETs), with a prevalence of 1 in 10 000 in the UK.[1] The coexistence of acromegaly, hyperprolactinaemia, and Cushing's disease within a single MEN1-associated pituitary complex is exceptionally rare. We present a rare case of MEN1-associated silent triple pituitary hormonal hypersecretion.

Case Presentation: A 48-year-old Caucasian man presented with asymptomatic hypercalcaemia (adjusted calcium 2.8 mmol/L) and elevated PTH (8.3 pmol/L) with severe osteoporosis (Z-scores: −3.2 lumbar spine, −1.6 right total hip, −4.3 right forearm), bilateral nephrolithiasis. Parathyroid ultrasound and 99mTc-sestamibi SPECT-CT identified bilateral superior parathyroid adenomas. He was listed for 3.5-gland parathyroidectomy.

Genetic testing confirmed a pathogenic heterozygous MEN1 frameshift variant (c.1517_1530del; p.Thr506Serfs*20).

MRI pituitary revealed showed equivocal areas of reduced enhancement, raising suspicions of microadenomas. He had raised monomeric prolactin (2974 mIU/L), elevated IGF-1 (41.7 nmol/L) unsuppressed GH on OGTT (nadir 2.2 mcg/L), and a low free testosterone of 0.201 nmol/L, LH: 4.4 U/L and FSH:1.9 U/L He was started on cabergoline 1500 mcg weekly.

CT Chest Abdomen Pelvis showed multiple stable p-NETs (largest 11 mm) and a stable non-functioning left adrenal adenoma (3.7 cm). Metanephrines and Aldosterone Renin Ratio were normal. He failed an ONDST (cortisol 301 nmol/L), and subsequent LDDST confirmed ACTH-dependent Cushing's syndrome. Inferior petrosal sinus sampling further confirmed a pituitary source.

He underwent trans-sphenoidal surgery, however post-operative cortisol remained elevated (300-500 nmol/L), suggesting non-remission. Prolactin nadir was 43 mIU/L and IGF-1 of 48.2 nmol/L.

Histology suggested PIT-1 lineage but co-expression of SF-1 and PIT-1 transcription factors suggested native anterior pituitary tissue.

This patient had no symptoms of acromegaly or Cushing's syndrome. The only tell-tale signs were severe osteoporosis (disproportional to mild hypercalcemia) and intermittent hyperglycaemia (HbA1c 38 mmol/mol).

Discussion and Conclusion: This case highlights an exceptionally rare MEN1 presentation with silent triple pituitary hormonal hypersecretion (prolactin, GH and ACTH) detected only through biochemical surveillance. The patient's severe osteoporosis and PTH dependent hypercalcaemia were the only indicators of endocrine dysfunction, emphasising the importance of comprehensive hormonal assessment in MEN1 even when asymptomatic.

Persistent post-operative hypercortisolaemia reflects the challenges of treating MEN1-related Cushing's disease and reinforces the importance of multidisciplinary, iterative evaluation. As pituitary surgery did not likely cure the Cushing's disease, he is planned for further dynamic function tests, functional imaging and re-discussion with neurosurgeons.

Reference

1. Genomics Education Programme. Multiple endocrine neoplasia type 1; 2015. https://www.genomicseducation.hee.nhs.uk/wp-content/uploads/2015/07/Multiple-endocrine-neoplasia-type1.pdf

Abstract citation ID: lvag096.1837

EP1803 - LBA_ECE_1461 - Management of carbimazole-induced neutropenia in Graves' disease: a case report of alternative therapeutic strategies

Helena Fahmi, Dilini Abeyratne, Hyma Rachabattula and Nilukshana Yogendranathan

King's College Hospital NHS Foundation Trust, London, United Kingdom

Introduction: Antithyroid drug-induced neutropenia occurs in less than 0.5% of patients with Graves' disease, typically within 90 days of therapy. Carbimazole can cause minor adverse effects including pruritus and major complications such as agranulocytosis requiring immediate discontinuation. When antithyroid drugs are contraindicated, alternative approaches are needed to achieve biochemical control prior to definitive treatment. This case demonstrates successful management using cholestyramine and lithium carbonate as bridging therapy to radioactive iodine ablation.

Case Presentation: A 55-year-old female presented with palpitations, bone pain, and weakness. Examination revealed tachycardia, fine tremor, and palpable goiter. Laboratory investigations confirmed severe thyrotoxicosis (TSH <0.01 mIU/L, FT4 48.5 pmol/L, FT3 >30.7 pmol/L) with elevated TRAb (16.75 U/L), confirming Graves' disease. Carbimazole 30 mg daily and propranolol 40 mg three times daily were initiated. At 3-week follow-up, thyroid function partially improved (FT4 27.6 pmol/L, FT3 14.1 pmol/L), but the patient developed pruritus and neutropenia (neutrophil count 0.97×10^9/L, WBC 3.1×10^9/L). Carbimazole was discontinued immediately. Three weeks later, her repeat blood tests showed that her White cell and neutrophil counts had normalized, but thyroid function was worsened (FT4 >64.3 pmol/L, FT3 >30.7 pmol/L, TRAb 34.93 U/L). Cholestyramine 4 g every 6 hours was initiated but required dose reduction to 4 g three times daily following the symptoms of diarrhea. Lithium carbonate 200 mg twice daily was introduced. Persistent fluctuating neutropenia ($0.62\text{-}1.46 \times 10^9$/L) despite 4 months off carbimazole prompted hematology consultation, suggesting benign ethnic neutropenia. Technetium-99m uptake scan showed diffuse uptake of 25%. 2-week follow-up following lithium initiation demonstrated clinical improvement on combination therapy with improving thyroid function (FT4 36.7 pmol/L, FT3 18.4 pmol/L, TSH < 0.01). The patient opted for radioactive iodine ablation as a definitive treatment.

Conclusion: This case illustrates effective management of Graves' disease when antithyroid drugs are contraindicated. Cholestyramine interrupts enterohepatic circulation of thyroid hormones, producing significant reductions in hormone levels at 4 weeks. Lithium carbonate inhibits thyroid hormone release and serves as effective bridging therapy, with studies demonstrating significant reductions in free T4 and T3 after median exposure of 37 days. Persistent neutropenia after carbimazole

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

discontinuation highlights the importance of distinguishing drug-induced neutropenia from ethnic neutropenia, a benign condition affecting individuals of African, Middle Eastern, and West Indian descent. Combination therapy with cholestyramine and lithium provided effective biochemical control as a bridge to definitive radioactive iodine treatment, demonstrating the value of individualized approaches and multidisciplinary collaboration in managing Graves' disease complications.

Abstract citation ID: lvag096.1838

EP1804 - LBA_ECE_1058 - Genetic distribution of FCS in 6 countries of Latin America

Alejandro Roman-Gonzalez[1], Alejandro Castellanos[2], Claudia Monsalve[3], Johnayro Gutierrez Restrepo[1], Juliana Lores[4], Cristina Armijos[5], Maria Sanchez[6], Virgilio Melgar Manzanilla[7], Sonia Chavez[8], Laura Olate[9], Melissa Chacon[9], Alejandro Cob[10], Karla Garay[11], Juan Pozo[12], Natalia Agudelo[13], Diana Sanchez[13], Josefina Gonzalez[13] and Heidi Mateus[13]

[1]Endocrinology, Universidad de Antioquia, Medellín, Colombia; [2]Centro Médico Santa Clara, Monteria, Colombia; [3]Universidad Pontificia Bolivariana, Medellín, Colombia; [4]Clínica Imbanaco, Cali, Colombia; [5]Hospital San Rafael, Pereira, Colombia; [6]Hospital Roosevelt, Bogota, Colombia; [7]Hospital Faro del Mayab, Mexico, Mexico; [8]Hospital Juarez, Mexico, Mexico; [9]Hospital Clinica Biblica, Costa Rica; [10]Clinica Los Yoses, Costa Rica; [11]Hospital Eugenio Espejo, Quito, Ecuador; [12]Universidad de Cuenca, Cuenca, Ecuador; [13]PTC Therapeutics, Bogota, Colombia

Background and Aims: Familial chylomicronemia syndrome (FCS) is an ultra-rare genetic disorder caused by pathogenic variants in fivegenes (LPL, APOA5, APOC2, LMF1, and GPIHBP1), characterized by severe hypertriglyceridemia and a high risk ofacute pancreatitis. The available evidence, derived mainly from European and North American cohorts, identifiesLPL as the most frequently implicated gene (Hegele et al.), with limited representation of Latin Americanpopulations. The aim of this study was to characterize the genetic and demographic profile of patients with FCSacross six Latin American countries and to compare these findings with those reported in the literature.

Methods: This was a retrospective study of 83 patients with genetically confirmed FCS. Anonymized data from the PTCTherapeutics Diagnostic Program, collected between 2020 and 2025, were analyzed.

Results: A total of 83 cases from Colombia, Costa Rica, Ecuador, Guatemala, Mexico, and Panama were included, with amean age of 33.2 ± 20.5 years and a female predominance (63.0%). LPL was the most frequently affected gene (55.4%), followed by APOA5 (15.7%), GPIHBP1 (12.0%), LMF1 (12.0%), and APOC2 (3.6%). Differences wereobserved across countries, with greater genetic heterogeneity in Ecuador. Compared with the literature, the LatinAmerican cohort showed a lower proportion of LPL-associated cases and a greater relative contribution of non-LPLgenes.

Conclusions: FCS in Latin America appears to exhibit greater genetic heterogeneity than that described in European and NorthAmerican cohorts, underscoring the need for further characterization.

Abstract citation ID: lvag096.1839

EP1805 - LBA_ECE_1177 - A pilot trial of a nutraceutical based on bergamot (*Citrus bergamia*), berberin (*Berberis aristata*), fenugreek (*Trigonella foenum-graecum*) and probiotic (*Lactobacillus plantarum*), for mild dyslipidemia

Claudia Arnas-Leon[1,2], Rosa María Sanchez-Hernandez[3], Sara Andrada-Diaz[4], Agnieszka Kuzior[2], Evigeni Fierro-Milla[2], Lucia Belen Zele-Alvarez[2], Ana Martinez-Martinez[2], Inmaculada Molinero-Marcos[1], Borja Santana-Ojeda[1] and Francisco Javier Martinez-Martin[1,2]

[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain; [3]Complejo Hospitalario Universitario Insular Materno-Infantil, Las Palmas de Gran Canaria, Spain; [4]Bioksan Naturalmente Juntos, Medical Advisory, Las Palmas de Gran Canaria, Spain

Introduction: Monacolins from red yeast rice are a safety concern, with potential adverse effects even at low intakes. Bergamot extracts contain flavonoids that may help improve lipid profiles in patients with statin intolerance or unwillingness to initiate statin therapy. We conducted an open-label pilot trial to evaluate the LDL-cholesterol lowering efficacy of a novel nutraceutical based on bergamot, berberin and fenugreek extract plus a probiotic.

Methods: We recruited patients with low-to-moderate cardiovascular risk, LDL cholesterol <190 mg/dL who rejected statins. Participants received one daily capsule containing 375 mg of standardized bergamot extract (40% flavonoids, including naringin, neoeriocitrin, and neohesperidin), 250 mg of berberine and fenugreek extract, and 30 mg of the probiotic *Lactobacillus plantarum*.

All patients provided written informed consent and underwent baseline anthropometric and laboratory assessments before starting treatment. These measurements were repeated after 3-4 months. Health-related quality of life was assessed using the EuroQoL-5D-3L questionnaire at baseline and follow-up. Adverse effects and treatment satisfaction (Likert scale) were also recorded.

Results: A total of 29 patients (86% female; mean age 53.7 years) completed both visits. LDL cholesterol showed a non-significant reduction of 3.22% (139.4 ± 26.6-134.9 ± 25.4 mg/dL; $P = .291$, paired t-test).

Changes in body mass index (−0.26%), waist circumference (−2.05%), systolic (−0.50%) and diastolic (−0.80%) blood pressure, heart rate (−2.76%), triglycerides (−2.15%), total cholesterol (−1.72%), HDL cholesterol (+1.21%), non-HDL cholesterol (−2.85%), apolipoprotein B (−5.30%), lipoprotein(a) (+1.64%), and SCORE2 cardiovascular risk (−2.49%) were also not statistically significant.

Similarly, no significant changes were observed in glucose metabolism (glucose −1.88%, insulin +8.09%, HOMA-IR +5.25%, HbA1c +0.31%), liver enzymes (AST −4.38%, ALT 0.00%, GGT +9.77%, alkaline phosphatase −2.59%, LDH +2.28%, total bilirubin +4.11%), FIB-4 score (−9.88%), renal function (eGFR −0.71%, albumin/creatinine ratio −8.65%), vitamins B_9 (−0.37%) and B_{12} (+0.96%), calcium (−0.21%), phosphate (−0.81%), C-reactive protein (−1.16%), and creatine-kinase (+0.30%).

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Quality of life remained unchanged (+4.3% index score; +6.11% health status). No serious adverse effects were reported, and 79.2% of patients reported high/very high satisfaction with the treatment.

Conclusions: The supplement demonstrated excellent tolerability, with high patient satisfaction. However, it showed no significant effect on LDL cholesterol or on cardiovascular, hepatic, or renal risk markers. These findings suggest that more effective therapeutic alternatives are needed for this patient population.

Abstract citation ID: lvag096.1840

EP1806 - LBA_ECE_1372 - Hidden cardiovascular risk in obese adults with normal routine parameters: association of waist-to-height ratio with carotid IMT and hepatic steatosis

Juliana Karanxha[1] and Mirjeta Guni[2]
[1]Cardiology, America Hospital, Tirane, Albania; [2]Endocrinology, America Hospital, Tirane, Albania

Background: Obesity is a major driver of cardiometabolic disease; however, individuals with normal routine laboratory parameters may still harbor significant subclinical organ damage. Anthropometric indices such as waist-to-height ratio (WHtR) may better reflect visceral adiposity and associated metabolic risk compared to traditional measures.

Objective: To evaluate the association between WHtR and early markers of subclinical cardiovascular and metabolic damage, including carotid intima-media thickness (cIMT) and hepatic steatosis, in obese adults with otherwise normal routine parameters.

Methods: This single-center observational study included adult patients with obesity (BMI $\geq$30 kg/m^2) and normal routine laboratory parameters (lipid profile and fasting glucose). Anthropometric measurements, including WHtR, were recorded. Carotid ultrasound was performed to assess cIMT, and hepatic ultrasound was used to evaluate the presence of steatosis. Associations between WHtR and markers of subclinical organ damage were analyzed using descriptive and correlation methods.

Results: Despite normal routine laboratory findings, a considerable proportion of patients demonstrated increased cIMT and evidence of hepatic steatosis. Higher WHtR values were associated with increased cIMT and a higher prevalence of hepatic steatosis. Patients with elevated WHtR showed clustering of subclinical cardiovascular and metabolic abnormalities, suggesting the presence of hidden cardiometabolic risk.

Conclusions: WHtR appears to be a simple and effective marker for identifying hidden cardiovascular and metabolic risk in obese individuals with otherwise normal routine parameters. These findings support the need for broader screening strategies incorporating anthropometric indices to detect early organ damage and improve risk stratification in obesity.

Keywords obesity, WHtR, carotid IMT, hepatic steatosis, visceral adiposity, cardio metabolic risk

Abstract citation ID: lvag096.1841

EP1808 - LBA_ECE_1094 - Familial 11β-hydroxylase deficiency associated with a CYP11B1 mutation: phenotypic variability across two generations, including a severe form with salt-wasting syndrome

Meryem Eladla[1], Sanae El Moudden[2] and Sanae Abourazak[3]
[1]Endocrinology, University Hospital Center, Fez, Morocco; [2]Pediatric Endocrinology, University Hospital, Fez, Morocco; [3]Endocrinology, Pediatric Endocrinology, University Hospital, Fes, Morocco

Introduction: 11β-hydroxylase deficiency is an autosomal form of congenital adrenal hyperplasia, accounting for 5%-8% of cases. It results in impaired cortisol synthesis, leading to an accumulation of precursors that causes hyperandrogenism and, in some cases, hypertension. This study describes the clinical, biological, and progressive characteristics of a familial deficiency observed in three sisters born to an affected mother.

Materials and Methods: A retrospective descriptive study conducted in the pediatric endocrinology department at Hassan II University Hospital in Fez. Clinical, laboratory, genetic, therapeutic, and follow-up data for the patients were collected from their medical records.

Results: Patient 1 (14 years old): neonatal sexual differentiation disorder with testosterone 2.5 ng/mL, 17-OHprogesterone 12 ng/mL, Δ4-androstenedione 17 ng/mL, 11-deoxycortisol 24 ng/mL, cortisol 2.8 µg/dl, ACTH 95 pg/mL, hyponatremia, normal serum potassium. CYP11B1 mutation confirmed. Started on hydrocortisone at birth, vaginoplasty at age 3. Course marked by poor compliance, melanoderma, and episodes of hyponatremia, with advanced bone age.

Patient 2 (10 years old): similar neonatal presentation, identical CYP11B1 mutation. Early replacement therapy and corrective surgery. Favorable outcome without melanoderma, initial short stature and low weight with gradual catch-up.

Patient 3: comparable neonatal presentation but with hyponatremia and hyperkalemia; identical mutation. Death at age 1 due to salt-wasting syndrome.

All three patients are daughters of an asymptomatic mother who was diagnosed secondarily after her daughters were diagnosed with 11β-hydroxylase deficiency and placed on hydrocortisone. Two other daughters, treated with antenatal dexamethasone (SRY-negative), had a favorable outcome.

Conclusion: This case illustrates the phenotypic variability of a CYP11B1 mutation within the same family, ranging from a compensated form to severe salt-wasting disease. It underscores the importance of family screening, genetic counseling, and strict adherence to treatment to prevent progressive complications.

Abstract citation ID: lvag096.1842

EP1810 - LBA_ECE_1361 - A rare case of ectopic adrenal found in liver

Bhavna Sharma[1], Smita Singh[2], Kiran Agarwal[2] and Shivali Sehgal[2]
[1]Endocrinology, Queen Mary University of London, London, United Kingdom; [2]Lady Hardinge Medical College, New Delhi, India

Background: Ectopic adrenal tissue or adrenal rests refer to adrenal gland tissue located in abnormal regions. Adrenal ectopia has a reported incidence of less than 1% in adults, with a predominance in males.[1]

Common locations include along the path of embryological descent (especially near reproductive tissues), tests or spermatic cord, the ovaries or the broad ligament or in the retroperitoneum. Ectopic adrenal tissue is often a remnant due to faulty migration during embryonic development.[2]

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

These, even though mostly are asymptomatic, may become significant when they enlarge, produce hormones, or be misdiagnosed as another tumour.[1]

Rarely, these may be involved in endocrine conditions, including congenital adrenal hyperplasia.

In this clinical case, we highlight its potential for misdiagnosis, as this was found in the liver.

Case Summary: A 31-year-old female of Indian origin with no past medical history presented with abdominal pain. She was asymptomatic with no signs or symptoms to suggest adrenal axis pathology.

She had no hormonal profiles done pre-op due to no clinical suspicion.

Ultrasound abdomen revealed a well-defined cystic lesion at segments VI and VII of the liver of size $7.2 \times 7.5 \times 7.8$ cm with an ill-defined hyperechoic mural nodule. CT abdomen found a hypodense lesion in the liver with a calcific nodule. Both radiological investigations were suggestive of a complex Hydatid cyst.

Excision was performed.

Gross examination of the excised tissue was described as multiple flap-like tissue pieces varying in colour from grey-white to yellow. On microscopic examination, strips of fibrocollagenous tissue with numerous congested blood vessels and focal chronic inflammatory infiltrate were described. Encapsulated adrenal tissue was identified, adjacent to which a few cystic spaces lined by flattened cells (CK Negative and CD34 Positive) were present. A diagnosis of Adrenal ectopia with endothelial cyst was made.

Discussion: This case highlights the importance of careful preoperative evaluation and emphasises the need to consider adrenal ectopia when encountering unusual hepatic lesions. Consideration of possible secretion is cautioned; however would be extremely challenging.

References

1. Schechter DC. Aberrant adrenal tissue. *Ann Surg*. 1968;167(3):421-426. https://doi.org/10.1097/00000658-196803000-00017
2. Hafiz B, Alturkistani F. Adrenal cortical rests in the fallopian tube: a case report and review of the literature. *Cureus*. 2022;14(8):e27649. https://doi.org/10.7759/cureus.27649

Abstract citation ID: lvag096.1843

EP1811 - LBA_ECE_1252 - Silent hyperandrogenism: a functioning gonadotroph adenoma presenting as pituitary apoplexy without clinical features of androgen excess

Helena Fahmi, Dilini Abeyratne, Nilukshana Yogendranathan, Charmaine Ilangaratne and Eleni Maratos
King's College Hospital NHS Foundation Trust, London, United Kingdom

Introduction: Functioning gonadotroph adenomas (FGAs) are rare pituitary neuroendocrine tumors (PitNETs) that secrete biologically active gonadotropins. While gonadotroph-lineage tumors are the most common subtype among clinically non-functioning pituitary adenomas, functioning cases with elevated sex steroids are exceedingly rare in males. In adult men, FGAs with secondary testosterone elevation do not produce a recognizable clinical syndrome, making preoperative diagnosis challenging. We report a functioning gonadotroph PitNET presenting with features of pituitary apoplexy and biochemically elevated androgens without clinical signs of androgen excess.

Case Presentation: A 57-year-old male with no prior medical history presented with acute severe frontal headache and right-sided diplopia. Examination revealed hypertension, right ptosis, and a right visual field defect. CT demonstrated a large pituitary mass with suprasellar extension compressing the optic chiasm. Empirical intravenous hydrocortisone was administered. MRI confirmed a $21 \times 26 \times 32$ mm macroadenoma extending into the suprasellar cistern, sphenoid sinus, and bilateral cavernous sinuses with possible carotid encasement, though no definitive hemorrhage was identified. Hormonal evaluation revealed elevated testosterone (35.5 nmol/L), free androgen index (101.7%), FSH (24.9 IU/L), LH (10.6 IU/L), and mildly elevated prolactin (1086 mIU/L) consistent with stalk effect. Secondary hypothyroidism was present. The patient denied symptoms of androgen excess, and examination revealed no hyperandrogenic features.

Ophthalmological assessment demonstrated progressive compressive visual field changes, prompting urgent transsphenoidal surgery. Histopathology confirmed a gonadotroph PitNET with widespread LH, FSH, and pan-α-subunit positivity, diffuse SF-1 expression, and bone and sinonasal mucosal invasion with a low Ki-67 index (2%-3%). Postoperatively, visual fields normalized. Hormonal reassessment revealed low testosterone (0.5 nmol/L) with normalized gonadotropins and suboptimal cortisol and growth hormone responses on insulin stress testing. The patient was commenced on testosterone replacement and hydrocortisone with good response.

Conclusion: This case highlights a rare functioning gonadotroph PitNET presenting with features of pituitary apoplexy. Despite biochemically elevated androgens and gonadotropins, no clinical features of androgen excess were observed, consistent with reports that elevated sex steroids in male FGAs lack a recognizable clinical syndrome. The 2022 WHO classification, emphasizing SF-1-based lineage identification, has improved recognition of gonadotroph PitNETs. Transsphenoidal resection resolved visual deficits and hormonal hypersecretion while providing tissue for definitive classification. This case underscores the importance of comprehensive hormonal evaluation in pituitary macroadenomas, as functioning gonadotroph tumors may be underdiagnosed due to the absence of a distinct clinical phenotype in males.

Abstract citation ID: lvag096.1844

EP1812 - LBA_ECE_1462 - Pachydermoperiostosis mimicking acromegaly: a case report

Doha Dahmani, Aziouaz Fatima and Benkacem Mariem
Endocrinology and Metabolic Diseases Department, Mohammed VI University Hospital, Tangier, Morocco

Introduction: Pachydermoperiostosis is a rare disorder characterized by skin thickening and periosteal bone formation, often mimicking acromegaly and complicating the differential diagnosis. We report a case illustrating this diagnostic challenge.

Observation: A 70-year-old woman with a history of poorly differentiated thyroid carcinoma was referred for suspected

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

acromegaly. She reported a more than 20-year history of progressive enlargement of the hands and feet, increased shoe size, skin thickening, and facial dysmorphism. Clinical examination showed coarse facial features with a broadened nasal base, mandibular prognathism, and spade-like hands and feet. Serum IGF-1 levels were normal. Radiographs revealed periosteal apposition involving the metacarpals, metatarsals, and long bones. Extensive evaluation excluded secondary hypertrophic osteoarthropathy, including pulmonary, cardiac, neoplastic, hepatic, and inflammatory causes. The diagnosis of incomplete pachydermoperiostosis was retained.

Discussion: Pachydermoperiostosis is a rare genetic disease, usually autosomal dominant with variable penetrance, typically beginning in adolescence and predominantly affecting males.

It classically associates acromegaloid features, periostosis, and pachydermia, with possible hyperhidrosis and seborrhea. Osteoarticular manifestations include bone pain, mechanical arthralgia, and recurrent joint effusions, with bilateral symmetrical periosteal new bone formation without erosions.

Diagnosis relies on clinical criteria such as those proposed by Borochowitz, and requires exclusion of secondary hypertrophic osteoarthropathy, particularly paraneoplastic pulmonary causes, as well as cardiac, hepatic, gastrointestinal, hematologic, and endocrine disorders.

Management is mainly symptomatic, including nonsteroidal anti-inflammatory drugs, corticosteroids, colchicine, retinoids for cutaneous involvement, and bisphosphonates or tamoxifen in severe cases.

Conclusion: Although rare, pachydermoperiostosis is an important differential diagnosis of acromegaly. The association of periostosis, digital clubbing, and pachydermia in the absence of systemic disease strongly supports this diagnosis and should alert endocrinologists.

Abstract citation ID: lvag096.1845

EP1813 - LBA_ECE_1418 - A sight-threatening form of TED in an elderly woman—case presentation

Porcereanu Natalia[1], Ina Dusa[1], Lorina Vudu[2] and Tatiana Magla[1]
[1]IMSP SCR, "Timofei Moșneaga", Chișinău, Moldova; [2]USMF, "Nicolae Testemițanu", Chișinău, Moldova

Introduction: Thyroid eye disease (TED) is the major extrathyroidal manifestation of Graves' disease (GD). Although in only 1% of patients TED presents a sight-threatening form, requiring an urgent medical intervention, the elderly represent a specific group at risk, due to the physiologic changes and the disease's particularities.

Case Presentation: A 72 years old woman was first referred to an endocrinologist with a 2 months history of thyrotoxic symptoms (palpitations, tremor, weight loss). Blood tests show primary thyrotoxicosis (TSH - 0.01 mIU/mL, fT4 - 2.54 ng/dl, fT3 - 7.06 ng/dl) with positive TRAb (50 IU/l). TED was appreciated as Moderate-severe, Clinical Activity Score (CAS) 6 points OD, 6 points OS.

Patient was started on Thiamazole 30 mg/day, Propranolol 30 mg/day and 500 mg methylprednisolone (MP) pulse therapy was started. After the discharge, the patient continued the pulse scheme with 500 mg MP for 2 weeks (total dose of MP 2g), then she missed 1 dose. Three days after withdrawal, TED symptoms evolved rapidly to marked redness, severe chemosis and the vision loss, and the patient was admitted to the hospital. An improvement in thyroid hormones was found: TSH from 0.01 to 0.1 (N 0.27-4.20 mlU/mL); T4f from 20.2 to 13.7 pmol/l (N 12-22 pmol/l). The ophthalmologic exam showed OD lagophthalmos, protrusion, diffuse conjunctival injection, chemosis and corneal ulceration. The CAS score was: OD - 10 points, OS - 5 points. The severe, sight-threatening form of TED with corneal ulceration requiredprompted intervention and three ivMP pulses (1000 g) given alternate days was administrated. Topical treatment with NSAIDs, antibiotic, lubrication was started and a protective contact lense was applied. After 2 weeks, an improvement of the CAS was noted (5p OD, 4p OS), and the recovery of gross vision and of the color vision was noticed.

Discussion: Old age is one of the known risk factors for TED worsening and poor response to treatment. The ocular surface disease in elderly patients precipitates the TED occurring in this category of patients. Corneal breakdown demands expeditious and intensive multimodal management—topical and systemic medications and orbital decompression surgery in particular cases.

Conclusion: Early identification of the progression of TED to more severe forms has a profound impact on the quality of life of the patients. Elderly patients with TED must be counseled to avoid the progression lubrication, nighttime protection and bandage lenses.

Abstract citation ID: lvag096.1846

EP1814 - LBA_ECE_1433 - Multimodal management of silent corticotroph tumors with Crooke's cell features transforming into severe Cushing's disease—the ERCUSYN Kraków cohort

Aleksandra Gilis-Januszewska[1], Aleksandra Gamrat-Żmuda[1,2], Anna Bogusławska[1], Ewelina Rzepka[1], Mari Minasyan[1], Wiktoria Suchy[1] and Alicja Hubalewska-Dydejczyk[1]
[1]Department of Endocrinology, Jagiellonian University Medical College, Krakow, Poland; [2]Doctoral School of Medical and Health Sciences, Jagiellonian University Medical College, Krakow, Poland

Background: Silent corticotroph tumors (SCTs) are pituitary neuroendocrine tumors of corticotroph lineage characterized by T-PIT positivity without clinical or biochemical hypercortisolism at diagnosis. Transforming into overt ACTH-dependent Cushing's disease (CD) has been reported in approximately 4% of cases, representing a rare but clinically significant phenomenon.

Methods: We report three patients from the ERCUSYN Kraków cohort with initially silent corticotroph PitNETs with Crooke's cell features who subsequently developed overt CD during long-term follow-up.

Results: A 53-year-old woman underwent resection of a non-functioning pituitary macroadenoma measuring up to 40 mm. Histopathology demonstrated a densely granulated corticotroph tumor with scattered Crooke's cells (Ki-67 approximately 3%). Proton radiotherapy was subsequently performed. Six years later, rapid tumor progression involving the sella and left cavernous sinus was observed together with biochemical

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

ACTH-dependent hypercortisolism (loss of circadian rhythm, late-night cortisol 19.3 µg/dL, urinary free cortisol 308-445 µg/24 h, ACTH 97.7 pg/mL), despite only mild clinical manifestations. The progression was accompanied by severe mass-effect symptoms, including visual field impairment, ptosis, and convergent strabismus. Combination therapy with pasireotide LAR and temozolomide was initiated. Temozolomide was discontinued after the first cycle due to bone marrow aplasia, while continued pasireotide therapy resulted in radiological stabilization and normalization of cortisol levels.

An 80-year-old man underwent incomplete transsphenoidal resection of a 35 mm nonfunctioning macroadenoma (Knosp grade 2). Histopathology confirmed a corticotroph PitNET with Crooke's cell features, followed by adjuvant radiotherapy. Approximately nine years later, the patient developed clinically overt ACTH-dependent CS without significant radiological tumor progression. Initial treatment with pasireotide was insufficient. Due to severe hypercortisolism, osilodrostat was initiated directly in a block-and-replace regimen (up to 30 mg/d) with hydrocortisone supplementation, resulting in biochemical remission and clinical improvement.

A 71-year-old woman underwent four transsphenoidal resections of a corticotroph macroadenoma within two years followed by radiotherapy. Five years later, marked tumor progression (Knosp grade 4) occurred with severe mass-effect symptoms including convergent strabismus and impaired ocular motility. Treatment with pasireotide and temozolomide was initiated; however, overt CD developed during therapy. Osilodrostat was introduced and administered for six months, achieving biochemical control of hypercortisolism. Subsequently, temozolomide therapy was continued, and after seven cycles the patient remains clinically stable with radiological tumor regression.

Conclusions: SCTs with Crooke's cell features may transform into severe CD many years after the initial diagnosis, sometimes even without marked radiological progression. These observations highlight the importance of long-term endocrine surveillance and often necessitate multimodal therapeutic strategies including surgery, radiotherapy, and targeted medical therapy.

Abstract citation ID: lvag096.1847

EP1815 - LBA_ECE_1182 - The impact of Semaglutide and Tirzepatide intervention on the metrics of metabolic function, bioimpedance analysis, and dietary behaviors in individuals receiving treatment

Gamze Akkus[1], Irem Kolsuz Türker[1], Erdem Ince[1], Ali Örs[1,2] and Gulsah Seydaoğlu[2]
[1]Endocrinology, Cukurova University, Adana, Turkey; [2]Cukurova University, Adana, Turkey

Introduction: In the present investigation, our objective is to conduct a comparative analysis of the biochemical, metabolic, bioimpedance, and dietary habitus subcriteria among patients receiving treatment with either semaglutide or tirzepatide.

Methods: We enrolled a cohort of 57 individuals diagnosed with obesity (comparing Tirzepatide and Semaglutide; 39 vs 18), utilizing a prospective study design. We meticulously documented various parameters, including weight, body mass index, fasting plasma glucose, liver function tests, and lipid profiles of the participants both prior to and following the therapeutic intervention. All subjects underwent bioelectrical impedance analyses, which encompassed measurements of fat percentage (fat%), fat mass, free fat mass (FFM), and total body water (TBW) both before and after treatment, approximately 12 weeks post-initiation). Additionally, we solicited information from the patients regarding their alimentary practices, encompassing three factors, namely: uncontrolled eating, emotional eating, and restrictive eating.

Results: Both cohorts demonstrated a statistically significant reduction in body weight and body mass index (BMI) ($P < .001$).Within the semaglutide cohort, BMI exhibited a reduction from 36.03 to 32.94 kg, while body weight diminished from 98.25 to 89.89 kg. Conversely, in the tirzepatide cohort, BMI declined from 35.52 to 31.57 kg, accompanied by a weight reduction from 94.87 to 84.12 kg. The average change in Body Mass Index (BMI) was −1.97 kg/m^2 within the semaglutide cohort and −3.17 kg/m^2 within the tirzepatide cohort. The percentage of body fat exhibited a decline of −1.86% and −3.96%, correspondingly, while the total fat mass demonstrated reductions of −4.59 kg and −7.12 kg. Both cohorts demonstrated enhancements in nutritional habits prior to and subsequent to the intervention ($P < .001$). In the intergroup comparison, the decrease in uncontrolled and emotional eating scores was more pronounced and statistically significant in the tirzepatide group ($P = .004$ and $P = .006$, respectively). The increase in restrictive and mindful eating scores was also found to be stronger in favor of tirzepatide ($P = .021$ and $P = .028$).

Conclusion: Although glucagon-like peptide-1 (GLP-1) receptor agonists yield considerable reductions in body weight, enhancements in glycemic control, and favorable modifications in body composition, Tirzepatide demonstrated a greater efficacy in ameliorating the parameters related to adipose tissue mass and dietary behaviors, notably resulting in a diminished score pertaining to emotional and uncontrolled eating while simultaneously fostering an increase in mindful and restrictive eating practices.

Abstract citation ID: lvag096.1848

EP1816 - LBA_ECE_1394 - A rare cause of male infertility: SRY-negative 46,XX testicular DSD associated with SOX3 duplication

Filipa Sales[1], Maria Luís Mazeda[1], Bruna Silva[1], Catarina Chaves[1], Ana Saavedra[1], Catarina Cidade Rodrigues[1,2], Alexandra Araujo[3], Ana Morgado[4], Mário Laço[5] and Margarida Almeida[1]
[1]Endocrinology, ULS Tâmega e Sousa, Penafiel, Portugal; [2]Endocrinology Department of the Centro Hospitalar do Tâmega e Sousa, Porto, Portugal; [3]Endocrinology, ULS Matosinhos, Matosinhos, Portugal; [4]Obstetrics and Gynecology, ULS Tâmega e Sousa, Penafiel, Portugal; [5]Genetics, ULS Tâmega e Sousa, Penafiel, Portugal

Introduction: 46,XX testicular disorders of sex development (DSD) are rare and most cases result from translocation of *SRY* to an X chromosome, producing SRY-positive 46,XX males. In contrast, *SRY*-negative 46,XX testicular DSD is much less frequent and has been associated with gain-of-function or increased dosage of alternative testis-determining genes, including *SOX3*, and shows a variable clinical phenotype ranging from nearly typical male development to overt DSD.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Case Report: A 40-year-old phenotypic male was referred to endocrinology for primary infertility. His history included epilepsy, Hashimoto thyroiditis with hypothyroidism, prediabetes, and dyslipidemia. He reported more than 10 years of infertility, decreased libido, and anejaculation, and described normal, spontaneous pubertal development. There was no family history of DSD, infertility, or other relevant endocrine or genetic disorders. Physical examination showed bilateral gynecomastia, reduced facial and truncal hair, and bilaterally small testes, with otherwise normal male external genitalia. Baseline biochemistry revealed normal renal and hepatic function, with prediabetes and dyslipidemia, controlled hypothyroidism and hypogonadism with total testosterone 0.6 ng/mL, free testosterone 1.57 pg/mL, SHBG 84.6 nmol/L, and DHEA-S 0.49 mg/mL. Gonodatrophins were slightly elevated (LH 9.4 mUI/mL (1.2-8.6) and FSH 21.1 mUI/mL (1.3-19.3)) and prolactin was normal. Scrotal ultrasound documented markedly reduced testicular volume (2 mL bilaterally), mildly heterogeneous echotexture, reduced vascularization, and a moderate left varicocele, without focal lesions; pituitary MRI was unremarkable. Conventional karyotyping revealed 46,XX; one chromosome X with an abnormal long arm. Chromosomal microarray showed an approximately 6.5 Mb duplication at Xq27.1q27.3 consistent with a female genomic profile and including *SOX3*, compatible with 46,XX testicular DSD. Subsequent testing for *SRY* was negative, and multiplex ligation-dependent probe amplification *for NROB1, NR5A1, SOX9*, and *WNT4* disclosed no clinically relevant alterations. The patient declined gonadotropin therapy and started intramuscular testosterone 250 mg every 4 weeks, with improved libido, normalization of total testosterone, and modest improvement of the lipid profile. He was referred for assisted reproductive techniques and genetic counseling.

Discussion: This *SRY*-negative 46,XX testicular DSD due to a large Xq27.1q27.3 duplication including *SOX3* broadens the clinical spectrum of *SOX3*-associated sex development disorders, demonstrating that normal pubertal development and a fully male external phenotype may coexist with severe primary testicular failure and infertility. It reinforces the need to incorporate high-resolution genomic analysis with specific evaluation of *SOX3* dosage into the work-up of *SRY*-negative 46,XX males with hypergonadotropic hypogonadism, and underlines the importance of multidisciplinary long-term management with endocrine, reproductive, and genetic counseling.

Abstract citation ID: lvag096.1849

EP1818 - LBA_ECE_1407 - Rapid visual recovery and decreasing prolactin levels in a giant prolactinoma with extreme hyperprolactinemia under low-dose dopamine agonist therapy

Jacob Ritter[1,2], Leonard Kozarzewski[1,2], Cinzia Tarallo[1,2], Linus Hesse[1,2], Christian J. Strasburger[1,2], Linus Haberbosch[1,2], Knut Mai[1,2,3] and Dominik Soll[1,2]
[1]*Department of Endocrinology and Metabolism, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Charité—Universitätsmedizin Berlin, Berlin, Germany;* [2]*Humboldt-Universität zu Berlin, and Berlin Institute of Health, Pituitary Tumor Center of Excellence at Charité—Universitätsmedizin Berlin, Berlin, Germany;* [3]*Department of Human Nutrition, German Institute of Human Nutrition Potsdam-Rehbrücke, Potsdam, Germany*

Background: Giant prolactinomas are rare pituitary adenomas, accounting for approximately 2%-5% of all prolactin-secreting pituitary tumors, characterized by extreme hyperprolactinemia and significant mass effects (>4 cm), often including optic chiasm compression. Dopamine agonist treatment as first-line therapy can achieve rapid tumor shrinkage and biochemical remission, thereby avoiding acute neurosurgical intervention to improve visual impairment. However, the optimal initial dosing strategy remains undefined, particularly in patients with acute visual compromise, and is currently being addressed in ongoing prospective research.

Case Presentation: We report a 41-year-old male patient presenting with a 2-month history of progressive diplopia, blurred vision, and increasing visual fatigue, culminating in bitemporal hemianopsia, which was confirmed by medical examination. Cranial MRI demonstrated a large 4×4×3 cm sellar and suprasellar mass, consistent with a giant pituitary adenoma. Initial prolactin was markedly elevated at 17 300 µg/L (normal range: 4.00-15.20 µg/L), confirming the diagnosis of a giant prolactinoma. Macroprolactinemia was excluded by PEG precipitation. Endocrine workup revealed mild hypogonadotropic hypogonadism without other pituitary deficiencies. Cabergoline 0.25 mg every other day was started immediately.

Results: Visual symptoms improved within 5 days of treatment initiation (MD values: 20 -> 15.2). Serial computer-assisted perimetry performed at each follow-up demonstrated consistent and objective improvement in visual field defects. In addition, a rapid and profound decline of prolactin was observed within 48 hours to 12 800 µg/L and 5 days to 1659 µg/L. Continued decline was documented after 46 days (534 µg/L).

Conclusion: This case illustrates the dramatic and rapid reversibility of severe neuro-ophthalmologic deficits in giant prolactinoma with extreme hyperprolactinemia. Despite presentation with impending blindness, dopamine agonist therapy resulted in rapid biochemical reduction and early visual recover. As part of ongoing research, this case supports the hypothesis that even low-dose dopamine agonist therapy may induce rapid and clinically meaningful recovery in high-risk giant prolactinoma.

Abstract citation ID: lvag096.1850

EP1820 - LBA_ECE_1225 - A case of co-existence of prediabetes and insulinoma and the advantages of EUS-RFA

Maria Pandelieva[1], Nevena Chakarova[2], Tsvetalina Tankova[2] and Petko Karagyozov[3]
[1]*University Specialized Hospital for Active Treatment in Endocrinology 'Acad. Ivan Penchev', Sofia, Bulgaria;* [2]*Clinic of Diabetology, University Specialized Hospital for Active Treatment in Endocrinology 'Acad. Ivan Penchev', Sofia, Bulgaria;* [3]*Acibadem City Clinic University Hospital Tokuda, Sofia, Bulgaria*

Insulinomas are functional neuroendocrine tumors (NETs) of the pancreatic β-cells characterized by inappropriate insulin secretion, resulting in recurrent episodes of hypoglycemia. Endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) is an innovative, minimally invasive technique for treatment of small (≤2 cm) pancreatic NETs, especially for comorbid patients with high surgical risk. EUS-RFA enables localized thermal destruction, under real-time endoscopic ultrasound guidance, leading to coagulative necrosis of tumor mass, preserving surrounding pancreatic tissue.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

We present the case of a 61-year-old man with obesity—BMI 40.1 kg/m^2, and confirmed episodes of severe hypoglycemia over the last 2 years. Initially, based on OGTT results consistent with prediabetes and severe insulin resistance—HOMA IR 12.2, a diagnosis of functional hypoglycemia was assumed. Treatment with a GLP-1 receptor agonist and insulin sensitizers was initiated, and because of the persistence of episodes of severe hypoglycemia further diagnostic evaluation was performed. MRI was negative while PET/CT 68Ga DOTA-TATE revealed a linear parenchymal structure with increased accumulation in the head of the pancreas, without the typical characteristics of insulinoma. A supervised fasting test lasting for 12 hours confirmed the presence of endogenous hyperinsulinism—a serum glucose of 2.3 mmol/l and unsuppressed insulin secretion with an extremely high insulin level—126.8 mIU/l (2-25 mIU/l) and C-peptide level—10.2 ng/mL (1.1-3.5 ng/mL). Endoscopic ultrasound showed a 18 mm hypoechoic mass and the immunostaining of the biopsy material confirmed NET G1. The patient refused surgery and EUS-RFA was performed without complications with immediate resolution of hypoglycemia. At the first follow-up 1 month after the intervention, the OGTT revealed persistence of prediabetes and severe insulin resistance—HOMA-IR 15.5, with stimulated insulin secretion reaching over 350 mIU/l during the test. The fasting test was performed in full 72 hours without registering a hypoglycemia. The test was terminated at a serum glucose of 4.5 mmol/l, low beta-hydroxybutirate level of 0.4 mmol/l, insulin 21.36 mIU/l and C-peptide 4.51 mmol/l. At this early stage, it was assumed that there is no evidence on the persistence of endogenous hyperinsulinism.

This case underscores the possibility of coexistence of prediabetes and insulinoma and the difficulty in the interpretation of hyperinsulinemia in this setting. The case also underlines the importance of follow-up after EUS-RFA as the complete effect of the procedure takes several months. On the other hand another advantage of this treatment modality is the possibility to repeat in case of persistence of the endogenous hyperinsulinism.

Abstract citation ID: lvag096.1851

EP1821 - LBA_ECE_1120 - Obesity in wartime Ukraine: evidence from 10 years of real-world data

Daria Lahoda[1,2], Valentyna Velychko[3] and Veronika Neporada[4]

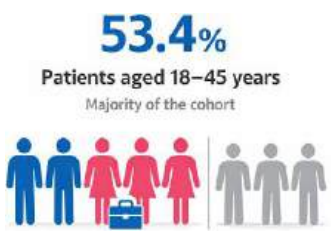
[1]Odesa National Medicine Univercity, Odesa, Ukraine; [2]Medical House Odrex, Odesa, Ukraine; [3]Odesa National Medicine University, Odesa, Ukraine; [4]Medical Hub Odrex, Odesa, Ukraine

Background: Obesity is a major global public health challenge with rapidly increasing prevalence and significant cardiometabolic risks. In Ukraine, epidemiological data remain limited, particularly in the context of ongoing war. Real-world clinical evidence is essential to understand current trends, identify high-risk groups, and improve early detection and multidisciplinary management strategies.

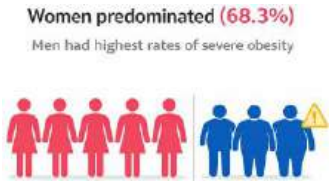
Materials and Methods: A retrospective single-center study analyzed 8760 electronic medical records of patients aged 18-75 years (2016-2025). Demographics, BMI categories, and referral patterns were assessed. Descriptive and comparative statistical methods were applied to evaluate trends, age- and sex-related differences, and associations between BMI and specialist referrals.

Aim: To analyze obesity trends in Ukraine during wartime using 10 years of real-world clinical data, focusing on BMI categories, age and sex differences, and patient referral pathways.

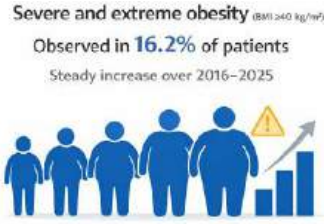
Results: The majority of patients were of working age (18-45 years), accounting for 55.0% of the cohort



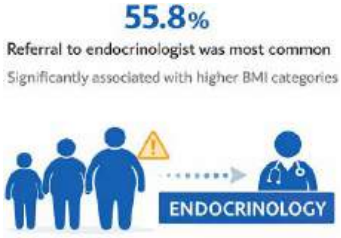
Women predominated (67.9%), while men more frequently presented with severe obesity



Severe and extreme obesity (BMI ≥40 kg/m^2) was observed in 15.3% of patients, with a steady increase over 2016-2025



Referral to endocrinologists was most common (56.1%) and was significantly associated with higher BMI categories



Conclusions:

1. Obesity increasingly affects individuals of working age, highlighting a growing impact on the active population and healthcare systems.
2. Gender differences suggest distinct clinical patterns, with women more likely to seek care, while men present with more advanced disease.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

3. The rising burden of severe obesity and its link to specialist referral emphasizes the need for earlier detection and structured care pathways.

Abstract citation ID: lvag096.1852

EP1825 - LBA_ECE_1464 - Elevated serum selenium as a potential marker for destructive thyroiditis: insights from a clinical case series

Natia Vashakmadze[1,2]

[1]*Department of Endocrinology, Ilia State University, Tbilisi, Georgia;* [2]*Department of Endocrinology, Israeli-Georgian Medical Research Clinic "Healthycore", Tbilisi, Georgia*

Selenium is a part of selenoproteins in thyrocytes, aiding thyroid hormone production and protecting the thyroid gland.

This case series investigates how serum selenium correlates with different types of thyroid dysfunction. Despite a small sample size, significant pathophysiologic patterns emerged. Patients with destructive thyroiditis and thyrotoxicosis showed high serum selenium, while those with non-destructive conditions had normal levels.

Case	Age	Sex	Disease	TSH	FT4	FT3	Thyroid US	TRAB	Anti-TPO	Serum selenium
#1	19	M	Graves' Disease	<0.005 mIU/mL	4 µg/mL (0.9-1.7)	14 ng/dl (2.5-5)	Nodular goiter; Volume - 46.4 cm^3	2.7 U/L (<1.6)		119 µg/l (79-120)
#2	28	F	AIT, newly diagnosed Hypothyroidism	19.5 mIU/mL	FT4 – 12.9 pmol/l (12-22)		Nonhomogeneous without nodules, volume – 8.0 cm^3		55.2 (<30)	119 µg/l (79-120)
#3	73	M	Amiodarone induced overt hypothyroidism	9.1 mIU/mL	8.1 pg/mL (12-22)		Multinodular Goiter, multiple cystic-solid nodules. volume 14.7 cm^3.		9.0 IU/mL (<34)	100 µg/l (79-120)
#4	59	F	Amiodarone induced thyrotoxicosis type 1	0.009 mIU/m	18.3 pg/mL (8.9-17)	2.85 pg/mL (2-4.2)	Volume- 17.6 cm^3; Nodular goiter;	0.98 IU/L (<1)		90 µg/l (50-120)
#5	58	M	Contrast induced thyroiditis, subclinical thyrotoxicosis	0.193 mIU/mL	FT4 – 1.55 ng/dl (0.9-1.7)		Structure normal, volume – 12.5 cm^3	<1.1 U/L (<1.5)		145 µg/l (79-120)
#6	40	F	Subacute thyroiditis + overt thyrotoxicosis	<0.09 mIU/mL	35.4 pmol/l (7-18)	13.9 ng/dl (3.6-6.9)	Thyroid painful, volume – 20 cm^3, markedly nonhomogeneous	<1 U/L (<1.5)		129 µg/l (60-120)
#7	35	F	Postpartum thyroiditis + thyrotoxicosis	0.012 mIU/mL	34.00 pmol/l (12.00-22.00)	6.69 pmol/l (3.10-6.80)		<1.1 mIU/mL (<1.5)	13.6 IU/mL (<34)	137 µg/l (60-120)
#8	66	F	Recurrent thyrotoxicosis due to exacerbation of subacute thyroiditis after steroid withdrawal *(After 2 weeks from steroid* withdrawal)	0.011 mIU/mL	40.10 (12.00-22.00) pmol/l	9.18 (3.10-6.80) pmol/l;	Thyroid painful, volume – 25.3 cm^3, markedly nonhomogeneous + multinodular goiter;	<1.1 mIU/mL (<1.5)		78 µg/l 50-120
#9	49	M	Amiodarone induced thyrotoxicosis mixed type	0.01 mIU/mL	3.21 ng/mL (0.9-1.75)	7.47 (2-4.2 pg/mL)	Thyroid volume 37 cm^3. Multinodular Goiter;	0.51 IU/L (<1.5)		132 µg/l (50-120)
#10	54	M	Amiodarone induced thyrotoxicosis type 2	0.01 mIU/mL	2.45 µg/mL (0.9-1.75)	6.46 pg/mL (2-4.2)	Volume – 14.5 cm^3; Non-Homogenous	0.25 IU/L (<1.5)		160 µg/l (50-120)

Consulsion: We hypothesize that follicular cell destruction releases selenium into the bloodstream. Therefore, elevated serum selenium could potentially serve as a diagnostic marker for thyrotoxicosis induced by various types of destructive thyroiditis.

Abstract citation ID: lvag096.1853

EP1829 - LBA_ECE_1443 - Dramatic response to cabergoline in a non-operable macroprolactinoma presenting with atypical tremor

Ezgi Yılmaz, Gulsah Elbuken and Sayid Zuhur

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Endocrinology and Metabolism, Tekirdağ Namık Kemal University, Tekirdağ, Turkey

Background: Invasive giant prolactinomas are rare subtypes of prolactin (PRL)–secreting pituitary neuroendocrine tumors (PİT-NETS), measuring >40 mm accounting for only 4.4% of all prolactinomas. Neurological manifestations such as tremor are highly uncommon and may obscure the diagnosis. We report a case of giant invasive macroprolactinoma presenting primarily with head tremor,without prominent classical endocrine symptoms.

Case Presentation: A 61-year-old male patient with no known disease presented to the neurology department with tremor in his head while looking at his phone for 3-5 years. A contrast-enhanced cranial magnetic resonance imaging (MRI) revealed a macroadenoma measuring 43*33*31 mm extending into the supracellar cistern,significantly compressing the optic chiasm and showing invasion of the right cavernous sinus. He was referred to the endocrinology outpatient clinic .The patient didn't present with typical symptoms of prolactinoma such as galactorrhea, erectile dysfunction,headache or visual field loss.His initial PRL level was 2259 ng/mL (4.04-15.2). Hooke's effect was ruled out .There were no abnormalities in the anterior pituitary panel except for hypogonadism. Visual field examination was normal . The patient was started on cabergoline 0.25 mg. The PRL level measured after 1 month was 148 ng/mL, and after 2 months it was 32.2 ng/mL. A pituitary MRI performed 1 month later after cabergoline showed the lesion regressed to 33 * 23 mm . Since the patient refused surgery, he kept under close observation with medical therapy. Patient's symptoms completely resolved.

Conclusion: This case is notable for its atyp,cal presentaton, as tremor was leading and only symptom of macroprolactinoma. The rapid biochemical and clinical response further supports the effectiveness of dopamin agonists, even in cases with very high prolactin levels and huge adenoma sizes.

Keywords prolactinoma, macroprolactinoma, giant

Abstract citation ID: lvag096.1854

EP1833 - LBA_ECE_1128 - Effect of a nutraceutical based on white mulberry leaves, fenugreek, niacin, chrome, zinc and a probiotic in a female patient with prediabetes, obesity and polycystic ovary syndrome: a case report

Borja Santana-Ojeda[1], Inmaculada Molinero-Marcos[1], Sara Andrada-Diaz[2], Claudia Arnas-Leon[1,3], Ricardo Jose de Leon-Durango[1], Agnieszka Kuzior[3], Carmen Acosta-Calero[4], Estefani Alcantara-Manzueta[1], Lisette Ojeda-Sanchez[1] and Francisco Javier Martinez-Martin[1,3]

[1]*Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain;* [2]*Medical Advisory, Bioksan Naturalmente Juntos, Las Palmas de Gran Canaria, Spain;* [3]*Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain;* [4]*Cardiology, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain*

Introduction: Polycystic ovary syndrome (PCOS) is closely linked to insulin resistance, a key driver of its metabolic and reproductive manifestations. This report describes a woman with obesity and prediabetes treated with a nutraceutical targeting insulin resistance, highlighting the causal role of metabolic dysfunction in PCOS and its therapeutic implications.

Methods: Review of the patient's clinical records and the relevant scientific literature.

Results: A 40-year-old administrative worker with overweight was referred for endocrine evaluation. She was reluctant to adopt dietary and exercise interventions.

She initially presented to Gynecology with irregular menses and hirsutism and was diagnosed with PCOS and prediabetes. She was subsequently referred to Endocrinology for metabolic control and weight management.

On physical examination, body mass index (BMI) was 29.7 kg/m^2, blood pressure 137/86 mmHg, heart rate 67 bpm. She had Ferriman–Gallwey grade II/IV hirsutism on the lower back (other areas depilated), waist circumference of 104 cm, and hepatomegaly (2 fingerbreadths). Acrochordons and acanthosis nigricans were present on the neck and axillae.

Baseline laboratory results showed: fasting glucose 102 mg/dL, HbA1c 6.2%, insulin 13.2 µIU/mL, total cholesterol 238 mg/dL, HDL-C 41 mg/dL, LDL-C 158 mg/dL, triglycerides 195 mg/dL, AST 68 U/L, ALT 43 U/L, GGT 83 U/L, and testosterone 0.98 ng/mL.

In addition to lifestyle advice, the patient was prescribed a nutraceutical based on white mulberry leaf, with demonstrated beneficial effects on insulin sensitivity.

After 6 months, the patient reported good tolerability and 94% adherence. She did not significantly modify diet or physical activity and experienced minimal weight loss (0.5 kg). However, she was very satisfied, reporting regular menstrual cycles over the previous 4 months.

On follow-up, BMI was 29.5 kg/m^2, blood pressure 126/78 mmHg, heart rate 64 bpm, with reduced acanthosis nigricans. Laboratory tests showed: fasting glucose 94 mg/dL, HbA1c 5.5%, insulin 6.4 µIU/mL, total cholesterol 233 mg/dL, HDL-C 49 mg/dL, LDL-C 152 mg/dL, triglycerides 160 mg/dL, AST 39 U/L, ALT 35 U/L, GGT 71 U/L, and testosterone 0.68 ng/mL.

HOMA2-IR improved from 1.75 to 0.84, FIB-4 from 1.52 to 0.92, and SCORE2 cardiovascular risk from 1.4% to 1.0%. Prediabetes resolved to normoglycemia.

Conclusion: This case illustrates that targeting insulin resistance can lead to meaningful metabolic and reproductive improvements in PCOS, including normalization of glycemia and menstrual cycles, even in the absence of significant weight loss. It supports a causal role of insulin resistance in PCOS and highlights the potential utility of nutraceutical-based interventions.

Abstract citation ID: lvag096.1855

EP1835 - LBA_ECE_1329 - Reversible nyctalopia from severe vitamin A deficiency and effective management of late weight regain with semaglutide after malabsorptive biliopancreatic diversion: a dual-outcome case report

Borja Santana-Ojeda[1], Marta Sánchez[1], David Rodriguez-Cruz[2], Inmaculada Molinero-Marcos[1], Claudia Arnas-Leon[1,3], Ricardo Jose de Leon-Durango[1], Alba Hernandez-Lazaro[1,4], Agnieszka Kuzior[1,3],

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Carmen Acosta-Calero[5] and Francisco Javier Martinez-Martin[1,3]
[1]Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [2]Ophthalmology, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain; [3]Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain; [4]Servei d'Endocrinologia i Nutricio, Parc Taulí Hospital Universitari, Sabadell, Barcelona, Spain; [5]Cardiology, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain

Background: In malabsorptive bariatric procedures such as biliopancreatic diversion (Scopinaro), late weight regain remains a frequent post-surgery challenge. These procedures also carry substantial long-term risk of fat-soluble vitamin deficiencies, particularly vitamin A, which can manifest as nyctalopia (night blindness), a potentially sight-threatening complication, yet reversible if addressed promptly.

We describe a paradigmatic case in which targeted micronutrient repletion reversed severe nyctalopia despite prior parenteral failure, while GLP-1 receptor agonist therapy effectively countered weight regain.

Methods: Review of the patient's clinical records and of the relevant scientific literature.

Results (Case Presentation): A 51-year-old woman with laparoscopic Scopinaro biliopancreatic diversion (2015; preoperative weight 149.5 kg, nadir 99 kg) presented in 2024 with progressive weight regain to 116 kg (waist circumference 124 cm) and refractory nyctalopia unresponsive to previous intramuscular vitamin A.

Biochemistry revealed profound deficiencies: vitamin A 0.09 µg/mL (lower normal limit 0.3 µg/mL), 25-OH vitamin D_3 7.8 ng/mL (lower normal limit 30 ng/mL), secondary hyperparathyroidism (PTH 119 pg/mL), and lumbar osteopenia (T-score −2.3).

Ophthalmologic evaluation confirmed preserved acuity (0.8/1), normal fundoscopy/Optical Coherence Tomography (OCT), consistent with functional nyctalopia.

Dual intervention included: (1) high-dose oral vitamin A (50 000 IU thrice daily) plus 25-OH vitamin D_3 loading/maintenance; and (2) weekly parenteral semaglutide titration for weight control. At six months: weight decreased to 106 kg (waist circumference 117 cm), vitamin A was almost normalized (0.29 µg/mL) with near complete nyctalopia resolution, vitamin D reached 88 ng/mL, PTH declined, and glycemic stability persisted (fasting glucose 96-100 mg/dL).

Conclusions: This case delivers two pivotal messages:

1. Severe vitamin A deficiency-induced nyctalopia after malabsorptive bariatric surgery remains reversible with sustained high-dose oral repletion, even after parenteral inadequacy, emphasizing the primacy of aggressive enteral strategies in compliant patients
2. GLP-1 receptor agonists like high-dose parenteral semaglutide offer a powerful, evidence-supported tool to reverse late weight regain, achieving substantial body weight reduction in a challenging post-bariatric cohort.

Lifelong multidisciplinary surveillance and multimodal therapy are essential to mitigate late complications such as these.

Abstract citation ID: lvag096.1856

EP1836 - LBA_ECE_1421 - Challenges and successful management of amiodarone-induced thyrotoxicosis: a report of two cases

Dilini Abeyratne, Helena Fahmi and Nilukshana Yogendranathan
Diabetes and Endocrinology, Princess Royal University Hopsital, King's College NHS Foundation Trust, Orpington, Kent, United Kingdom

Introduction: Amiodarone, an iodine-containing antiarrhythmic, is associated thyroid dysfunction ranging from subclinical biochemical abnormalities to overt disease. Amiodarone-induced thyrotoxicosis (AIT) may arise from increased thyroid hormone synthesis (AIT-1) or from destructive thyroiditis with the release of preformed hormones (AIT-2). Accurate differentiation is essential for guiding management; however, overlapping/ mixed forms are common, posing diagnostic and therapeutic challenges.

Case Presentations: Case 1: A 67-year-old man with prior ablation for atrial tachycardia (September 2023) presented with recurrence in October 2024 and new thyrotoxicosis (FT4 39.8 pmol/L, FT3 8.5 pmol/L, TSH <0.01 mIU/L), with previously normal thyroid function tests (TFTs). He had received amiodarone 200 mg daily for 3 months (November 2023–January 2024). He reported weight loss and intermittent diarrhoea, with no autoimmune family history. He was started on daily doses of carbimazole 20 mg, prednisolone 30 mg, and sotalol. Thyroid Stimulating Receptor Antibodies (TRAb) were negative; Thyroid ultrasound demonstrated normal dimensions, echotexture and vascularity. A nuclear medicine (NM) thyroid scan showed diffusely increased uptake, consistent with AIT-1.

Prednisolone was rapidly tapered and discontinued. Carbimazole was down titrated and was stopped by February 2026 following biochemical improvement. He remained euthyroid and discharged to primary care after one year of monitoring. Annual TFTs was recommended due to risk of late-onset hypothyroidism.

Case 2: A 55-year-old man presented to endocrinology in May 2025 with palpitations and weight loss following prolonged amiodarone use (200 mg daily, April 2023–January 2025). He had no goitre, ophthalmopathy or family history of thyroid disease. TRAb were negative. Ultrasound demonstrated bilateral hypoechoic micronodularity with normal vascularity, suggestive of thyroiditis.

NM scan demonstrated markedly reduced uptake of 0.09% (normal range = 1%-3%) consistent with AIT-2. He was treated with prednisolone 30 mg daily and short-term carbimazole, subsequently discontinued. Prednisolone was tapered and stopped by January 2026 following normalized TFTs. He remains euthyroid off treatment undergoing follow-up.

Conclusion: These two cases highlight the spectrum of AIT and the importance of distinguishing AIT-1 and AIT-2. Despite similar clinical presentations, differing underlying mechanisms necessitate tailored management, guided by biochemical, imaging, and antibody testing. Mixed/overlapping features, variable latency following amiodarone exposure and non-specific clinical findings pose diagnostic challenges. Therapeutically, balancing antithyroids and corticosteroids, while monitoring response and

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

avoiding overtreatment can be complex. These cases underscore the importance of close follow-up to optimize outcomes and detect potential late-onset hypothyroidism.

Abstract citation ID: lvag096.1857

EP1838 - LBA_ECE_1326 - Functional transformation of metastatic neuroendocrine carcinoma presenting with refractory hyperinsulinemic hypoglycemia in type 2 diabetes: a bi-directional dynamic glycemic phenotype

Rawan Alghawi, AlAnood AlQahtani and Azmi Mohammed
Department of Endocrinology and Metabolism, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia

Functional transformation of poorly differentiated, non-functioning neuroendocrine neoplasms is rare and often clinically under-recognised. We report a 78-year-old man with metastatic high-grade poorly differentiated pancreatic neuroendocrine carcinoma and hepatic metastases. He had long-standing type 2 diabetes mellitus, previously stable on oral therapy. After receiving systemic palliative chemotherapy, he developed recurrent hypoglycaemia, marking a transition from chronic hyperglycaemia to unexplained hypoglycaemia. Continuous glucose monitoring and serial laboratory glucose measurements confirmed frequent episodes with plasma glucose levels reaching 47 mg/dL. Biochemical evaluation during spontaneous hypoglycaemia showed inappropriately elevated insulin (77.3 µU/mL; reference 2-25 µU/mL) and C-peptide (9.15 ng/mL; reference 0.78-5.19 ng/mL), confirming endogenous hyperinsulinaemic hypoglycaemia. Insulin autoantibodies were negative. Adrenal insufficiency was excluded. There was no exposure to exogenous insulin or insulin secretagogues. Repeat histopathological evaluation was not feasible.

Subsequently, Diazoxide was started and effectively suppressed hypoglycaemia. However, after receiving lanreotide for oncologic management, the patient developed progressive hyperglycaemia. This necessitated the discontinuation of Diazoxide. He was transitioned to basal insulin, then to basal-bolus insulin therapy. Serial measurements over three months demonstrated a declining trend in C-peptide despite continued hyperglycaemia (5.87 ng/mL at glucose 337 mg/dL, then 1.89 ng/mL at glucose 156 mg/dL).

This case illustrates a bi-directional glycaemic phenotype driven by tumour-associated insulin secretion under therapeutic modulation. Notably, such functional transformation, although described in isolated reports, is exceptionally uncommon in poorly differentiated neuroendocrine carcinomas, in which hormone secretion is typically absent. These sequential changes reflect tumour plasticity and highlight the need for vigilant metabolic surveillance and adaptive multidisciplinary management.

Abstract citation ID: lvag096.1858

EP1841 - LBA_ECE_1249 - Does testosterone therapy resolve endometriosis symptoms in young transgender men? A retrospective study

Francisco Javier Martinez-Martin[1,2], Borja Santana-Ojeda[1], Inmaculada Molinero-Marcos[1], Estefani Alcantara-Manzueta[1], Lisette Ojeda-Sanchez[1], Alba Hernandez-Lazaro[1,3], Ricardo Jose de Leon-Durango[1], Claudia Arnas-Leon[1,2], Agnieszka Kuzior[1,2] and Carmen Acosta-Calero[1,4]
[1]*Endocrinology & Nutrition, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain;* [2]*Endocrinology & Nutrition, Hospitales Universitarios San Roque, Las Palmas de Gran Canaria, Spain;* [3]*Servei d'Endocrinologia i Nutricio, Parc Taulí Hospital Universitari, Sabadell, Barcelona, Spain;* [4]*Cardiology, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas de Gran Canaria, Spain*

Background and Objectives: Approximately half of transgender men receiving gender-affirming hormonal therapy (GAHT) with testosterone report nonmenstrual pelvic pain, and around one in eleven are diagnosed with endometriosis, according to a recent systematic review (doi: 10.1016/j.jmig.2025.08.009). Given that endometriosis is an estrogen-dependent condition, it has been hypothesized that testosterone therapy may improve symptoms by suppressing ovarian estrogen production, ovulation, and menstruation, and by inducing endometrial atrophy. However, evidence supporting this effect remains limited, heterogeneous, and largely observational. Furthermore, some individuals may retain hormonally active endometrial tissue. Potential mechanisms for persistent disease include peripheral aromatization of testosterone to estrogens, local estrogen production within endometriotic lesions, and progesterone resistance.

This study aimed to retrospectively assess the clinical course of symptomatic endometriosis in transgender men undergoing GAHT with testosterone in a real-world clinical setting.

Methods: We conducted a retrospective review of clinical records from transgender men aged <45 years who initiated testosterone therapy in our Transgender Clinic from January 2015 and had at least one year of follow-up. Patients with a prior diagnosis of endometriosis or diagnosed after presenting with chronic nonmenstrual pelvic pain at the initial visit were included. Data collected included persistence, improvement, or resolution of pelvic pain, as well as referral for total hysterectomy with bilateral adnexectomy (THBA).

Results: A total of 258 transgender men met inclusion criteria. Seventeen (6.6%) had endometriosis: 12 with a prior diagnosis and 5 diagnosed after their initial evaluation. All reported chronic nonmenstrual pelvic pain at baseline. Median follow-up after initiation of GAHT was 4.3 years.

During follow-up, six patients (35%) reported complete resolution of symptoms, and three (18%) experienced clear and sustained improvement. However, eight patients (47%) continued to report persistent pelvic pain, although none described consistent worsening. Among these, five reported occasional spotting, but none resumed regular menses.

Four patients (23.5%) were referred for THBA due to persistent symptoms. Surgical intervention resulted in symptom resolution or significant improvement in four patients (80%), while one (20%) continued to report chronic pelvic pain.

Conclusions: Testosterone therapy was associated with symptom improvement or resolution in approximately half of transgender men with endometriosis; however, a substantial proportion experienced persistent symptoms. THBA appears to be more resolutive, although not universally. These findings indicate that GAHT alone does not reliably resolve endometriosis and that additional interventions, including surgery, may

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

be required. Further prospective studies are needed to better define optimal management strategies in this population.

Abstract citation ID: lvag096.1859

EP1842 - LBA_ECE_1005 - Homozygous familial hypobetalipoproteinemia with abetalipoproteinemia-like phenotype: a rare multisystemic substrate crisis with negative MTTP sequencing

Beren Ayşe Altunsaray[1], Hanne Beyza Ayalan[1], Mina Gulfem Temizturk[2] and Muge Kuzu Kumcu[1,2]
[1]Faculty of Medicine, Atilim University, Ankara, Turkey; [2]Ankara, Turkey

Introduction: Abetalipoproteinemia (ABL) and Homozygous Familial Hypobetalipoproteinemia (HHBL) are ultra-rare lipid metabolism disorders. While ABL is typically caused by MTTP mutations, HHBL results from codominant APOB mutations. Both lead to a near-complete absence of apolipoprotein B-containing lipoproteins, creating a critical substrate crisis for fat-soluble vitamins and cholesterol, which precipitates hepatic, hematologic, and neuro-ophthalmological dysfunction.

Case Presentation: A 28-year-old female presented with menstrual irregularities, fatigue, and persistent steatorrhea. Laboratory screening revealed severe hypolipidemia (LDL-C <5 mg/dL). Diagnosis was confirmed by ApoB <20 mg/dL, Vitamin E 2.36 µg/mL (critical deficiency), and Vitamin A 520 ng/mL. Hormonal evaluation showed suppressed Estradiol (26 pg/mL). Peripheral smear demonstrated pathognomonic acanthocytosis.

Multidisciplinary screening revealed no irreversible pathologies. Hepatobiliary USG showed hepatomegaly (15.5 cm) with Grade 2 steatosis. Family screening confirmed a familial pattern: the 52-year-old father and 50-year-old mother exhibited significant asymptomatic hypolipoproteinemia (LDL-C: 27.8 and 61 mg/dL, respectively). Although there is no known consanguinity, both parents originate from the same small geographical region (approximately ≤250 000 inhabitants), suggesting a potential founder effect. This profile directs the diagnosis toward HHBL despite the severe phenotype.

Genetic Evaluation: Targeted MTTP sequencing detected no pathogenic mutations. Since MTTP defects are a regulatory prerequisite for official orphan drug access (eg, Lomitapide), the patient was ineligible for such targeted therapies. To explore the underlying pathology explaining this favorable clinical course, an expanded genetic panel is currently pending.

Management & Conclusion: Management involved a strict Low-LCT diet supplemented with Medium-Chain Triglyceride (MCT) oil. Initially, high-dose oral Vitamin E (400 IU 2 × 3) and Vitamin A (30 000 IU 1 × 3) were administered. The high cost of orphan drugs and the non-orphan status of MCT oil posed significant therapeutic barriers. Due to clinical stabilization and financial constraints, treatment was optimized to daily maintenance doses (1 × 1), aligning with state-covered insurance limits. This case underscores the challenges in drug access when canonical markers are absent. Aggressive ADEK supplementation remains the gold standard for stabilizing this phenotype, even when advanced pharmacological options are inaccessible.

Abstract citation ID: lvag096.1860

EP1843 - LBA_ECE_1388 - Resistant hypertriglyceridaemia associated with low-molecular-weight heparin in heterozygous LPL variant carriers

Murat Tozman[1], Adam D. McIntyre[2], Robert Hegele[2], Ilgin Simsir[1] and Gökçen Ünal Kocabaş[1]
[1]School of Medicine, Ege University, Izmir, Turkey; [2]University of Western Ontario, Ontario, Canada

Introduction and Objective: Biallelic pathogenic variants in the apolipoprotein (APO) C2, APOA5l, glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1 (GPIHBP1), lipase maturation factor 1 (LMF1), and lipoprotein lipase (LPL) genes cause familial chylomicronemia syndrome (FCS). Although heterozygous carriers typically exhibit a milder phenotype, severe hypertriglyceridemia (HTG) may develop in the presence of secondary triggers. Low-molecular-weight heparin (LMWH) can increase the release of LPL from the endothelium, potentially leading to an initial transient reduction in triglyceride (TG) levels; however, with continued use, rapid clearance of circulating LPL and limited resynthesis capacity may result in depletion of the functional LPL pool. In this report, we present a possible association between enoxaparin use and resistant HTG in a patient carrying a heterozygous pathogenic LPL variant.

Case Presentation: A 49-year-old man presented with a TG level of 5502 mg/dL (63.3 mmol/L), without a history of alcohol consumption. His medical history was notable for myocardial infarction 14 years earlier, 11 episodes of pancreatitis, and portal and splenic vein thrombosis following a severe pancreatitis episode six months prior, as well as pancreatitis-related secondary diabetes mellitus. Glycemic control was stable, with a hemoglobin A1c level of 6.4% at presentation.

Genetic analysis identified a heterozygous pathogenic variant in the LPL gene, c.347G>C (p.Arg116Pro). Although the patient's sister carried the same heterozygous variant, her TG levels had been reported to be no higher than 500 mg/dL (5.6 mmol/L).

Despite treatment with fenofibrate, rosuvastatin, nicotinic acid, orlistat, and intravenous insulin infusion, the TG level remained elevated at 4770 mg/dL (53.9 mmol/L), without a meaningful reduction. After treatment reassessment, LMWH was discontinued due to its potential contributory role, and rivaroxaban was initiated. Following this modification, the TG level decreased to 1516 mg/dL (17.1 mmol/L).

Discussion and Conclusion: The marked interindividual variability in phenotypic severity among heterozygous LPL variant carriers suggests a substantial contribution of secondary modifiers. In our patient, persistently elevated TG levels despite intensive lipid-lowering therapy and adequate glycemic control suggested an ongoing precipitating factor. The substantial decline in TG levels following discontinuation of LMWH suggests that anticoagulant therapy may have had a clinically relevant impact in the setting of genetically limited LPL activity.

This observation underscores the importance of carefully reviewing not only metabolic determinants but also concomitant pharmacologic treatments in patients with severe and refractory HTG. In individuals with an underlying genetic predisposition, LMWH use should be assessed on an individual basis for its potential contributory role.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1861

EP1848 - LBA_ECE_1170 - Dual-mechanism life-threatening hyponatraemia: NSAID-induced hyporeninemic hypoaldosteronism unmasking Sheehan's syndrome latent for four decades

Zain Komal[1,2], Haroon Arshad[3], Asif Mehmood[1], Ma Pyeh Kyithar[1] and Jayant Sharma[1]
[1]Endocrinology, Midland Regional Hospital, Portlaoise, Ireland; [2]Endocrinology, Internal Medicine, Midland Regional Hospital, Portlaoise, Ireland; [3]Midland Regional Hospital, Portlaoise, Ireland

Introduction: Severe hyponatraemia refractory to saline resuscitation typically prompts investigation of a single cause. We report the first characterisation of concurrent NSAID-induced hyporeninemic hypoaldosteronism and panhypopituitarism from Sheehan's syndrome, two pathologies that synergised to produce refractory salt-wasting hyponatraemia through dual peripheral and central mechanisms, identifiable through parallel mineralocorticoid and pituitary axis evaluation. Given widespread NSAID use and increasing migrant populations with undiagnosed peripartum pituitary injury across Europe, this combination may be under-recognised.

Case Description: A 64-year-old woman presented with bilateral lower limb pain, proximal myopathy, weight loss (>7 kg), fatigue and polyuria after three months of NSAID use and recent radiocontrast exposure. She had a prior episode of severe hyponatraemia (Na 112 mmol/L) four years earlier without aetiological workup. Sodium was 121 mmol/L on admission, dropping to 110.8 mmol/L despite 0.9% normal saline 1 litre TDS–QDS and repeated 2.7% hypertonic saline boluses throughout a 32-day admission with 30 days in ICU. Urinary sodium was 160 mmol/L with output peaking at 7185 mL/24 h, representing daily renal sodium losses exceeding 500 mmol. Serum osmolality was 231 mOsmol/kg against inappropriately concentrated urine (656 mOsm/kg) with flat IVC on ultrasound. A desmopressin challenge worsened hyponatraemia (133-123 mmol/L), excluding SIADH and confirming salt-wasting physiology.

Results: Parallel axis evaluation identified two mechanistically distinct pathologies. Mineralocorticoid axis: aldosterone 39 pg/mL (ref 68-249), renin 3.4 pg/mL (suppressed), ARR 11.47, with hypokalaemia and low bicarbonate at normal anion gap, confirming hyporeninemic hypoaldosteronism. Pituitary axis: fasting cortisol 96 nmol/L, ACTH 12.4 pg/mL (inappropriately low, confirming central aetiology), FT4 4.1 pmol/L (ref 9.8-23), FT3 2.1 pmol/L (ref 4.7-7.2), TSH 0.38 mIU/L (inappropriately low), prolactin 64 mIU/L (low), IGF-1 12 µg/L (ref 36-244). MRI revealed empty sella with tiny residual pituitary. Autoimmune screen was negative. Collateral history uncovered prolonged labour, lactation failure and premature menopause, consistent with Sheehan's syndrome undiagnosed for four decades. This coexistence has not been previously described.

Conclusions: Fludrocortisone, hydrocortisone and levothyroxine normalised sodium to 136-140 mmol/L. At three-month follow-up, aldosterone normalised (39-158 pg/mL) and fludrocortisone was discontinued, establishing the NSAID-induced component as transient, while permanent pituitary deficiency required ongoing replacement, with complete resolution of myopathy confirming the diagnosis. This case establishes that refractory salt-wasting hyponatraemia can arise from simultaneous peripheral and central endocrine failure, distinguishable only through systematic parallel evaluation of mineralocorticoid and pituitary axis. We propose this approach for any patient with NSAID exposure presenting with unexplained, refractory or recurrent hyponatraemia.

Abstract citation ID: lvag096.1862

EP1851 - LBA_ECE_1409 - Primary amenorrhea revealing idiopathic premature ovarian insufficiency with early bone compromise: a missed opportunity for early diagnosis

Dilini Abeyratne, Helena Fahmi and Nilukshana Yogendranathan
Diabetes and Endocrinology, Princess Royal University Hopsital, King's College NHS Foundation Trust, Orpington, Kent, United Kingdom

Introduction: Primary amenorrhea is an important clinical presentation in adolescence. Evaluation is guided by hormonal assessment, with progestin or combined estrogen–progestin challenge tests helping differentiate central, ovarian, and outflow tract causes.

Premature ovarian insufficiency (POI) is a rare cause of primary amenorrhea, and may present diagnostic challenges. We report a 16-year-old girl who presented with primary amenorrhea and was ultimately diagnosed with idiopathic POI following a thorough evaluation, with negative genetic and autoimmune workup. In this case, a delay in diagnosis following initial presentation to primary care, contributed to compromised bone health at the time of diagnosis. This report underscores the importance of early recognition and prompt evaluation of primary amenorrhea to reduce the risk of long-term complications.

Case Presentation: A 16-year-old female presented with primary amenorrhea despite normal secondary sexual characteristics. She denied anosmia, galactorrhea, hirsutism, headaches, visual disturbances, weight changes, or cyclical abdominal pain. Past medical, drug, and family histories were unremarkable.

On examination, BMI was 15.5 kg/m^2 with normal blood pressure. She had Tanner stage IV breast development and stage II-III pubic hair, with no dysmorphic features or clitoromegaly.

Initial investigations demonstrated elevated gonadotropins (FSH 85.7 U/L, LH 25.3 U/L) with low estradiol (<92 pmol/L), consistent on repeat testing. Anti-Müllerian hormone (AMH) was markedly reduced (<0.2 pmol/L). Prolactin, thyroid function, Dihydroepiandrostendione, 17 hydroxy-progesterone, and androgen profiles were normal. Ovarian and adrenal antibodies were negative. Autoimmune screening, including, anti-thyroid peroxidase, anti-intrinsic factor, anti-diabetic antibodies and celiac screen were negative.

Pelvic ultrasound revealed small ovaries without follicles and a normal-sized uterus. No outflow tract abnormalities were identified. Progesterone challenge produced withdrawal bleeding. Genetic testing confirmed a normal 46,XX karyotype. Full genetic panel testing for POI including FMR1 premutation were negative. Very low AMH favoured against possible FSH/LH resistance

Conclusion: A diagnosis of idiopathic POI was made. Initial bone densitometry showed osteopenia. The patient was commenced on oestrogen–progesterone replacement therapy, resulting in regular withdrawal bleeds, with ongoing management focused on bone health preservation.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Early evaluation of primary amenorrhea is essential, as prompt diagnosis of conditions such as idiopathic POI allows timely initiation of hormone replacement therapy, which is critical to preserve bone health and reduce long-term metabolic and reproductive complications. Delayed diagnosis may result in preventable morbidity, underscoring the need for early and thorough assessment at first presentation.

Abstract citation ID: lvag096.1863

EP1854 - LBA_ECE_1118 - Discordant growth hormone dynamics and hyperprolactinaemia associated with migraine-related hypothalamic dysfunction

Ciaran Walsh, Uroosa Moqeem and Aneliya Sirkova
London, United Kingdom

A woman in her 30s was referred to Endocrine clinic for persistent galactorrhoea and intermittent mild hyperprolactinaemia. She had a history of migraine with aura. Insulin-like growth factor-1 concentrations were mildly elevated but consistently remained below recognised diagnostic thresholds for acromegaly, with normal insulin-like growth factor binding protein-3. Pituitary magnetic resonance imaging was normal. Oral glucose tolerance testing demonstrated elevated basal growth hormone concentrations with failure of suppression. Despite these biochemical findings, there was no clinical or radiological evidence of acromegaly. The constellation of discordant growth hormone dynamics, mild hyperprolactinaemia, and migraine supports hypothalamic inhibitory dysfunction affecting multiple pituitary axes rather than autonomous endocrine disease. This case highlights the importance of recognising functional hypothalamic–pituitary dysregulation as a cause of abnormal dynamic endocrine testing and avoiding misdiagnosis of pituitary tumours.

Abstract citation ID: lvag096.1864

EP1855 - LBA_ECE_1309 - Parathyromatosis presenting as severe hypercalcemia after multiple parathyroid surgeries: a diagnostic challenge

Eirini Melidou[1], Artemis Kyriakidou[1], Xanthippi Tsekmekidou[1], Maria Zikopoulou[1], Konstantinos Sapalidis[2], Maria Grammatiki[1], Litsa Rakitzi[1], Kyriakos Chatzopoulos[3] and Kalliopi Kotsa[1]
[1]*Division of Endocrinology and Metabolism—Diabetes Center, 1st Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA University Hospital, Thessalonki, Greece;* [2]*3rd Surgical Department, Aristotle University of Thessaloniki, AHEPA University Hospital, Thessaloniki, Greece;* [3]*Laboratory of General Pathology and Pathological Anatomy, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Objective: Parathyromatosis is a rare cause of persistent or recurrent primary hyperparathyroidism, typically occurring after parathyroid surgery. We present a case of severe hypercalcemia caused by parathyromatosis in a patient with multiple previous cervical surgeries for primary hyperparathyroidism.

Case Presentation: A 65-year-old woman presented with nausea, dizziness and generalized weakness. Her medical history included hemithyroidectomy with postoperative hypothyroidism, type 2 diabetes mellitus and surgically treated primary hyperparathyroidism. The patient had recently discontinued cinacalcet therapy. Clinical examination revealed a palpable painless mass near the angle of the left mandible. Laboratory evaluation showed severe hypercalcemia (Ca: 16 mg/dL), elevated parathyroid hormone levels (PTH: 188 pg/mL; reference range 14.9-56.9 pg/mL), hypomagnesemia (Mg: 1.38 mg/dL) and hypophosphatemia (P: 1.6 mg/dL). The patient was treated with intravenous hydration, diuresis, reintroduction of cinacalcet and magnesium supplementation, resulting in gradual improvement of calcium levels and symptoms. Review of the patient's medical history revealed five previous cervical surgeries for primary hyperparathyroidism and the presence of a 3-cm left adrenal lesion compatible with an adenoma that had not been previously investigated. Neck ultrasound demonstrated a 1.3-cm hypoechoic lesion posterior to the left thyroid lobe compatible with an enlarged parathyroid gland, as well as suspicious lymph nodes. Parathyroid scintigraphy revealed hyperfunctioning parathyroid tissue in two locations adjacent to the upper and lower poles of the left thyroid lobe. Based on imaging findings and surgical history, parathyromatosis was suspected, with parathyroid carcinoma considered in the differential diagnosis. Additional imaging with 4D CT revealed multiple nodular lesions in the left lateral cervical region, the esophageal wall and along the sternocleidomastoid muscle, suggestive of disseminated parathyroid tissue. Due to persistent hypercalcemia despite maximal cinacalcet therapy (360 mg/day), surgical treatment was recommended by the multidisciplinary tumor board.

Follow-up: Histopathological examination confirmed parathyromatosis. Seven months after surgery, the patient remains asymptomatic without medical therapy and maintains normal calcium and parathyroid hormone levels.

Conclusion: Parathyromatosis is a rare but important cause of persistent or recurrent hyperparathyroidism following parathyroid surgery. It may present with severe hypercalcemia and can mimic parathyroid carcinoma. Diagnosis requires careful correlation of clinical history, imaging findings and histopathological confirmation. Early recognition is essential to guide appropriate surgical management and prevent complications related to prolonged hypercalcemia.

Abstract citation ID: lvag096.1865

EP1856 - LBA_ECE_1316 - Kallmann syndrome mimicking as Müllerian agenesis: a diagnostic challenge

Selma Jusufovic, Enra Desevic, Anisa Sahbaz, Ilma Sirbegovic and Lamija Mlaco
Department of Reproductiv Endocrinology, Clinical Center University of Sarajevo, Clinic for Endocrinology, Sarajevo, Bosnia and Herzegovina

Introduction: Hypogonadotropic hypogonadism is a rare but important cause of primary amenorrhea. Kallmann syndrome, characterized by gonadotropin-releasing hormone deficiency and anosmia, may be misdiagnosed when prolonged estrogen deficiency results in non-visualization of reproductive organs.

Case Presentation: A 26-year-old woman with primary amenorrhea and absent pubertal development had previously been diagnosed with uterine and ovarian agenesis. Hormone replacement therapy had been recommended but not initiated. At presentation, she had poor breast development (Tanner stage II), normal external genitalia, and pubic hair consistent

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

with Tanner stage III/IV. Her history revealed progressive hyposmia evolving into anosmia. Hormonal evaluation confirmed hypogonadotropic hypogonadism, and the karyotype was 46, XX. Initial imaging again failed to visualize the uterus and ovaries, raising suspicion of Müllerian agenesis. Pituitary MRI showed hypoplasia, and bone densitometry revealed osteopenia. Estrogen therapy was initiated. Follow-up ultrasound demonstrated uterine development with appropriate endometrial thickness and visualization of adnexal structures. After five months, transvaginal ultrasound confirmed a normal uterus with a trilaminar endometrium and both ovaries, excluding Mayer-Rokitansky-Küster-Hauser syndrome. MRI of the olfactory region showed hypoplastic olfactory structures, confirming Kallmann syndrome. Progesterone was added, resulting in regular withdrawal bleeding.

Conclusion: This case highlights that prolonged estrogen deficiency can lead to misdiagnosis as Müllerian agenesis on imaging. Timely recognition and hormone therapy are essential for accurate diagnosis, restoration of reproductive anatomy, and preservation of bone and reproductive health.

Keywords Kallmann syndrome, hypogonadotropic hypogonadism

Abstract citation ID: lvag096.1866

EP1859 - LBA_ECE_1300 - Patient with anaplastic thyroid carcinoma evolving from papillary thyroid carcinoma ten years after initial diagnosis

Chrysanthi Balodimou, Georgios Christantoniou, Constantina Philippidou, Charalampos Papadopoulos, Eleana Zisimopoulou, Maria Boudina and Alexandra Chrisoulidou

Department of Endocrinology, Theagenio Cancer Hospital, National Center of Endocrine Oncology, Thessaloniki, Greece

Background: The majority of anaplastic thyroid carcinomas (ATC) derives from preexisting papillary thyroid carcinomas (PTC). Although ATC is a rare entity, when it occurs, it is more often detected at the site of the primary tumor or at cervical lymph nodes and less often at distant metastases, such as lungs, breast and retroperitoneum.

Case Presentation: A 61-year-old female underwent total thyroidectomy and right lateral lymph node dissection ten years ago. The histology revealed a papillary thyroid carcinoma sized 2 cm, with foci of solid nests, no evidence of extrathyroidal extension, but metastases in 8 out of 36 cervical lymph nodes. The patient underwent RAI ablation and active surveillance thereafter, due to persistent high thyroglobulin levels. During her close follow-up, ultrasound findings were consistent with remnant pathological right lateral lymph nodes and she developed pulmonary nodules. She was then subjected to RF ablation of right lateral lymph nodes, followed by a second dose of radioiodine treatment. Due to deterioration of secondary pulmonary lesions (progressive disease according to RECIST criteria), initiation of treatment with Lenvatinib was decided. Three years after treatment with TKIs, she presented a sudden right-sided neck swelling. The ultrasound revealed enlargement of right lateral cervical lymph nodes. The patient underwent central and right lateral neck lymph node dissection and histopathology revealed that 19 lymph nodes and 2 lymph blocks out of 31 excised lymph nodes were infiltrated by ATC.

Conclusions: Increased vigilance and close follow-up are required for patients with differentiated thyroid carcinoma, whose histopathology subtypes and characteristics imply aggressive behavior.

Abstract citation ID: lvag096.1867

EP1860 - LBA_ECE_1034 - Metachronous hormonal syndromes in digestive neuroendocrine tumors: a case of sequential gastrin and ACTH secretion

Solène Eon[1], Marine Briand[1], Morgane Mauger[1], Nina Kissel[2], Florence Pihan-Le Bars[2], Daniela Hurjui-Jarnet[2], Anne-Laure Coulon[2], Oana Ionesco[2], Mélanie Priou[2] and Patricia Vaduva[1]

[1]Rennes University Hospital, Rennes, France; [2]Saint-Brieuc Hospital, Saint-Brieuc, France

Background: Metachronous hormonal syndromes (MHS) occur in 3.4%-6.8% of digestive neuroendocrine tumors (NETs), predominantly in pancreatic locations. This report examines the rare metachronous association of gastrinoma and paraneoplastic ACTH secretion, a combination characterized by high clinical severity.

Case Presentation: We report the case of a 75-year-old patient with hepatic lesions discovered during follow-up of a previously treated sarcoma. Liver biopsy revealed a well-differentiated grade 2 NET (Ki-67 8%), initially non-functional. Six months later, the patient presented with hematemesis, and duodenal biopsies confirmed a grade 2 NET with gastrinoma. Clinical and radiological stability was initially achieved with proton pump inhibitors and somatostatin analogues. One year later, new-onset diabetes associated with severe hypokalemia led to the diagnosis of ACTH-dependent Cushing's syndrome, with markedly elevated urinary free cortisol (58 times upper limit of normal), suggesting paraneoplastic secretion. Osilodrostat was initiated. Due to tumor progression, repeat liver biopsy demonstrated focal ACTH expression and an increased Ki-67 index (15%), supporting tumor evolution. In the context of severe hypercortisolism and hypergastrinemia, the biopsy was complicated by duodenal perforation, requiring high-dose proton pump inhibitors and temporary intravenous etomidate. Despite biochemical control of hypercortisolism and systemic chemotherapy (temozolomide–capecitabine), the disease progressed with hepatic and bone metastases, leading to death three years after diagnosis.

Discussion: Pathophysiologically, MHS likely stems from clonal evolution or the emergence of distinct cell subpopulations, often correlating with an increased Ki-67 index and tumor grade progression. Diagnostic confirmation is frequently hindered by heterogeneous hormone expression, underscoring the necessity for repeated biopsies during clinical progression. Management remains complex and multimodal, requiring urgent hormonal stabilization alongside systemic therapy. Ultimately, MHS illustrates the biological plasticity of NETs; recognizing these transitions is vital, as secondary hormonal functionalization significantly alters therapeutic priorities and patient prognosis, necessitating lifelong clinical vigilance.

Conclusion: Metachronous hormonal syndromes (MHS) in digestive neuroendocrine tumors are rare but pose significant clinical challenges. This case highlights the sequential emergence of

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

gastrinoma and paraneoplastic ACTH secretion and its major clinical impact. Early recognition of new endocrine symptoms is essential, as secondary hormonal secretions profoundly alter therapeutic priorities and patient survival.

Abstract citation ID: lvag096.1868

EP1862 - LBA_ECE_1040 - Type 1 diabetes mellitus (T1DM) in real-world clinical practice in Odessa, Ukraine: a six-year retrospective analysis of prevalence, age, and gender of patients for the period 2019-2025

Veronika Neporada
Дім Медицини, MH "Odrex", Clinic, Одеська міська громада, Ukraine

Materials and Methods of the Study: According to the design of the study, it was a retrospective single-center observational study. The study material was the medical records of patients who were treated at MH "ODREX" in the period from January 1, 2019. to December 31, 2025.

The study included 121 electronic medical records of patients aged 14-90 years. The inclusion criteria were: consent to the processing of personal data, the presence of a confirmed diagnosis of T1DM according to the protocol, initial treatment or hospitalization within the specified period (to avoid duplication of patients).

The study was conducted in compliance with the ethical standards of biomedical research and the principles of the Declaration of Helsinki. All patient data were depersonalized and used exclusively for scientific purposes.

Table 1 Age characteristics of patients with T1DM by 2019 year.

Age	*n*	%
14-18 years	0	**0%**
18-44 years	7	**22.6%**
45-59 years	5	**16.1%**
60-74 years	13	**41.9%**
75-90 years	6	**19.4%**
31 patients		

Table 2 Gender characteristics of patients with T1DM by 2019 year.

Gender	*n*	%
Women	24	77
Men	7	31
Total	31	**100**

Table 3 Age characteristics of patients with T1DM by 2025 year.

Age	*n*	%
14-18 years	7	**7.7%**
18-44 years	28	**31.1%**
45-59 years	26	**28.9%**
60-74 years	23	**25.6%**
75-90 years	6	**6.7%**
90 patients		

Table 4 Gender characteristics of patients with T1DM by 2025 year.

Gender	*n*	%
Women	57	63
Men	33	37
Total	90	**100**

Conclusions: The proportion of patients increased by 190% (2.9 times or 59 people)—this indicates a steady trend towards an increase in the proportion of patients with T1DM during the period 2019-2025.

In the total sample of patients, there was a predominance of women compared to men

Abstract citation ID: lvag096.1869

EP1863 - LBA_ECE_1163 - Semaglutide and contraceptive efficacy: insights from FAERS and patient experiences

Nithin Tumkur Prasad
Bengaluru, India

Introduction: Semaglutide delays gastric emptying and may alter absorption of oral medications, including combined oral contraceptives. The real-world implications of this interaction remain uncertain, representing a potentially important patient safety concern in women of reproductive age.

Aim: To evaluate whether semaglutide is associated with disproportionate reporting of contraceptive-related pregnancy outcomes in women of reproductive age and to explore patient-reported experiences to identify potential signals from real-world data.

Methods: A retrospective pharmacovigilance study was conducted using the U.S. Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) from January 2018 to January 2026. Female reports involving semaglutide were identified. Disproportionality was assessed using reporting odds ratio (ROR) and proportional reporting ratio (PRR) with predefined signal detection thresholds (ROR 95% CI >1, PRR ≥2, χ^2 ≥4). Complementary thematic analysis of 635 publicly available posts from X and Reddit was performed, including posts clearly discussing semaglutide use and contraceptive experiences, with duplicates removed to ensure unique patient perspectives.

Results: Among 37 733 female semaglutide reports, 16 involved pregnancy while on oral contraception. Disproportionality analysis revealed a significant signal (ROR 5.15, 95% CI 3.15-8.42; PRR 5.15), with the lower confidence interval exceeding the predefined threshold. Signal strength was highest for obesity-indicated formulations. Social media analysis identified users reporting unintended pregnancies and concerns regarding contraceptive efficacy, frequently alongside gastrointestinal adverse effects.

Conclusion: A pharmacovigilance signal for contraceptive-related pregnancy was identified with semaglutide. While causality cannot be established, these findings highlight a potential real-world safety concern not fully captured in pharmacokinetic studies.

Impact: Endocrinologists and obesity specialists should discuss potential contraceptive efficacy concerns with women starting

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

semaglutide, especially during dose escalation, and review alternative or additional contraceptive options.

Abstract citation ID: lvag096.1870

EP1864 - LBA_ECE_1317 - SGLT2 inhibitor–associated euglycemic diabetic ketoacidosis: the importance of early acid–base assessment

Nikolaos Davanellos, Rafail Giannas, Nikolaos Kouris, Dimitrios Argiropoulos and Mixalis Apergis
Ermoupoli, Greece

Background: SGLT2 inhibitors increase the risk of euglycemic diabetic ketoacidosis (EDKA), a potentially life-threatening condition that may be overlooked due to near-normal glucose levels.

Case Presentation: A 43-year-old man with type 2 diabetes treated with empagliflozin–linagliptin–metformin presented with vomiting and diffuse abdominal pain for 16 hours following reduced oral intake and a urinary tract infection. On admission, he was mildly dehydrated and tachycardic (HR 111 bpm), with plasma glucose of 173 mg/dL. Despite the absence of marked hyperglycemia, early arterial blood gas analysis revealed severe metabolic acidosis (pH 7.15, HCO_3^- 8.7 mEq/L) with low lactate (0.8 mmol/L). Serum ketones were markedly elevated (7.1 mmol/L), confirming EDKA precipitated by infection and fasting. The SGLT2 inhibitor was discontinued, and the patient was treated with intravenous fluids, insulin infusion, dextrose, and potassium replacement. Metabolic parameters normalized within 24 hours, and he was discharged on basal–bolus insulin with appropriate education.

Conclusion: EDKA should be suspected in SGLT2-treated patients presenting with gastrointestinal symptoms even in the absence of hyperglycemia. Early arterial blood gas analysis is critical for prompt diagnosis and timely management. Delay in recognition may lead to severe metabolic deterioration and increased morbidity.

Abstract citation ID: lvag096.1871

EP1865 - LBA_ECE_1230 - Rare case of phaeochromocytoma presenting with pancreatitis, complicated by duodenal fistulation and massive upper gastrointestinal haemorrhage from a splenic artery pseudoaneurysm

Neha Fatima[1,2], Aiyappa Biddanda[1], Emily Goodchild[3], Scott Akker[3], William Martyn Drake[3], Sulmaaz Qamar[1] and Ravi Menon[1]
[1]*North Middlesex University Hospital, Royal Free London NHS Foundation Trust, London, United Kingdom;* [2]*North Middlesex University Hospital, London, United Kingdom;* [3]*Barts Health NHS Trust, London, United Kingdom*

Background: Phaeochromocytoma typically presents with catecholamine excess, while pancreatitis, diabetic ketoacidosis (DKA) and delayed catastrophic gastrointestinal haemorrhage are distinctly uncommon manifestations. We report a complex case of residual biochemically active left phaeochromocytoma complicated by duodenal fistulation and massive upper gastrointestinal bleeding from a splenic artery pseudoaneurysm, highlighting the importance of coordinated multi-centre stabilisation and intervention.

Case Presentation: A 35-year-old man initially presented in 2022 with acute pancreatitis, severe hypertriglyceridemia (triglycerides 140 mmol/L) and DKA. Cross-sectional imaging revealed a 63 mm necrotic left adrenal mass. Biochemistry showed plasma normetanephrine >10 000 pmol/L and elevated 3-methoxytyramine, consistent with a noradrenergic/dopaminergic-secreting phaeochromocytoma. Germline testing using an 11-gene susceptibility panel was negative. Following staging and alpha-blockade, he underwent left adrenalectomy in January 2024. Resection was difficult because of extensive pancreatitis-related adhesions involving the pancreatic tail, splenic flexure and tumour bed. Histology confirmed a 7.5 cm phaeochromocytoma with central necrosis, retained SDHB staining and Ki-67 up to 10% in hotspot areas, without vascular invasion. Despite surgery, post-operative imaging and biochemistry remained concerning for persistent locoregional disease, including an FDG-avid 26 mm lesion in the adrenalectomy bed, ongoing normetanephrine elevation and a suspicious 10 mm retroperitoneal node at the coeliac axis. Stereotactic ablative radiotherapy was administered to the tumour bed. In October 2025, he presented to a district general hospital with severe abdominal pain, diarrhoea, haematochezia and haemodynamic instability. Haemoglobin fell from 122 to 75 g/L, requiring transfusion of 3 units of packed red cells. Urgent upper gastrointestinal endoscopy identified clot and a suspected bleeding source beyond the distal duodenum. After initial stabilisation with blood products, he was transferred to a tertiary centre. Triple-phase CT demonstrated a gas-containing cavity at the adrenalectomy bed with direct communication to D4, consistent with potential fistulation, and a splenic artery pseudoaneurysm causing haemorrhage. He underwent urgent splenic artery embolisation, which resolved the bleeding, and was discharged with endocrine follow-up for repeat plasma metanephrines, interval imaging and ongoing multidisciplinary discussion regarding management of persistent disease. During admission, no additional alpha-blockade was given because of ongoing hypotension and low catecholamine burden, which was considered inconsequential to his haemodynamic status.

Conclusion: This case illustrates an exceptionally rare and clinically important trajectory of phaeochromocytoma, from presentation with pancreatitis and DKA to persistent locoregional disease and delayed massive upper gastrointestinal haemorrhage due to duodenal fistulation and splenic artery pseudoaneurysm. It emphasises the need for coordinated endocrine, radiological, surgical and interventional management in complex residual phaeochromocytoma.

Abstract citation ID: lvag096.1872

EP1869 - LBA_ECE_1302 - A case report of a 17 year old male patient presenting with tetany and secondary hyperparathyroidism. A diagnostic revision

Eirini Biliou[1,2], Maria Tzoraki[2], Sofia Leka-Emiri[2], Stefanos Fakiolas[3], Evanthia Kassi[1] and Elpis Vlachopapadopoulou[2]
[1]*Endocrine Unit, First Department of Propaedeutic and Internal Medicine, Medical School, National and Kapodistrian University of Athens, C.E.R.E.D, Laiko General Hospital of Athens, Athens, Greece;* [2]*Department of Endocrinology, Growth and Development, Children's Hospital P. & A. Kyriakou, Athens, Greece, Athens, Greece;*

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

[3]Biochemical Department, 'P. & A. Kyriakou' Children's Hospital of Athens, Athens, Greece

Background: Pseudohypoparathyroidism (PHP) is a group of heterogeneous genetic disorders, characterized by kidney and bone unresponsiveness to PTH, with hypocalcemia, hyperphospatemia and elevated parathormone levels. It is divided into PHP Type 1 and 2. Type 1 demonstrates diminished cAMP and phosphate excretion in urine and Type 2 shows normal cAMP response but blunted phosphate excretion. PHP type 1b is defined as resistance to PTH in the kidney and normal PTH response in bone. Unlike patients with PHP type 1a and 1c patients with type 1b do not have phenotypic expression of Albright hereditary osteodystrophy (AHO). The differential diagnosis of hypocalcemia includes hypoparathyroidism, Vitamin D deficiency and chronic kidney disease.

Clinical Case: A 17-year-old boy presented with tetany. He had no notable prior personal of family medical history, skeletal abnormalities or intellectual impairment.

During physical examination Chvostek sign was positive and intermittent carpometacarpal spasms were present. Biochemical testing revealed Calcium: 5.7 mg/dl, PTH: 188 pg/mL (12-65), 25(OH)VitD:35 ng/mL.

Imaging studies were normal. He received intravenous calcium and alfacalcidol when normocalcemia was achieved, he was switched to oral treatment with calcium carbonate, alfacalcidol and cholecalciferol.

In his first follow up visit,patient demonstrated normal calcium levels, hyperphosphatemia, normal creatinine,high parathormone and suboptimal 25(OH)D_3(19.7 ng/mL) levels. Due to limited resources, genetic testing was not performed and the patient was treated as a suspected case of pseudohypoparathyroidism type 1.

During his follow up visits, primary hypothyroidism was diagnosed and he achieved adequate 25(OH)VitD_3 levels (>30 ng/mL) for a limited period.

On his last visit at the pediatric department, his lab exams showed normal calcium, parathormone and 25(OH)VitD_3 levels.

In view of these results, the initial diagnosis was re-considered.The patient discontinued treatment for one month, after which a repeat biochemical workup was performed revealing normal calcium,phosphorus, parathormone, suboptimal 25(OH)VitD_3 and normal 1,25$(OH)_2$VitD_3 levels (Ca: 9.9 mg/dl, P: 4.5 mg/dl Creat: 1 mg/dl, Alb: 4.2 g/dl, PTH: 44 pg/mL, 25(OH)VitD_3: 17 ng/mL, Mg: 2 mg/dl, 1,25Vit(OH)D_3 46 pg/mL). The results were evaluated, revising the diagnosis to secondary hyperparathyroidism due to Vitamin D deficiency. The patient will receive cholecalciferol monotherapy until his next follow-up appointment.

Conclusion: This case illustrates the diagnostic challenges of calcium disorders, as the initial diagnosis of pseudoparathyroidism, was re-evaluated during follow-up and the patient was managed as a case of severe and prolonged Vitamin D deficiency and secondary hyperparathyroidism.

Reference

1. Mantovani G, Bastepe M, Monk D, et al. Diagnosis and management of pseudohypoparathyroidism and related disorders: first international Consensus Statement. *Nat Rev Endocrinol*. 2018;14(8):476-500. https://doi.org/10.1038/s41574-018-0042-0

Abstract citation ID: lvag096.1873

EP1872 - LBA_ECE_1395 - Delayed diagnosis of Turner syndrome in an adolescent presenting with progressive lower limb spasticity

Maria Tzoraki[1], Ioanna Kosteria[1], Marina Kontitsi[2], Christina Karastathi[2], Anastasia Konidari[2] and Elpis Vlachopapadopoulou[1]

[1]Department of Endocrinology-Growth and Development, Children's Hospital P. & A. Kyriakou, Athens, Greece; [2]Second Department of Pediatrics, Children's Hospital P. & A. Kyriakou, Athens, Greece

Background: Turner syndrome (TS) is typically diagnosed in childhood on the basis of short stature, dysmorphic characteristics and coarctation of the aorta, or in pubertal age with delayed or absent pubertal development. However, diagnosis may be delayed, particularly in patients with atypical features.

Case Presentation: We report the case of a 15-year-old Roma adolescent referred for progressive gait disturbance and bilateral lower limb pain, short stature and primary amenorrhea. Symptoms initially affected the right lower limb and subsequently involved the left and had a 3 months duration. She reported no menarche but an episode of transient vaginal bleeding.

Clinical Evaluation: Height: 148 cm (<3rd Percentlie), weight: 36.8 kg, BP: 114/67 mmHg. Thyroid: Non-palpable. Head circumference: 54 cm. No dysmorphic features but a small triangular mandible. Tanner stage I for breast and II for pubic hair.

Neurological examination revealed hypertonia and increased deep tendon reflexes.

Laboratory Investigations: Brain and spine MRI were unremarkable, and cerebrospinal fluid analysis was normal. Metabolic and autoimmune investigations were negative. Bone age was delayed (10-11 years compared to chronological age of 15 years), and bone mineral density was significantly reduced (DEXA Z-score TBLH: −3.4, Lumbar spine: −3.5). Pelvic ultrasound failed to visualize the ovaries. Hormonal evaluation showed elevated gonadotropins and undetectable estradiol (FSH 61 IU/L, LH 31.9 IU/L, estradiol <5 pg/mL). Thyroid evaluation: TSH: 2.19 μIU/mL, FT4: 1.45 ng/dl, antiTPO: 3.97 IU/mL, antiTg: 6.08 IU/mL. IGF-1: 291.9 ng/mL.

The presence of hypergonadotropic hypogonadism and short stature alluded the possible diagnosis of Turner's syndrome. Thus, cytogenetic analysis was performed and revealed a structural X chromosome abnormality, 46,X,idic(X)(q13.1), consistent with a Turner syndrome variant.

Conclusion: This case illustrates a delayed diagnosis of Turner syndrome in an adolescent with atypical neurological presentation. Karyotype analysis should be performed in all girls with short stature, furthermore when it is associated with delayed puberty the likelihood of Turner's syndrome is very high and should prompt endocrine evaluation and karyotype analysis, even when non-endocrine symptoms predominate, in order to ensure timely diagnosis and appropriate management.

Abstract citation ID: lvag096.1874

EP1875 - LBA_ECE_1447 - Severe familiar hypercholesterolemia in a patient with hypothyroidism due to Hashimoto thyroiditis

Adishah Çerma

Internal Medicine, Kukës Regional Hospital, Kukës, Albania

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Introduction: Hypothyroidism is associated with hyperlipidemia due to modifications in lipid synthesis, absorption and metabolism, mainly with increased total cholesterol and LDL-cholesterol. The case presented is that of a 40-year-old patient with primary hypothyroidism and severe hypercholesterolemia, with a positive familiar history for both.

Case Presentation: Patient A.B, 40 years old, presents to the clinic with tiredness and pain in her neck, starting after viral tonsillitis. She reported a positive family history for thyroid disorders including her mother and sisters. Her thyroid ultrasound showed diffuse goiter with heterogenous structure and small hypoechoic areas, which were slightly painful on examination. TSH was 0.023 μU/L, Anti-TPO 2000 IU/mL with a slightly elevated CRP of 0.64 mg/dl. Ibuprofen was started to treat the subacute thyroiditis and selenium 200 μg/day. After the subacute thyroiditis resolution, she was reevaluated and TSH resulted 28.648 μU/L with normal ft4 and ft3. A lipid profile was requested: Total Cholesterol was 319 mg/dl, LDL-cholesterol 248 mg/dl, Triglycerides 113 mg/dl and HDL-cholesterol 55 mg/dl. She takes no medication to affect lipid metabolism. Diabetes, hepatitis, nephrotic syndrome and other hormonal alterations were excluded. On further questioning, she recalls that both her sisters had been taking statins for hypercholesterolemia, before the age of 40. No early cardiac event was reported. On physical examination, no xanthoma or xanthelasma were present. Her peripheral doppler and heart ultrasound were normal. No genetic testing was possible.

Patient was started on Levothyroxine 75 mcg/day and Rosuvastatin 20 mg/day, with dietary restrictions. Her TSH remained high (57.524 μU/L) in a 2-month follow-up, with a decrease in Total Cholesterol 239 mg/dl and LDL-cholesterol 150 mg/dl. TSH dosage was raised again to 100 mcg/day, advising her on the medication compliance. After 5 months of follow-up, her TSH was 17.301 μU/L and total cholesterol elevated at 301 mg/dl and LDL-cholesterol 202 mg/dl, despite medication and slight dietary changes. Ezetimibe 10 mg was added and Levothyroxine 125 mcg/day. No changes were seen in the follow up (total cholesterol 319 mg/dl and LDL-cholesterol 231 mg/dl). Rosuvastatin dosage was raised to 30 mg/dl and a strict daily diet recommended. After almost a year of treatment, her TSH normalized (0.880 μU/L) and total cholesterol 135 mg/dl with LDL 76 mg/dl. She continues to be on close follow-up.

Conclusion: Severe hypercholesterolemia should be carefully evaluated in every patient, to determine primary and secondary causes, including hypothyroidism. Treatment and follow-up are necessary to avoid future cardiac complications.

Abstract citation ID: lvag096.1875

EP1877 - LBA_ECE_1047 - FSH resistance syndrome in a young woman with primary amenorrhea

Evangelia Makri[1], Georgios Kostopoulos[1], Konstantinos Ravanos[2], Ioannis Papoulidis[3] and Foteini Adamidou[1]

[1]*Endocrinology, Hippokration General Hospital of Thessaloniki, Thessaloniki, Greece;* [2]*Embryolab Next Gen IVF, Thessaloniki, Greece;* [3]*Clinical Genetics Laboratory, Access To Genome—ATG, Thessaloniki, Greece*

Introduction: FSH-resistant ovary syndrome is a rare cause of primary or secondary amenorrhea. It is characterized by menopausal levels of FSH and LH, low estradiol levels, normal anti-Müllerian hormone (AMH) levels, and the presence of immature ovarian follicles with impaired maturation due to mutations in the FSH receptor (*FSHR*) gene. Patients present with anovulation and infertility and are commonly diagnosed with premature ovarian insufficiency.

Case Presentation: A 32-year-old woman with a history of primary amenorrhea presented for fertility evaluation. The patient had normal secondary sexual characteristics and had been treated with cyclic hormonal therapy with estrogen and progesterone since adolescence. Laboratory evaluation showed a normal female karyotype, elevated FSH/LH levels (101.9 mIU/mL and 41.4 mIU/mL, respectively), low estradiol levels (17.2 pg/mL), and normal AMH levels (1.7 ng/mL). Transvaginal ultrasound demonstrated normal internal genitalia, with an antral follicle count of 10. There was no known family history of infertility.

The patient underwent ovarian stimulation with follitropin alfa 300 IU, without follicular development.

Genetic testing revealed a novel homozygous missense variant in the FSHR gene, c.1412T>G p.(Ile471Ser), classified as likely pathogenic, confirming the diagnosis of FSH resistance syndrome.

The patient was referred for further specialized assisted reproductive treatment.

Conclusions: FSH resistance should be suspected in women of reproductive age presenting with primary or secondary amenorrhea, when elevated FSH and LH levels are found alongside low/normal estradiol levels, but preserved ovarian reserve. The combination of clinical evaluation, laboratory findings, and genetic testing enables early recognition and appropriate

counseling. In these cases, conventional ovarian stimulation has low likelihood of success, and recommended reproductive strategies include in vitro maturation (IVM) of oocytes and oocyte donation.

Abstract citation ID: lvag096.1876

EP1879 - LBA_ECE_1137 - Adrenal hemangioma: an unusaul cause of abdominal pain

Eleftheria Kakargia[1], Danai Georgakopoulou[1], Akrivi Kostopoulou[2], Giorgos Zografos[3], Labrini Papanastasiou[1], Athanasios Fountas[1] and Athina Markou[1]

[1]*Department of Endocrinology and Diabetes Center, Center of Excellence of Rare Endocrine Adrenal Disorders, Athens, Greece;* [2]*Department of Pathology, General Hospital of Athens G.Gennimatas, Athens, Greece;* [3]*First Departmennt of Surgery, G. Gennimatas' General Hospital of Athens, Athens, Greece*

Background: Adrenal hemangioma is a rare benign vascular tumor of uncertain pathogenesis, most often identified incidentally. Fewer than 100 cases have been reported in the literature since it was first described approximately 70 years ago. Herein, we present a rare case of an adrenal hemangioma presenting with abdominal pain.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Case Report: A 61-year-old woman with a recent history of a transient ischemic attack secondary to a patent foramen ovale was referred to our clinic after an adrenal mass was detected on abdominal CT, performed for intermittent abdominal pain. CT demonstrated a 3.5 cm bilobed and heterogeneous right adrenal lesion with large calcifications and no contrast enhancement. The left adrenal gland was unremarkable and there was no lymph node enlargement. Further assessment with gadolinium-enhanced MRI revealed a complex right adrenal mass with heterogeneous T1 and T2 signal intensity and prominent cystic components. There were no clinical features suggestive of a secreting adrenal tumor, which was confirmed by comprehensive hormonal evaluation excluding cortisol, aldosterone, adrenal androgens and catecholamines excess. Adrenal tuberculosis was included in the differential diagnosis, given that adrenal calcifications are a characteristic imaging finding in tuberculous adrenalitis, and subsequently excluded. To further characterize the lesion a ^{18}F-FDG PET/CT was performed, which demonstrated a photopenic lesion without FDG uptake, as well as a ^{68}Ga-DOTATATE PET/CT, which showed no increased uptake in the right adrenal gland. Taking into account the suspicious imaging features of the adrenal mass and the absence of definite diagnosis the option of adrenalectomy was offered to the patient. An uneventful laparoscopic right adrenalectomy was performed followed by complete resolution of the abdominal pain. Histopathological examination was indicative of an adrenal hemangioma.

Conclusion: Our case highlights the challenges in the diagnostic evaluation of an adrenal hemangioma. Despite being benign, it may present as a radiologically suspicious adrenal mass and mimic malignant lesions including adrenocortical carcinoma, metastases or pheochromocytomas. Pre-operative diagnosis is difficult and given its rarity and non-specific imaging features surgical resection is ultimately needed to establish the diagnosis.

Abstract citation ID: lvag096.1877

EP1881 - LBA_ECE_1313 - When fluid restriction makes it worse: cerebral salt wasting masquerading as SIADH after traumatic brain injury

Paul Chatee, Muhammad Waqar Khan, Nur Fatin Aqilah Binti Suharinizam and Paul Pravin
Endocrinology, Univeristy Hospital Limerick, Limerick, Ireland

Background: Hyponatraemia is a frequent complication following acute brain injury and is most commonly attributed to Syndrome of Inappropriate Antidiuretic Hormone Secretion. However, Cerebral salt wasting represents an important alternative diagnosis. Distinguishing between these entities is critical, as management strategies are opposing. Misclassification may worsen hyponatraemia and increase morbidity.[1]

Case Presentation: A 44-year-old male was admitted following a mechanical fall. CT brain demonstrated bilateral intraparenchymal haemorrhages with subarachnoid haemorrhage. Neurosurgical review advised conservative management, and antiepileptic therapy was commenced.

On day 8, serum sodium declined from 139 to 123 mmol/L. The patient appeared clinically euvolaemic, although subtle hypovolaemia may have been masked. Urine sodium was 150 mmol/L and urine osmolality 639 mOsm/kg. Urine output remained elevated at >3 L/day. Thyroid function and cortisol were normal. SIADH was initially diagnosed.

Fluid restriction (1 L/day) was instituted; however, hyponatraemia worsened, with sodium approaching levels requiring escalation to high-dependency care for hypertonic saline. The lack of response, alongside ongoing natriuresis and high urine output, prompted reconsideration of the diagnosis.

Cerebral salt wasting was suspected, and isotonic fluid replacement was initiated. This resulted in stabilisation and subsequent improvement in serum sodium, confirming the diagnosis.

Discussion: SIADH and CSW share overlapping biochemical features, including hyponatraemia with elevated urine sodium and osmolality, and may appear clinically euvolaemic. However, CSW is characterised by renal sodium loss, likely mediated by natriuretic peptides, leading to hypovolaemia and high urine output.

Failure of standard therapy should prompt reconsideration of diagnosis. Early misclassification may expose patients to inappropriate fluid restriction and progression to severe hyponatraemia requiring critical care intervention. Response to fluid administration may provide a useful diagnostic distinction.[2,3]

Conclusion: Accurate differentiation between SIADH and CSW is essential following brain injury. This case highlights that worsening hyponatraemia despite guideline-directed therapy should trigger diagnostic reassessment, as incorrect classification may delay treatment and worsen outcomes.

References

1. Spasovski G, et al. *Eur J Endocrinol*. 2014.
2. Palmer BF. *Trends Endocrinol Metab*. 2003.
3. Sherlock M, et al. *Clin Endocrinol*. 2006.

Abstract citation ID: lvag096.1878

EP1886 - LBA_ECE_1112 - Association between waist-to-height ratio as an indicator of central obesity and glucose dynamics during oral glucose tolerance test in individuals with prediabetes

Irem Sonmezoglu Kutuk[1], Fidan Yusifova[2], Ethem Turgay Cerit[1], Mehmet Muhittin Yalcin[1], Mujde Akturk[1], Fusun Toruner[1], Ayhan Karakoc[1] and Altinova Alev[1]
[1]*Department of Internal Medicine, Division of Endocrinology and Metabolism, Gazi University Faculty of Medicine, Ankara, Turkey;* [2]*Department of Internal Medicine, Gazi University Faculty of Medicine, Ankara, Turkey*

Introductıon: Central obesity plays an important role in the development of insulin resistance and type 2 diabetes. Although body mass index (BMI) is widely used, it may not adequately reflect visceral adiposity and the associated metabolic risk. In recent years, waist-to-height ratio (WHtR) has been suggested as a more sensitive marker for evaluating central obesity. In this study, it was aimed to evaluate the relationship between WHtR and glucose dynamics obtained during the oral glucose tolerance test (OGTT) in individuals without diabetes.

Methods: A total of 86 individuals who underwent OGTT, had no diagnosis of diabetes, and had prediabetes were included in this cross-sectional study. Demographic characteristics,

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

HbA1c levels and anthropometric measurements of the participants were recorded. Using plasma glucose values at 0, 30, 60, 90 and 120 minutes during OGTT, total glucose area under the curve (AUC), early AUC, late AUC, peak glucose level and glucose excursion were calculated. Central obesity was defined as WHtR ≥0.5. The relationships between WHtR and BMI with OGTT parameters were evaluated by correlation analyses and OGTT parameters were compared according to WHtR categories.

Results: The mean age of the participants was 51 ± 12 years and 70.6% were female. Mean HbA1c was 5.96 ± 0.22% and BMI was 26.46 ± 3.44 kg/m^2. WHtR showed significant correlation with 30-minute glucose level ($r = 0.222$, $P = .042$), peak glucose ($r = 0.247$, $P = .022$), early AUC ($r = 0.249$, $P = .022$) and delta glucose (peak glucose—0-minute glucose) ($r = 0.245$, $P = .023$). In contrast, no significant relationship was found between BMI and OGTT glucose dynamics.

In individuals with WHtR ≥0.5, 30-minute glucose level (150.5 ± 21.9 vs 136.2 ± 22.9 mg/dL, $P = .041$) and delta glucose (82.1 ± 27.6 vs 63.1 ± 28.9 mg/dL, $P = .031$) were found to be higher. Additionally, WHtR values were found to be significantly higher in individuals with 60-minute glucose ≥155 mg/dL ($P = .029$).

Discussion and Conclusion: Waist-to-height ratio, which indicates central obesity, was found to be associated with early glucose abnormalities occurring during OGTT before the development of diabetes, whereas this relationship was not observed with BMI. These findings suggest that WHtR may be a more sensitive anthropometric marker than BMI in determining early metabolic risk demonstrated during OGTT and may be a clinically more valuable measurement in detecting glycemic abnormalities occurring before the development of diabetes.

Abstract citation ID: lvag096.1879

EP1887 - LBA_ECE_1064 - Functional adrenocortical oncocytoma with androgen excess and subclinical hypercortisolism: a rare cause of infertility

Arnautu Ana Maria[1], Catalina Petrescu[1], Claudia Nacea[1], Mirona Dinca[1,2], Beatrice Grecu[1], Dana Tilici[1,2], Adina-Ioana Onofrei[1], Ruxandra Costinescu[1] and Diana Paun[1,3]

[1]Ploiesti, Romania; [2]Doctoral School of "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [3]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Background: Oncocytic neoplasms are predominantly benign tumors most commonly identified in the kidney, thyroid, parathyroid, and salivary glands. Adrenocortical oncocytomas are exceptionally rare and are typically non-functioning. However, a subset may exhibit hormonal activity, and a proportion demonstrates features suggestive of uncertain or malignant biological potential.

Case Presentation: We report the case of a 23-year-old woman initially referred to gynecology for evaluation of infertility, where markedly elevated DHEA-S levels (approximately four times the upper limit of normal) were identified.

Subsequent endocrine assessment revealed mild chin acne on clinical examination. An extended hormonal evaluation confirmed elevated adrenal androgens, associated with lack of cortisol suppression following the 1 mg overnight dexamethasone suppression test and loss of circadian cortisol rhythm, while ACTH levels remained within the normal range.

Contrast-enhanced abdominal CT demonstrated a large (86 × 80 × 93 mm), well-circumscribed, heterogeneous right adrenal mass, with an attenuation of 40 HU and washout >50%, exerting significant mass effect on adjacent structures.

The patient underwent laparoscopic right adrenalectomy. Histopathological examination revealed an adrenocortical oncocytic neoplasm of uncertain malignant potential. According to Lin–Weiss–Bisceglia criteria, major criteria included equivocal venous invasion, while minor criteria comprised large tumor size (maximum diameter 105 mm), capsular invasion, and equivocal sinusoidal invasion. Immunohistochemistry showed a Ki-67 index of 2% and negative staining for inhibin, Melan-A, MCK, vimentin, PHH3, and MSA.

Postoperative evolution was favorable. At 3-month follow-up, the patient had a normal clinical examination and significant improvement in biochemical hyperandrogenism, with only mild persistent elevation of total testosterone and 17-hydroxyprogesterone (measured in the luteal phase). Follow-up CT imaging showed no evidence of recurrence.

Given the uncertain malignant potential, periodic follow-up with hormonal assessment and imaging at 3-month intervals was recommended.

Conclusion: Adrenocortical oncocytomas are uncommon adrenal tumors, typically non-functional, but occasionally associated with clinically relevant hormone secretion. This case underscores the need to include functional oncocytic tumors in the differential diagnosis of hyperandrogenism and infertility. Establishing their biological behavior remains challenging and relies on thorough histopathological and immunohistochemical assessment, given the limited ability of preoperative investigations to reliably distinguish them from malignant adrenal lesions.

Abstract citation ID: lvag096.1880

EP1888 - LBA_ECE_1077 - Demographic profile and symptoms distribution in patients with diabetic peripheral neuropathy in Armenia

Naira Zohrabyan, Yeranuhi Khanoyan and Yelena Aghajanova

Endocrinology, Yerevan State Medical University after Mkhitar Heratsi, 'Muratsan' University Hospital, Yerevan, Armenia

Background: Diabetic peripheral neuropathy is a common complication of diabetes, that results damage to multiple peripheral nerves. It is characterized by sensory, motor, and/or autonomic nerve dysfunction, with symptoms including pain, burning, numbness and weakness in the limbs, as well as disturbances in digestion, urination, sweating and cardiovascular regulation. Understanding the demographic profile and symptom patterns of patients with DPN is essential for improving diagnosis, management, and patient outcomes. This study aims to describe key characteristics of patients diagnosed with DPN in ambulatory clinics of RA, focusing on pain status, age distribution, and possible sex differences.

Objectives: The primary objective of this study was to describe the demographic and clinical characteristics of patients with

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

diabetic peripheral neuropathy in Armenia. Specifically, the study aimed to determine the proportion of patients with painful vs painless DPN, analyze the age and sex distribution of the patient population, assess the response to benfotiamine over one month of treatment.

Methods: A cross-sectional study was conducted on patients diagnosed with 383 completing the study. Incompletely or incorrectly completed questionnaires were excluded from the analysis. Patients were classified into two groups: those experiencing painful DPN and those with painless DPN. Data on patients' year of birth (ranging 1941-1973), sex, and presence or absence of neuropathic pain were collected using standardized clinical assessment forms. All patients received benfotiamine treatment, one tablet daily, for one month. Descriptive statistics were used to analyze and summarize the demographic and clinical features.

Results: Of the 383 patients included, 328 (85.6%) reported painful symptoms associated with DPN, whereas 55 patients (14.4%), had DPN without pain. The age of the patients varied, with birth years ranging between 1941 and 1973, indicating an adult to elderly population affected by DPN. The sex distribution showed a marked predominance of female patients, with 276 females (72.1%) and 107 males (27.9%). Painful DPN was more commonly observed across both sexes, however, no further stratification by sex was performed.

Conclusion: The findings indicate that painful DPN constitutes the majority of cases among patients with diabetic peripheral neuropathy in Armenia. Daily benfotiamine for one month was consistently applied and was associated with moderate to significant improvement in neuropathic symptoms, highlighting its benefit in DPN management. These findings underscore the importance of early detection and appropriate management of neuropathic pain in diabetic patients to improve quality of life and prevent further disability.

Keywords DPN, diabetes complications, benfotiamine, demographic characteristics

Abstract citation ID: lvag096.1881

EP1889 - LBA_ECE_1478 - PTH replacement therapy with palopegteriparatide in women with severe hypoparathyroidism—a case report

Jowita Halupczok-Żyła[1], Anna Brona[1] and Marek Bolanowski[2]

[1]Department of General and Experimental Pathology, Wroclaw Medical University, Wrocław, Poland; [2]Department and Clinic of Endocrinology and Internal Medicine, Wroclaw Medical University, Wrocław, Poland

Hypoparathyroidism is a rare disease usually characterized by a lack or deficiency of parathyroid hormone (PTH), which results in hypocalcemia and may lead to hyperphosphataemia. In most cases, hypoparathyroidism in adults is iatrogenic and caused by thyroid and parathyroid surgery or radiation to the neck. Conventional therapy consists of oral calcium and active vitamin D supplementation. However, this approach does not restore physiological PTH function. Palopegteriparatide, a PTH analogue, causes a sustained PTH effect, and therefore, it may be a promising option that will be more widely used in hypoparathyroidism.

A 52-year-old patient underwent total thyroidectomy due to retrosternal goiter. A few days after the surgery, she complained of typical symptoms of tetany. Laboratory examinations showed decreased concentrations of total calcium (7.1 mg/dl) and corrected calcium (7.28 mg/dl), and increased phosphorus (5.5 mg/dl). Postoperative hypoparathyroidism was diagnosed. She was treated with calcium carbonate (10 g/day), calcium citrate (1.2 g/day), calcitriol (1.5 μg), cholecalciferol (4000 IU/day), and hydrochlorothiazide (25 mg/day). After several months, treatment with palopegteriparatide was successfully initiated with a gradually increasing dose. The starting dose was one daily subcutaneous injection of 18 μg. During the therapy, skin redness at the injection site, nausea, diarrhea, and an increase in blood pressure occurred. After two months of treatment, the patient felt better and reported no side effects (27 μg/day). Laboratory results revealed normalization of total calcium (8.56 mg/dl) and phosphorus (3.69 mg/dl) levels. The use of palopegteriparatide allowed for a reduction in calcium doses (calcium carbonate - 2 g/day, calcium citrate - 0.8 g/day) and hydrochlorothiazide (12.5 mg/day). Calcitriol was discontinued. This case illustrates that palopegteriparatide may provide an effective therapeutic option in the management of severe postoperative hypoparathyroidism.

Abstract citation ID: lvag096.1882

EP1890 - LBA_ECE_1160 - Effects of exam-period lifestyle changes, sleep patterns, and stress awarness on fasting glucose levels in medical students in Georgia

Mariam Dumbadze[1], Ketevan Dundua[2] and Teona Gogitidze[3]

[1]Medicine, BAU International University, Batumi, Georgia; [2]David Aghmashenebeli University of Georgia, Tbilisi, Georgia; [3]Medicine, BAU International University, BAU International Hospital, Batumi, Georgia

Introduction: Medical students experience significant psychological and physiological stress due to demanding training and lifestyle. Mental health issues such as depression, eating disorders, and anxiety[1] are common. Lifestyle factors—including genetic predisposition, poor sleep,[2] irregular diet,[3] and chronic stress—also play an important role. These factors may lead to metabolic changes such as altered fasting glucose, weight fluctuations and reduced well-being. Studying these patterns helps clarify their link with fasting glucose and metabolic risk, especially in genetically predisposed individuals.

Aim: To evaluate the effect of exam-period lifestyle changes (sleep, stress, diet) on fasting glucose levels and metabolic risk among medical students, and to determine whether these changes are common.

Methods: A case-control survey was conducted among 200 medical students (1st–6th year) at BAU International University, Georgia. Participants represented diverse nationalities. Data were collected via questionnaire assessing demographics, chronic and genetic diseases, sleep, study habits, stress, and physical activity. Fasting glucose was measured during the final exam period. The analysis focused on associations between lifestyle factors and glucose levels.

Results: Among 200 students (mean age 21.8 years; 59% female), 93 (46.5%) without chronic disease or family history were

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

excluded. Data from 80 students were analyzed: 20% with chronic disease and family history of diabetes, and 20% with family history, without chronic disease. Among chronic cases, insulin resistance was present in 7%, PCOS in 4.5%, and type 1 diabetes in 0.5%. Many were likely pre-diabetic. Family history included type 2 diabetes in 48 (24%), type 1 in 14 (7%). During exams, 57% slept <6 hours and 73% reported moderate–severe anxiety. Symptoms such as fatigue, dizziness, tremor and poor concentration were reported by 76%. Physical activity decreased in 32%; weight gain occurred in 20%, 60% consumed unhealthy diets. Mean glucose was 91.3 and mean BMI 25.4.

Conclusion: Higher stress and shorter sleep were linked to increased fasting glucose and BMI, especially in insulin-resistant and pre-diabetic students. These findings suggest increased risk of dysglycemia. Greater awareness, lifestyle support, and preventive strategies are needed to improve both students' well-being and future patient care.

Keywords exam stress, sleep deprivation, lifestyle habits, fasting glucose, medical students

References

1. Sander J, Moessner M, Bauer S. Depression, anxiety, and eating disorders-related impairment: moderators in female adolescents and young adults. *Int J Environ Res Public Health*. 2021;18(5):2779. https://doi.org/10.3390/ijerph18052779
2. Sharma S, et al. Sleep, stress, and academic performance. *J Fam Med Prim Care*. 2025;14(5).
3. Khajuria A, et al. Diet and lifestyle in students. *J Lifestyle Med*. 2025;15(2).

Abstract citation ID: lvag096.1883

EP1894 - LBA_ECE_1304 - X-linked hypophosphatemic rickets and ulcerative colitis: a rare association requiring multidisciplinary management

Sabina Maria Dumitrache, Luminita Cima, Roxana-Elena Busioc, Diana Puscasu and Carmen Gabriela Barbu
Endocrinology, Elias University Emergency Hospital, Bucharest, Romania

Introduction: X-linked hypophosphatemic rickets (XLH) is a rare inherited disorder caused by PHEX mutations, characterized by FGF23-mediated renal phosphate wasting and impaired bone mineralization. Ulcerative colitis is a chronic inflammatory bowel disease with immune-mediated mechanisms. The coexistence of XLH and UC is poorly described in the literature. We report a case highlighting this association and its clinical implications.

Case Report: A 25-year-old male with genetically confirmed XLH (PHEX c.1224del, p.Phe409Leufs*15), diagnosed in childhood, was referred for endocrinological evaluation due to persistent hypophosphatemia and progressive skeletal complications despite long-term conventional therapy (active vitamin D and oral phosphate supplementation). Biochemical assessment revealed hypophosphatemia (~2.0 mg/dL), elevated alkaline phosphatase, reduced tubular phosphate reabsorption (TRP 76%), and low TmP/GFR, consistent with ongoing renal phosphate wasting. Imaging studies showed characteristic skeletal abnormalities, including femoral bowing, cortical thickening, periosteal reaction and decreased bone mineralization. A pseudofracture of the left femur was identified, and the patient was evaluated by orthopedic specialists for structural complications and functional impairment. Given the coexistence of a chronic inflammatory condition and a progressive metabolic bone disease, both potentially requiring targeted biological therapies, management was coordinated within a multidisciplinary team involving endocrinology and gastroenterology. Particular attention was given to the potential interactions and safety of introducing biologic treatment in the context of an underlying inflammatory disease.

Due to insufficient response to conventional XLH therapy and ongoing skeletal deterioration, treatment with Burosumab (anti-FGF23 monoclonal antibody) was initiated at a dose of 1 mg/kg every 4 weeks, with planned biochemical and clinical follow-up.

Discussion: This case raises the question of whether the coexistence of XLH and ulcerative colitis is incidental or may reflect a link between phosphate metabolism and chronic inflammation. FGF23 may have a role beyond phosphate regulation, including involvement in inflammation, while chronic inflammatory diseases can impact bone metabolism. To our knowledge, this coexistence has not been clearly described in the current literature. The coexistence of a condition requiring targeted therapy and a chronic inflammatory disease highlights the complexity of management. Further studies are warranted to investigate this potential association.

Abstract citation ID: lvag096.1884

EP1895 - LBA_ECE_1417 - Unrecognized primary hyperparathyroidism presenting with life- threating hypercalcemia

Hristina Vlavcheska[1], Biljana Todorova[1], Iskra Bitovska[1], Sasha Jovanovska Mishevska[1], Tatjana Prosheva Bajraktarova[1], Irfan Ahmet[1], Hristijan Petreski[2] and Tatjana Milenkovic[1]
[1]*Department of Endocrinology, Univerzitet Sveti Kiril i Metodij-Rektorat, University Clinic of Endocrinology, Diabetes and Metabolic Disorders, Skopje, North Macedonia;* [2]*Department of Internal Medicine, Endocrinology Unit, Opshta bolnica-Kichevo, Kichevo, North Macedonia*

Background: Primary hyperparathyroidism (PHPT) is most commonly diagnosed in older adults and typically presents as asymptomatic hypercalcemia. However, in younger patients, PHPT may lead to significant multisystem complications. This case highlights the diagnostic and clinical challenges of PHPT in a 31-year-old female patient presenting with recurrent hypercalcemia, gastrointestinal symptoms, and nephrolithiasis.

Case Presentation: A 31-year-old female presented with intermittent vomiting and epigastric pain, progressing to fatigue and palpitations requiring hospital admission. Endoscopy showed erosive antral lesions, and renal ultrasound confirmed bilateral nephrolithiasis. Labs revealed hypercalcemia, hypophosphatemia, elevated PTH, and increased creatinine, indicating renal impairment. Bone resorption (B-CrossLaps 6000, Osteocalcin 300.0) with decreased Vitamin D3 suggested high bone turnover and risk for osteoporosis. Dual-phase SPECT/CT parathyroid scintigraphy showed a pathological focus inferior to the left thyroid lobe, consistent with a parathyroid adenoma. The patient

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

underwent surgical parathyroidectomy. Postoperatively, hungry bone syndrome was managed with intravenous and oral calcium, vitamin D, and magnesium. Follow-up showed normalized calcium and improved bone markers.

Discussion: Hypercalcemia can be subclinical yet life-threatening, often presenting with nonspecific symptoms delaying diagnosis. Timely serum calcium measurement is crucial in patients with chronic multisystem complaints. Vitamin D deficiency may induce compensatory PTH hypersecretion, worsening bone metabolism. Standard imaging like cervical ultrasound may miss ectopic or small adenomas, whereas dual-phase SPECT/CT improves localization.

Conclusion: Hypercalcemia is a potentially life-threatening condition requiring prompt recognition and management, even when symptoms are nonspecific. Early evaluation with serum calcium and PTH is crucial to distinguish PTH-dependent from PTH-independent hypercalcemia. Delayed recognition of primary hyperparathyroidism can lead to severe metabolic, cardiac, neurocognitive, and skeletal complications. Surgical excision of the affected parathyroid achieved rapid biochemical remission, while careful perioperative monitoring and supplementation managed hungry bone syndrome. This case highlights the importance of systematic assessment, combined imaging for accurate lesion localization, anticipation of postoperative complications, and multidisciplinary care to ensure patient safety and long-term bone health.

Abstract citation ID: lvag096.1885

EP1897 - LBA_ECE_1063 - A rare cause of Iatrogenic Cushing's syndrome: prolonged oral corticosteroid therapy for chronic headache

Arnautu Ana Maria[1], Catalina Petrescu[1], Claudia Nacea[1], Dana Tilici[1,2], Ruxandra Costinescu[1], Adina-Ioana Onofrei[1], Beatrice Grecu[1], Mirona Dinca[1,2] and Diana Paun[1,3]
[1]Ploiesti, Romania; [2]Doctoral School of "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [3]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Background: Iatrogenic Cushing's syndrome (ICS) is the most common form of hypercortisolism and results from prolonged exposure to exogenous glucocorticoids. Although corticosteroids are widely used in neurological conditions, ICS associated with treatment of primary headache disorders is rarely reported. We present a case of severe ICS caused by intermitent, but prolonged oral corticosteroid use in a patient with chronic headache later diagnosed as hemicrania continua, complicated by multiple metabolic, endocrine and infectious manifestations.

Case Presentation: A 39-year-old man developed iatrogenic Cushing's syndrome after intermittent treatment with oral dexamethasone for chronic headache initially considered cluster-type. The headache syndrome began at the age of 16, and since 2021 the patient had been self-administering corticosteroids intermittently in variable doses. In 2025 he was diagnosed with hypercholesterolemia and diabetes mellitus, considered complications of chronic glucocorticoid excess.

At admission, the patient presented typical cushingoid features, including moon facies, central obesity, proximal myopathy, periorbital edema, and wide violaceous striae. Ulcerative lesions over the Achilles tendon and toenail onychomycosis were also observed. Laboratory evaluation revealed hematological changes suggestive of hypercortisolism, mild hepatic cytolysis, controlled LDL cholesterol under statin therapy, and hyperglycemia. Endocrine evaluation also showed central hypothyroidism likely related to chronic glucocorticoid exposure, as well as normal gonadotropins with undetectable testosterone levels consistent with functional hypogonadism.

Hormonal evaluation performed a week after glucocorticoid withdrawal demonstrated suppression of the hypothalamic–pituitary–adrenal axis, with undetectable basal cortisol, low ACTH, and decreased DHEAS levels. A 250 μg synthetic cosyntropin stimulation test confirmed severe secondary adrenal insufficiency, and glucocorticoid replacement therapy with prednisone 5 mg/day was initiated. A 1-mg intramuscular tetracosactide test induced a rapid cortisol rise during hospitalization, declining to the lower limit of normal by discharge.

Multidisciplinary management included dermatology and infectious disease consultations, which confirmed *Staphylococcus aureus* superinfection of the ulcerative lesions requiring targeted antibiotic therapy. Hyperglycemia initially required insulin therapy but was subsequently controlled with oral antidiabetic agents. During hospitalization, recurrent headache episodes prompted neurological evaluation, and an indomethacin test supported the diagnosis of hemicrania continua. Cardiology consultation revealed a right bundle branch block-like conduction abnormality, and psychiatric evaluation confirmed depressive disorder requiring SSRI therapy.

During follow-up, laboratory abnormalities improved progressively, with normalization of hematologic and hepatic parameters and gradual recovery of hormonal axes.

Conclusion: This case highlights the severe consequences of uncontrolled glucocorticoid exposure and the need for careful monitoring when corticosteroids are used in chronic headache disorders.

Abstract citation ID: lvag096.1886

EP1898 - LBA_ECE_1207 - Clinical, biochemical and tumoral characterization of adrenal hypercortisolism: a multicenter experience (2022-2026) in southwestern Colombia

Andres Garcia[1], Carlos Berrocal[1], Jhon Quintana[2], Diego Fernando Ocampo Cortes[3] and Alejandro Roman[4]
[1]Universidad del Valle, Cali, Colombia; [2]Clínica de Occidente—Universidad Santiago de Cali, Cali, Colombia; [3]Angiografia de Occidente, Cali, Colombia; [4]Facultad de Medicina U. De A, Universidad de Antioquia, Medellín, Colombia

Background and Aims: Adrenal hypercortisolism represents a clinical and biochemical spectrum ranging from mild autonomous cortisol secretion (MACS) to overt Cushing's syndrome, including rare malignant etiologies such as adrenocortical carcinoma. This study aimed to characterize the clinical presentation of patients with adrenal hypercortisolism from referral centers in southwestern Colombia.

Methods: We conducted a retrospective study of 12 patients with confirmed adrenal hypercortisolism (2022-2026). Demographics, metabolic comorbidities, biochemical profile, and imaging findings were analyzed.

Results: The cohort was predominantly female (91.7%), with ages ranging from 29 to 71 years. Most cases (75%) corresponded

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

to MACS, **followed by overt adrenal Cushing's syndrome and adrenocortical carcinoma**, and were associated with a high burden of metabolic comorbidities: dyslipidemia (66.7%), central obesity (58.3%), hypertension (41.7%), diabetes mellitus (25%), and osteoporosis/low bone mass (25%). Thrombotic events were identified in 16.7% of patients.

Biochemically, all cases showed an ACTH-independent profile (median ACTH: 8.4 pg/mL). Lack of suppression after DST was universal (median cortisol: 6.4 µg/dL; maximum: 25.2 µg/dL), with a median UFC of 102 µg/24 h.

Imaging revealed predominantly unilateral lesions, more frequently left-sided (66.7%). Adenomas ranged from 16 to 40 mm, while one patient presented severe hypercortisolism due to a 120 mm adrenocortical carcinoma, representing the extreme end of the disease spectrum. Surgical remission was achieved in 50% of followed cases.

Conclusions: Adrenal hypercortisolism exhibits a wide clinical spectrum, from subclinical forms associated with incidentalomas and significant metabolic burden to severe presentations caused by malignant tumors. These findings highlight the importance of early recognition and comprehensive evaluation of even mild cortisol excess.

Table Baseline characteristics: adrenal hypercortisolism ($N = 12$).

Variable	Frequency (n)/ Median	Percentage (%)/Range or IQR
Demographic and Clinical Profile		
Female Sex	11	91.7%
Age (years)	57.0	Range: 29-71
Incidental Diagnosis (MACS)	9	75.0%
Central Obesity	7	58.3%
Hypertension (HTN)	4	33.3%
Osteoporosis/Low Bone Mass	3	25.0%
Metabolic Profile (HbA1c)		
HbA1c (%)	5.86	Range: 5.4-7.46
Diabetes Mellitus (HbA1c $\geq$ 6.5%)	3	25.0%
Prediabetes/At risk (HbA1c 5.7%-6.4%)	5	41.7%
Normal (<5.7%)	3	25.0%
Biochemical Profile (Cortisol & ACTH)		
Plasma ACTH (pg/mL)	**8.4**	**IQR: 7.2 (Range: 1.5-84.2)**
ACTH Classification:		
- Suppressed/ Independent	7	58.3%
- Normal	3	25.0%
Cortisol post-1mg DST (µg/dL)	**6.4**	**IQR: 10.65 (Range: 2.07-25.17)**
24-hour Urinary Free Cortisol (µg/24 h)	**102.0**	**IQR: 198.6 (Range: 13.2-2950.0)**
Hypokalemia (K+ <3.5 mEq/L)	1	8.3%

Abstract citation ID: lvag096.1887

EP1899 - LBA_ECE_1457 - Steroid-replete but stress-deficient: hidden secondary adrenal insufficiency in a routine thyroid workup

Tabinda Dugal
Endocrinology Unit, Lusail, Qatar

Background: Non-specific symptoms such as fatigue and weight gain are frequently attributed to thyroid dysfunction or perimenopause. However, unrecognised glucocorticoid exposure remains an underappreciated cause of secondary adrenal insufficiency (SAI), with significant diagnostic and safety implications.[1,2]

Case: A 42-year-old woman presented with fatigue, impaired morning energy, and 3 kg weight gain. Past history included vitamin B12 and vitamin D deficiency and psoriasis. Examination was unremarkable (BMI 21 kg/m^2, BP 109/68 mmHg). Initial tests showed mildly elevated TSH (5 mIU/L), prompting broader endocrine evaluation.

Serum cortisol was profoundly suppressed at 4.4 nmol/L (reference 46-626). Targeted history revealed repeated intramuscular betamethasone injections over 3-4 years due to limited access to biologic therapy.

Interpretation: Betamethasone is a potent long-acting glucocorticoid (20-40× hydrocortisone potency; half-life 36-72 hours) that suppresses ACTH and endogenous cortisol production.[3,4] As it does not cross-react with cortisol immunoassays, measured cortisol appears extremely low despite ongoing glucocorticoid activity.[4] Patients are therefore "steroid replete" at baseline but unable to mount an adequate stress response, placing them at risk of adrenal crisis.[2,5]

Early SAI represents a key diagnostic trap: adrenal responsiveness may be preserved, leading to false-negative short Synacthen tests.[1,6] Definitive evaluation requires testing after steroid washout and, where necessary, dynamic assessment (eg, insulin tolerance or metyrapone testing). Suppression of ACTH-dependent adrenal androgens may further contribute to fatigue and reduced well-being.

Conclusion: This case highlights a critical and preventable cause of SAI in routine endocrine practice. Mild thyroid abnormalities may act as a diagnostic distraction. A careful drug history—including intermittent or depot glucocorticoid use—is essential. Patients receiving long-acting steroids must be counselled regarding adrenal suppression, issued steroid emergency cards, and managed with appropriate stress-dose precautions. Early recognition is key to avoiding unnecessary investigations and potentially life-threatening adrenal crisis.

References

1. Fleseriu M, et al. *Lancet Diabetes Endocrinol*. 2016.
2. Bornstein SR, et al. *J Clin Endocrinol Metab*. 2016.
3. Bancos I, et al. *Lancet Diabetes Endocrinol*. 2015.
4. Joseph RM, et al. *BMJ*. 2016.
5. Charmandari E, et al. *Lancet*. 2014.
6. Inder WJ, et al. *Clin Endocrinol (Oxf)*. 2012.

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Abstract citation ID: lvag096.1888

EP1902 - LBA_ECE_1476 - The changes in the patients profile with the different types of somatotroph PitNETs in the time progression

Mariana Solovey[1,2], Olena Danevych[1] and Mykola Guk[1]
[1]Romodanov Neurosurgery Institute, Kyiv, Ukraine; [2]Komisarenko Endocrinology and Metabolism Institute, Kyiv, Ukraine

Background: Acromegaly and acrogigantism are chronic systemic diseases caused by growth hormone (GH) hypersecretion predominantly due to pituitary neuroendocrine tumors (PitNETs). Epidemiological data on somatotroph PitNETs are heterogeneous and diagnostic delays contribute to the patient's outcomes.

Objective: To investigate the immunohistochemical and clinical profile of patients with GH-positive PitNETs surgically resected in our center over the past six years.

Materials and Methods: The study included 220 cases of somatotroph PitNETs surgically resected in our center from January 1, 2020 to December 31, 2025. The median age of diagnosis and the male-to-female ratio have been analyzed separately for each year period. Immunohistochemical profile of all GH-positive tumors was analyzed in males and females accordingly to the clinical presentation.

Results: The clinical presentation varied from totally silent to classic acromegaly picture or acrogigantism. The male-to-female ratio have been changed from 0.35 in 2020 and 0.26 in 2021 to 1.05 in 2023 and 1.08 in 2024. The median age of acromegaly diagnosis in females varied from 47 years in 2020 (IQR: 37-53 years) to 50 years in 2025 (IQR: 39-59 years). The median age of acromegaly diagnosis in males has been changed from 46.5 in 2020 (IQR: 34-50 years) to 36 in 2023 (IQR: 28-48 years) and 41.5 in 2025 (IQR: 33-46 years).

Silent somatotroph PitNETs represented 12.5% from 136 consecutive cases of GH-positive PitNETs in females and 14.3% from 84 somatotroph PitNETs in males. Pure somatotroph tumors constituted 59% of 99 patients with clinical acromegaly in females and 50.8% of 65 cases of acromegaly in males.

Conclusions: The gender predominance have changed from overt female to slight male predominance as well as the median age of acromegaly diagnosis in males due to the active screening in wartime. Clinical presentation of somatotroph PitNETs depends on the the immunohistochemical characteristics.

Abstract citation ID: lvag096.1889

EP1903 - LBA_ECE_1258 - Comparative effectiveness of sleeve gastrectomy, mini/one-anastomosis gastric bypass, and Roux-en-Y gastric bypass on 12-month weight and glycaemic outcomes: a real-world cohort study

Elamin Abdelgadir[1,2], Alaaeldin Bashier[1,2], Fauiza Rashid[1,2] and Fatheya Alawadi[1,2]
[1]Mohammed Bin Rashid University for Medicine and Health Sciences, Dubai, United Arab Emirates; [2]Dubai Hospital, Dubai, United Arab Emirates

Background: Comparative effectiveness evidence across bariatric procedures is heterogeneous and regionally underrepresented. We evaluated procedure-specific 12-month changes in BMI and HbA1c using robust multivariable modelling in a real-world cohort.

Methods: We analysed adults undergoing index primary sleeve gastrectomy (SG), mini/one-anastomosis gastric bypass (MGB/OAGB), or Roux-en-Y gastric bypass (RYGB). Outcomes were change in BMI at 6 and 12 months and change in HbA1c at 12 months. Multivariable linear regression adjusted for age, sex, baseline BMI, baseline HbA1c, baseline fasting insulin, and surgery year. Among participants with baseline HbA1c ≥6.5%, a biochemical remission proxy was defined as HbA1c <6.5% at 12 months.

Results: The cohort included 2978 individuals (SG $n = 1447$, MGB/OAGB $n = 899$, RYGB $n = 632$); mean age 33.9 years and 67.9% were female. At 12 months, compared with SG, MGB/OAGB achieved greater BMI reduction (adjusted beta -1.31 kg/m^2; 95% CI -1.67 to -0.96; $P = .0000$). For HbA1c, MGB/OAGB showed a greater reduction vs SG (beta -0.189%; 95% CI -0.231 to -0.147; $P = .0000$), while RYGB did not differ materially from SG (beta 0.047%; $P = .0881$). Among baseline HbA1c ≥6.5%, adjusted remission proxy probabilities were 83.4% (SG), 93.6% (MGB/OAGB), and 83.2% (RYGB). Relative to SG, MGB/OAGB increased odds of remission (OR 2.91; 95% CI 1.45-5.84; $P = .0027$), while RYGB was not different (OR 0.98; $P = .9620$).

Conclusion: In this real-world cohort, MGB/OAGB was associated with greater 12-month BMI and HbA1c improvements compared with SG and higher likelihood of biochemical remission proxy among those with diabetes-range baseline HbA1c.

EP1903 Table 1 Baseline characteristics by procedure (imputed dataset; descriptive).

Procedure	*n*	Age mean	Age SD	Pre BMI mean	Pre BMI SD	Pre HbA1c mean	Pre HbA1c SD	Pre insulin median	Pre insulin IQR
SG	1447	30.6	11.2	41.93	6.54	5.68	0.92	27.39	16.50
MGB/OAGB	899	35.8	10.0	42.55	6.61	6.09	1.45	25.30	15.41
RYGB	632	38.8	9.9	41.06	7.40	6.12	1.49	22.00	14.84

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Table 2 Adjusted between-procedure differences at 12 months (robust SE).

Outcome	Contrast	Beta	95% CI low	95% CI high	*P*-value
ΔBMI at 12 months (kg/m^2)	MGB/OAGB vs SG	−1.314	−1.673	−0.956	.0000
ΔHbA1c at 12 months (%)	MGB/OAGB vs SG	−0.189	−0.231	−0.147	.0000
ΔBMI at 12 months (kg/m^2)	RYGB vs SG	1.682	1.235	2.129	.0000
ΔHbA1c at 12 months (%)	RYGB vs SG	0.047	−0.007	0.100	.0881

Figure 1a

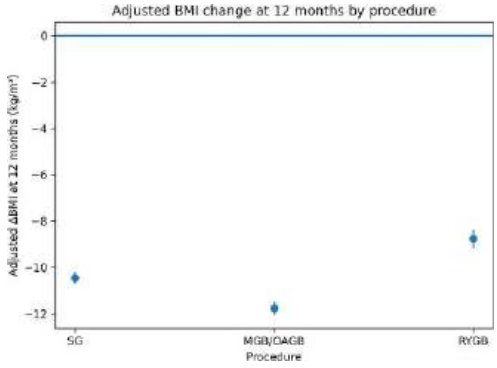
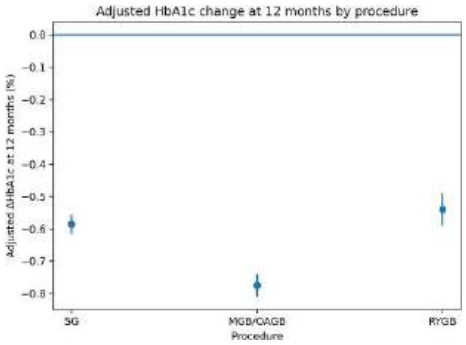


Figure 1b



Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Author Index

Abstract citation ID: lvag096.1890

Bold = Presenting author

Abainou, Lahoussaine EP1437
Abarca, Javier EP1158
Abarca Olivas, Javier EP1167, EP1124, P263
Abashidze, Ana EP1537
Abate, Andrea **P223**
Abbara, Ali P349, OC4.1, EP217, P351, OC4.2, P322, P325
Abbassy, Mahmoud Aly EP1227
Abbaszadeh, Sorena **P89**
Abbott, Taisha EP1610
Abd Mokti, Abdullah Shamshir **EP758**, **EP1607**
Abdalrazag, Osman **EP1494**, P99
Abdelgadir, Elamin EP74
Abdelgadir, Elamin **EP1736**, **EP1903**
Abdelhameed Osman, Ahmed **EP579**, **EP759**, **EP1227**
Abdelrazek, Ehab EP201
Abdelsalam Elsherbiny, Asmaa EP1227
Abdi, Lida RC7.1
Abdul Haseeb, Mohammed EP724
Abdulhayoğlu Erim, İrem RC5.4
Abdulla, Meshal EP1350
Abdul-Wahab, Suhail EP1799
Abdus-Salam, Sayad P448
Abella, Jacques EP363
Abelsen, Kari EP1136
Abeyratne, Dilini EP1811, **EP1851**, **EP1836**, EP1803
abid, sana EP1632
Abouglila, Kamal P186
abourazak, sanae EP1808
Abu Rashed, Nadim EP916
Abu-Lebdeh, Haitham **EP959**
Abuzzahab, Jennifer P255, P256, P142
Ach, Taieb EP1156, EP1487, EP571, EP1499, EP835
Achenbach, Sara J. EP1020
Acker, Güliz P284
Acosta-Calero, Carmen EP1703, EP1833, P497, EP1841, EP1835, EP1707, EP1773, EP1706, P498
Acosta-Merida, Asuncion EP1773
Adam, Clovis P242
Adam, Safwaan RC5.2, EP941
Adam, Viviana EP996, EP1491, EP1292, EP1337, EP159
Adamcova, Karolina EP445
Adamichou, Christina EP1508
Adamidou, Foteini EP1527, RC10.3, **EP332**, P415, EP1877
Adamidou, Sotiroula EP1541
Adamopoulos, Nektarios EP5, EP1596, EP327
Adamou, Dimitra P25
Adamska-Patruno, Edyta EP1721
Adamski, Jerzy P452
Adaş, Mine RC5.4
Adda, Guido EP1665
Addison, Helen EP160
Adekolu-John, Adelola **EP311**
Adiels, Martin P484
Adler, Ori EP1497
Adler, Scott OC10.4, OC10.1
Admoni, Osnat EP1317
Adoma, Rawia EP1545, EP1095, EP1180
Adoux, Lucie OC6.5
Afek, Arnon P128
Agapito Fonseca, Mariana **EP261**, **EP1534**, EP856, EP1449
Agarwal, Kiran EP1810
Agate, Laura RC7.6
Agbotounou, Wence P272
Agea Diaz, Leire EP244
Aggeli, Chrysanthi EP192, P59
Agha, Amar P283, P259
Aghajanova, Yelena EP544
Aghajanova, Yelena **EP1888**, EP1411
Agius, Charlton EP78
Agostini, Laura EP512
Agranyoni, Oryan EP499
Agrawal, Nidhi **EP1170**
Agrawal, NutanKumar EP689, EP639, EP403, EP509, EP565, EP640
Agrawal, Reshma EP257
Agrogiannis, George P138
Agudelo, Natalia EP1804
Aguennouz, M'Hammed P311
Agüera Sánchez, Alfonso P402
Aguiar Oliveira, Manuel H. OC5.5, EP1047, P457
Ahlqvist, Emma **1**, P137
ahluwalia, rupa EP1260, P37
Ahmad, Ammar **EP878**
Ahmad, Bushra EP953
Ahmad, Sabahat EP109
Ahmad, Tariq OC10.1, EP260, P72
Ahmadi, Hamid P480
Ahmed, Doua S **P416**
Ahmed, Faisal P228, EP125, EP34, EP973
Ahmed, Khaled EP1260
Ahmed, Mohammed **RC5.2**
Ahmed, Shayma EP546, EP987, EP667, EP142, **P369**, **EP1214**, EP653, **EP1371**, EP576, EP432, EP749
Ahmet, Irfan EP314, EP876, EP1895
Ahmeti, Irfan EP647
Ahn, Kyu Jeung EP517
Ahsen, Hilal P410
Aigbirhio, Franklin RC6.5
Aimaretti, Gianluca EP1138, EP1215
Aimaretti, Gianluca EP1455, P58, EP1186, EP189, P315, P278, EP497
Akad, Nada EP1641, EP354, **EP262**
Åkerström, Tobias RC6.5
Akgun, Ece **P478**
Akhtar, Muhammad EP89
Akhtar, Muhammad Sohail **EP1252**, **EP986**, **EP1216**
Akın, Leyla OC11.2
Akın, Senay P321
Akinci, Baris OC11.2
Akirov, Amit EP473, P268, P316, **RC3.5**, P129, EP1170
Akkaş, Merve EP733, EP1523
Akker, Scott EP1865
Akkiprik, Mustafa EP934
akkus, gamze **EP1212**, **EP1815**
Akmadžić, Anja EP793, EP794
Akpinar, Ebubekir EP1034, EP1201, EP1163
Aksoy, Seyma **RC3.6**
Aksoy Altınboğa, Ayşegül EP1484
Aksu, Cagri P78
Aksun, Seren **EP1755**, P463
Akter, Nazia P473
Akther, Sonia EP1485
Akturk, Mujde EP41, EP656, EP1797, P440
Akturk, Mujde EP1886
Akyea, Ralph EP1413
Al, Merve P502
Al Busaidy, Merah EP38
Al Hageh, Cynthia EP811
Al Jumaah, Ali EP1388
Al Mahmeed, Nada EP458
Al Mutasim, Mohammed EP1242
Al-Aamri, Amal P107
Alaaraj, Nada EP546, EP987, EP667, EP142, P369, EP1214, EP653, EP1371, EP576, EP432, **EP749**
Alabdurubalnabi, Zainab EP1732
Alakbarova, Shahla EP1605
Alam, Kh Imranul EP1581
Alamillo, Maria EP496
Alamuddin, Naji EP1674
Alano, Tina EP1676
Alawadi, Fatheya EP74
Alawadi, Fatheya EP1736, EP1903
Alay, Murat EP461
Albani, Adriana RC5.5
Albanki, Hessa EP1242
Albarel Loy, Frederique EP1002
Alberghi, Francesca OC8.2
Albert, Katherine P396
Albertelli, Manuela OC7.4
Albulescu, Adrian P230
Alcain Martinez, Guillermo EP467
Alcantara-Manzueta, Estefani EP1833, EP1841
Alcázar Lázaro, Victoria P267

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Al-Dabbagh, Tarek EP605
Alegria Neto, Teresa EP261, EP1534, **EP856**, EP1449
Aleidi, Yara EP58
Alejandro, Angel EP938
Aleksander, Natalia EP99
Alekseeva, Tatiana EP1080
Alemadi, Budoor EP74
Alenazi, Ali **EP180**
Alesina, Pier P470
Alessi, Ylenia P253
Alessi, Ylenia P258, **EP152**, EP1229
Alev, Altinova EP41, EP656, EP1797, P440, P500, EP1886
Alevizaki, Maria P426
Alexandraki, Krystallenia EP1733
Alexandrescu, Daniela P382
Alexandrescu, Octavian EP318
Alexandrino, Henrique EP457
Alexandrino, Jorge Henrique Carmona EP992
Alexiadou, Kleopatra EP430
Alexopoulou, Orsalia EP1046
Alfaro Martínez, José Joaquín P116
Alfian, Andi **EP1419**
Alfieri, Carlo OC11.6
AlGhawi, Rawan EP1838, EP1732
Alhambra Expósito, Mª Rosa **EP390**
Alhemaidi, Noora EP546, EP987, EP667, P369, EP432
AlHinai, Muzna **EP201**
Ali, AL-Bahrani EP302
Ali, Anyat **P99**
Ali, Farah P396
Ali, Khawla EP1350
Ali, Khiuaz **EP1288**
Ali, Muhammad **EP993**
Ali, Sadaf **EP397**
Ali, Sarah EP523
Ali Baig, Shams EP1325
Alibrandi, Angela P258, EP152
Alibrandi, Angela EP1229
Alieva, Sema **EP1540**
Alimussina, Malika P228
Alina, Fudulu P230
Alina Maria, Dumitru EP917
Aliyeva, Natavan EP1605
Aljohani, Hatim EP180
Al-Jorani, Hajir P22, P371, **EP135**
Alkaissi, Hussam OC7.2
Alkalefah, Reema EP58
Allahabadia, Amit EP1493
Allas, Soraya OC12.4, RC10.4
Allassonnière, Stéphanie P285
Allende, Fidel EP30
Allende, Janire EP372
Allosso, Francesca **P334**
Alluhayyan, Omar **EP58**, **EP605**
Almeida, Margarida EP1816
Almeida, Marta EP1188, EP1098, EP1267
Almeida, Marta **EP323**, **EP1621**
Almeida, Vânia EP1285
Almeida, VIVIANE OC5.5, P457
Almquist, Martin OC12.2
Al-Mrayat, Ma'en EP1153
Almudhammed, Rana **EP1725**, **P469**
Al-Mukhtar, Rania EP1679
Almutairi, Shaden EP58
Almutawa, Faisal EP58
Aloini, Maria Elena OC6.5, P253
Alonso Moreno, Bárbara EP924
Alotaibi, Rakan EP58
Alotaibi, Sultan EP605
AlQahtani, AlAnood **EP1838**
Alqaraishi, Ali EP605
Al-Qaysi, Amina **EP45**
Alrashed, Faisal EP605
Al-Saadi, Alhasan **EP211**
AlSalmi, Isa EP201
Alshamrani, Abdullah EP605
Alshamsi, Fatma **EP74**
Alstrup, Mathias P108, **P98**
Altabas, Velimir EP313
Altet, Charlotte P237
Altieri, Barbara OC7.3, OC12.5, EP1025
Altınbezer, Aslı EP726
Altıntop, Sabri Engin EP41, EP656, EP1797, P440, P500
Altun Özdemir, Buket EP1484
Altunsaray, Beren Ayşe **EP1842**
Alvarez Escola, Maria Cristina EP1125, EP151
Álvarez Escolá, Cristina P329
Alvarez-Guaita, Anna P143
Alvarez-Hernandez, Elisa P494
Alves, Eva EP261
Alves, Joana P77
Alves, Marta EP286
Alves Tavares, Lara **EP529**
Alvi, Sabah EP34
Alvisi, Fabricia P457
Alyafei, Fawziya **EP546**, **EP987**, **EP667**, EP142, P369, EP1214, EP653, EP1371, EP576, EP432, EP749
Alzhaxina, Alina **EP331**, **EP796**
Amann, Kerstin EP423
Amar, Laurence OC7.2, P452
Amaral, Claudia EP1027, P280
Amaro-Gahete, Francisco J. EP698
Amatrudo, Feliciana EP400
Amatrudo, Feliciana EP470, P169
Ambriashvili, Kristine EP1244
Ambrish, C EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Ambrosi, Thomas **2**
Ambroziak, Urszula EP906, EP183, EP928
Ambroziak, Urszula RC7.1, EP1416, EP63, EP480, EP1795
Ameismeier, Tobias EP657
Amer, Saad **EP1908**
Ameti, Adelina **EP1439**
Amilibia Achucarro, Ane EP978
Amin, Ayesha EP925
Amin, Sumayyah P339
amira, trigui EP1627, EP787
Amit, Akirov EP896
Amjad, Muhammad Masroor EP2, EP1279, **EP1490**
Ammoun, Abdulrahman EP1187
Amodeo, Alessandro EP1127, P501
Ampapa, Radek EP1210
Amzar, Daniela EP1148
Amzar, Daniela-Georgiana **EP1039**, **EP1105**, **EP1248**, EP1570
An, Eun Jin RC2.4
An, Guohua EP526
An, Hye In EP1747, **P499**
An, Solji **P409**
Ana Maria, Arnautu **EP1897**, **EP1887**, EP1522
Anadiotis, Athanasios P208
Anaforoglu, İnan **P442**
Anagnostis, Panagiotis **EP1116**, **P102**, **EP1340**
Anamaterou, Chrysanthi EP1365
Anand, Banmeet **OC2.2**, **EP739**, **P172**
Andela, Cornelie EP1067
Anderlova, Katerina EP445
Andersen, Marianne P327, RC11.3, P22, P371, EP1360, EP1364, EP135, P249
Andersen, Marianne Skovsager OC4.3, EP1316
Anderson, Kirstie EP1199
Anderson, Michelle EP157
Andjelkovic, Ana EP1351
Andoniadou, Cynthia OC9.3, RC5.6, OC5.6, OC7.6, OC3.6, OC5.4, RC6.1
Andova, Valnetina EP647
Andrada-Diaz, Sara P450, EP1703, EP1833, P497, EP1742, EP1805, EP1776, EP1777
Andrade, Marta EP1267
Andreassen, Mikkel EP1058, **P265**
Andreea, Bena EP1657, EP194, EP1263
Andreescu, Ioana EP969
Andreo-Lopez, María Del Carmen **EP253**
Andreozzi, Paola EP1635, EP683
Andrešić, Marina EP511
Andrews, Caroline P340
Andric, Jelena EP1327
Andronis, Christos P445
Androulakis, Ioannis P192
Androulakis, Ioannis P445
Androutsakos, Theodoros EP589
Androvitsanea, Ariadni P100, P94
Andrysiak-Mamos, Elżbieta EP1024
Andrzejak, Michalina P103, **EP1408**
Anemoulis, Marios P207
Angela, Romashko EP1031
Angelidou, Angeliki **P166**
Angelidou, Angeliki **EP145**, **EP519**, EP237, EP1387
Angelini, Flavia EP1060
Angelini, Francesco P444
Angelis, Nikolaos P182
Angelopoulos, Nicholas **P192**, **P401**, P445, P324, P343, P360
Angelousi, Anna RC10.1, **EP1045**, OC6.5, EP1496, EP927, **EP1262**, EP25, EP589, P141, **P471**
Angelousi, Anna P196
Anghel, Maria EP977, P299
Angileri, Filippo Flavio P311
Angileri, Filippo Flavio P258
Anguelova, Lia **EP1181**, **EP1313**
Anić, Sara EP793, EP794
Anna Venneri, Mary EP966, EP1026
Anne Jouinot, Anne RC12.4
Ansari, Narges Nasiri P138
Anselmo, João EP325
Anthony, Amarah P151
Antia, Tamara EP1244
Antic, Natalija EP444, P67, EP1351
Antoine, Loubet EP127
Antolić, Maja **EP426**
Anton, Gabriele P145
Anton, Nerea P83
Antonakis, Andreas P94
Antonakis, Pantelis EP1733
Antoni, Gunnar RC6.5

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Antonijević, Biljana EP1748
António, Mariana P366
Antonio Esteban, Jose P346
Antoniotti, Valentina EP590
Antoniou, Michael EP1748
Antonopoulou, Vasiliki EP519, EP453, EP591, EP237, EP139, EP115, EP1387, EP952, EP19
Antova, Emilija EP1611
Antsaklis, Panagiotis EP654
Antsiferov, Mikhail EP1080
Aouadi, Myriam **P78**, **RC10.4**
Aparici-Espot, Jordi EP496
Apaydin, Tugce **EP33**, **EP29**
Apergis, Mixalis EP1864
Apostolakis, Michalis EP1363
Apostoli, Daniele P444
Apostolidis, Stylianos EP1704
Apostolopoulou, Maria EP597, EP5, EP1596, **P170**, **EP327**
Appelman-Dijkstra, Natasha OC12.4, EP224, EP973
Appenzeller, Silke OC3.1
Appenzellers, Simone EP224
Arakelyan, Lusine EP544
Arampatzi, Panagiota OC3.1, RC11.1, EP423
Aranda, Juan Francisco EP259
Araujo, Alexandra EP1816
Araujo, Thiago **EP478**
Araújo, Bárbara EP245
Araujo Castro, Marta P267, P307, EP1205
Araújo-Vilar, David P188
Arcidiacono, Gaetano P97
Arcolesse, Lorenzo P12
ARDAH, HUSAM EP58
Ardura, Juan A. EP259
Arecco, Anna **P271**
Arecco, Federico EP219
Ares Blanco, Jessica **EP1677**
Aresta, Carmen EP51, EP163
Arffman, Riikka P350, EP1906
Argenta Model, Jorge Felipe OC11.5, EP424
Argiropoulos, Dimitrios EP1864
ARGÜELLES JIMÉNEZ, IÑAKI EP1191, EP1480
Argyrakopoulou, Georgia EP560, EP670
Ari Ostenfeldt, David P338, P372
Arias-Loza, Paula RC11.1
Arikan, Akif Enes P442
Arikan, Mehmet EP24
Aristizabal, Natalia EP82
Arlien-Søborg, Mai C EP1134, P249, **P244**
Arlt, Wiebke RC9.5, EP10, EP38, P151, RC7.1, EP1359, EP1348
Armani, Andrea P154
Armeni, Eleni EP1325
Armeni, Eleni **EP942**, EP523, **EP1791**, EP1799
Armeni, Eleni **EP1363**
Armijos, Cristina EP1804
Armstrong, Abigail EP38
Armstrong, Dawn EP1676
Arnaldi, Giorgio P462, P253
Arnas-Leon, Claudia P450, EP1703, EP1833, P497, **EP1742**, **EP1805**, EP1776, EP1777, EP1841, EP1835, EP1707, **EP1773**, EP1706, P498
Arnaudova, Mila EP732
Arnautu, Ana-Maria EP771, EP122
Aronica, Eleonora P250
Arranz, Raquel EP151
Arrondeau, Jennifer P285
Arroub, Shaimaa EP642
Arroyo-Millán, Laura **P219**, P210, EP1102
Arshad, Haroon EP1848
Arshad, Muhammad Fahad RC5.1
Arshad, Muhammad Fahad **EP124**
Arunkumar R EP689, EP639, EP403, EP509, EP565, EP640
Arvat, Emanuela EP1030, P253
Aschenbrenner, Bettina RC8.4
Ascione, Francesco EP911
Ashraf, Koushik P448
Ashrafi, Shadan EP458
Asia, Miriam Felicitas OC6.6
Asimakopoulou, Stavroula EP1045
Askitis, Dimitrios P445
Asla, Queralt P307
Asla Roca, Queralt OC3.4
Aslam, Muhammad Arif EP436
Aslan, Sinem EP1204
Aspelund, Thor EP49
Assaad, Samir EP579
Assad, Arfa Ahmed EP925, EP300
Assie, Guillaume P452
Assié, Guillaume RC9.3, P285, EP138, OC6.5, RC6.4
Assmann, Gunter EP224
Astl, Jaromir EP1521, P419, P375
Åsvold, Bjørn Olav P432
Aszkiełowicz, Sara P240, EP1629
Ataacar Aydınoğlu, Alara P442
Atapattu, Navoda P228
Atasoy, Bahar EP1092, EP935
Ateba, Sylvin Benjamin P238
Athanasiadou, Kleoniki I. EP654
Athukorala, t g EP277
Atikcan, Deniz Türküm EP292, **P385**, EP1481, P173
Atila, Cihan **OC3.4**, EP1081, EP991, OC3.3, OC5.2, EP1064, EP1109
Atkin, Stephen EP1350
Atkins, Jonathan S **P364**
Atkinson, Elizabeth EP1020
Atlas, Mor EP473
Atlivanchik, Alena EP334
Atoev, Tulkin **EP1749**
Atsama Mbede, Perpetue P238
Attard, Rebecca EP136
Attia, Amina **RC10.2**
Aubourg, Agnès EP1002
Auchus, Richard EP94, EP36, OC9.5, P21
Audhoe, Amber **EP994**
Auer, Matthias EP1108, OC9.6
Auernhammer, Christoph EP1108
Augoulea, Areti EP1363
Aulinas, Anna P267, P280
Aung, Htet Htet **EP1552**
Aurast, Zuzanna **EP1390**
Aureli, Alessia EP559
Auriola, Seppo P350
Ausín, María P79, OC10.3
Autin, Candice EP1908
Aversa, Tommaso OC8.5, P112
Avgousti, Sofia EP145
Avitan, Louis P191
Avkopashvili, Ana EP1207
Avluklu, Merve EP1212
Avventaggiato, Michele EP429
Aw, Tar Choon OC6.3
Awadin, Elhassan P99
Awounfack, Charline Florence P238
Ay, Hale P486
Ayada, Gida P129
Ayala, Alejandro P36, EP116, EP36
Ayala-Haedo, Juan OC1.3, EP1474
Ayalan, Hanne Beyza EP1842
Ayalon, Snait EP406, RC2.2
Aydin, Cevdet EP1711, P410, EP1484
Aydin, Fatih EP585
Aydin, Kadriye RC5.4, P314, EP943, P504, P486
Aydoğan, Ogün P390
Aykora, Damla P194
Aynaou, Hayat EP255
Azevedo, Luís RC5.3, RC4.6
Azhar, Shahroz **EP925**, **EP300**
Azimova, Makhbuba **EP1662**
Azirashvili, Mariami **EP1604**
Aziz, Ahmad P427
Azizol Rahman, Anis Syakirah EP815
Azketa, Ane **EP1096**
Aznar Ondoño, Itziar EP1478, EP199, EP784
Aznar Ondoño, Itziar EP1304, EP553
Azzam, Eman Zaky Ahmed AbdelAziz EP579, EP759, EP1227
Azziz, Ricardo P320, EP637
Azzoune, Assia **EP1634**
B. A. Higgins, Matthew EP1400
Baagar, Khaled EP785
Baalawi, Mohamed EP1281
Baalbaki, Diana P355, EP838, EP310
Baan, Janneke P260
Babacanlar, Nisa **EP1774**, P130
Baber, Ronny EP657
Babic, Jovana EP172, EP1651
Babich, Tanya P129
Babińska, Anna OC7.2, OC6.5
BABULAYEB, MUKHOPADHYAY **EP554**
Bacchi, Nicolò EP1130, EP1066
Bacha, Feyrous RC4.2
Bachar, Gideon P429
Bachega, Tania EP137, EP36
Bacila, Irina A EP34
Baciu, Ionela EP917, EP1251, EP1062
Baciu, Ionela EP1247
Backman, Samuel RC6.5
Bacmeister, Lucas EP135
Baculescu, Nicoleta EP1062
Bačun, Tatjana EP793, EP794, **EP1680**
Badan, Robert **EP1615**
Badenhoop, Klaus **EP1228**
Badiale, Chiara EP150
Badici, Adelina **EP757**
Badita, Ana-Iolanda P299
Badiu, Corin EP1258, EP17, EP1460, **3**, EP23, P382, P230, EP969, EP977, EP7, EP112, EP1149, EP919, P299
Badiuk, Deanna EP1684
Badnjevic-Cengic, Alma **EP1101**
Bae, Ja Seong P409
Bae, Ji cheol EP484
Bae, Ji Hyun P168
Bae, Sangjun **P7**
Baek, Chan Ju EP956
Baek, Ki-Hyun **EP1530**
Baena Ariza, Luis RC11.4, P180
Baffoni, Claudia EP219

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Bagaglini, Maria Flavia EP1315
Bagirova, Hanum EP1544
Bahadir, Adil EP1189, EP1204
Bahat, Gulistan P460
Bahl, Suhani RC1.6
Bahl, Suhani P449
Bahmani, Amir EP563
Bahougne, Thibault EP1002
Bahulikar, Yash EP689, EP639, EP403, EP509, EP565, EP640
Baikadamova, Kristina EP331, EP796
Baikštienė, Ieva EP1175, **EP999**
Baillargeon, Jean-Patrice EP408, RC11.2
Baima, Jessica EP590
Bain, Joshua OC6.6
BaÏzri, Hicham EP1437
Bajic, Jelena EP1464, P297, P120
Bak-Csiha, Sára P389
Baker, Elfreda EP1728, EP1729
Bakhit, Mohamed EP52
Bakirtas, Nihan P385
Bakirzhan, Madina **EP293**
Bakker, Leontine EP1067
Bakula-Zalewska, Elwira EP964
Bakuła-Zalewska, Elwira P411
Balacchi, Caterina P2
Balamoti, Christina EP383
Balas, Melania EP1039, EP1105, EP1248
Balas, Melania **EP1570**, EP1148
Balaško, Annemarie P222, EP910
Balasubramanian, Ravikumar EP1343
Balasubramanian, Sabapathy EP1493
Baldari, Michele **EP459**, **EP394**, EP512
Baldazzi, Giorgia Maria EP501
Baldelli, Sara P223
Baldeweg, Stephanie P23
Baldi, Matteo EP1030
Balibrea Ruiz, Ana P402
Balint, Bianca Andreea EP1779
Ballarino, Carolina EP1073, EP899
Ballesteros-Arias, Luna EP259
Balloni, Valentina P506
Bally, Lia P150
Balodimou, Chrysanthi EP1459, EP1859, EP1766, RC10.3
Balonov, Ilja EP463
Balosache, Daniela EP917
Baltić, Tamara **P324**, **P343**, **P360**
Baluta, Bogdan **EP14**
Bampilis, Andreas EP39, EP1230
Banas, Aleksandra EP79
Bancos, Irina RC3.4, OC7.2, OC6.4, EP94, RC7.1, EP1020, OC9.5, P21, EP27
Bandgar, Tushar P305
Bang, Hye Jung EP1747
Banu, Hurjahan **P475**
Banys, Valdas RC8.1
Bao, Yaru P407
Baptista, Carla EP944, EP1285
Barać, Uglješa P344, P324, P343, P360
Barac Nekic, Anja EP320, P222, EP910
Baraia Etxaburu Astigarraga, Beatriz EP562
Barale, Marco P96, P97
Baranceanu, Mihaela EP354, EP262
Barankiewicz, Joanna EP63
Barat, Maxime P285, RC6.4
Barath, Kristóf EP1006
Barbaros, Umut EP585
Barbosa, Ana Luísa **EP696**, P414, EP494, **EP1450**, **P400**
Barbosa, Ana Paula EP261, EP1534, P72, **EP731**, **P366**
Barbosa, David EP1267
Barbosa, Joana P77
Barbot, Mattia EP190, EP1086, P56, EP1094, RC9.4, P289, P253
Barbu, Carmen EP336
Barbu, Carmen Gabriela EP1894
Bârcă, Ana-Maria EP159
Barceló Álvarez, Nieves EP995
Barczynski, Marcin EP242
Bardadze, Mariam **EP908**, EP1524
Bardova, Kristina EP399
Barello, Sonia EP1030
Baretić, Maja **P156**, EP635
Bargiota, Alexandra **EP383**, **EP597**, **EP852**, EP5, EP1596, P170, EP327
Barham, Leela EP710
Bari, Aditya EP596, EP636, EP788
Barış, Zeren EP1523
Barjon, Jean-Noël EP1393
Barkas, Konstantinos EP1219, EP1335
Barlampa, Danai EP113, EP192
Barlas, Tugba **EP41**
Barmpa, Eleftheria EP597, EP852
Baron, Stephanie OC6.2
Baroncelli, Giampiero P97
Barragán, Alex EP821
Barranco, Alexandra P346
Barranco Ochoa, Juan de Dios EP1630
Barreto, Lohanna EP478
Barrie, Isata EP658
Barros Alves, Filipa **EP1123**, **EP483**
Barros Alves, Filipa EP238
Barry, Sayka EP1137
Bartolome Albistegui, Maria Jose EP1306
Bartoszewicz, Zbigniew EP1028
Bartsch, Detlef **4**
Baş Aksu, Özge **EP1154**, **P176**, **P204**
Başçıl Tütüncü, Neslihan EP292, P385, EP1481, P173
Bashari, Waiel EP1242
Bashier, AlaaEldin EP1736, EP1903
Basile, Christian P485
Basile, Vittoria RC12.5
Basmacı, Nergis EP1239, P16, P295
Basnet, Jelina RC4.4
Basolo, Alessio **EP1296**
Basolo, Alessio EP106, EP1291, P312
Bastarrika Alemañ, Gorka EP372
Baszczynska, Dorota EP352
Bathelt, Cemile OC5.2
Batman, Adnan **P502**
Batorek Lukač, Nina P328
Batsashvili, Salome **EP1207**
Battelino, Tadej EP1342
Battezzati, Alberto EP1127
Battista, Claudia EP337
Battista, Marie-Claude EP408
Batu, Alper EP1774
Baudrand, René EP30
Baumgartner, Clemens EP1017, P43, EP54, EP131, P455
Baumgärtner, Moritz RC8.4
Baumgartner-Parzer, Sabina EP50
Baussart, Bertrand P285
Bautista Recio, Carmen EP971, EP420
Bavaresco, Alessandro EP1094
Bavor, Petr EP1521, P375
Bayar, Ines EP1632
Bayburdyan, Gayane EP544
Bayer, Kathrin OC9.6
Baykal, Gökhan Rıza **EP84**, **EP726**
Bayram, Fahri EP1743
Bazarova, Anna EP1288, EP293
Beales, Phil L. **EP464**
Beard, Daisy P243, EP1584, P356
Bebek, Marko EP1466
Becerra-García, Diego EP253
Bechmann, NICOLE OC7.6
Bechmann, Nicole P30, EP55
Bechmann, Nicole **EP1790**
Beckers, Albert P252, P305
Bedatsova, Lucia **RC10.6**
Bednarczuk, Tomasz EP1028
Bégin, Marie-Josée EP283
Behary, Preeshila EP363
Beigi, Arshia **EP458**, EP1008
Beiglboeck, Hannes EP54, EP131
Beissert, Matthias P11
Beitz, Franziska EP657
Bekiaridou, Paschalia EP1045, EP1496, EP1262, EP25, P141
Bektas, Melih EP140
Bektas, Melih EP1204
Bektaş, Fatih P460
Belan, Matea RC11.2
Belardinelli, Elisabetta OC4.6, P323
Belheddad, Asma EP1756
Belińska, Agata EP939
Belis, Konstantinos EP1592, EP123, EP1394, EP685, EP1241
Bellach, Luise P43, EP54, EP131, P455
Bellakhel, Syrine EP202, EP1099, EP1652
Bellanger, Sylvain EP408
Bellido, Virginia EP496
Belo, Sandra EP494, P400
Belotserkovskaya, Tatyana EP1540
Beltsevich, Dmitry P215
Ben Abdessalem, Fatma EP1156, EP1487, EP571
Ben Amor, Bilel EP1632
Ben Jemaa, Yoldez EP1627, EP787
Ben Salah, Dhouha EP608
Ben Yamna, Hadami EP153
Bena, Andreea **EP1515**, **EP1503**
Benanteur, Nesrine **5**, **P285**, OC6.5
Bénard, Florence EP283
Ben-Chetrit, Eli P397
Bendfeldt, Hanna RC9.5
Bendlova, Bela EP1453, P161, EP1521, P419, P375
Benedetti, Arianna **P431**
Benelli, Elena EP150
Benetti, Zaira **EP150**
Bengt, Hallengren P89
Bengtsson, Daniel RC9.2
Benhamida, Jamal EP1676
Benhamou, Pierre-Yves P458
Benitez Avila, Rosa RC11.4, P180
Benkhellat, Mounia P285
Bennett, Kate **EP1759**
Benoit, Dominique D. EP469
Benoit, Timothé OC9.1
Benova, Andrea EP399
Benrezzak, Ouhida EP408

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Benrick, Anna EP1907
Ben-Shachar, Michaella P191
Bensing, Sophie P384, P38, EP11
Benso, Andrea EP1030
Bentivoglio, Valeria EP1182
Bentley, Conor EP686, EP768
Benvenga, Vanni EP638
Benyei, Erik **EP1700**
Bényei, Erik **EP1377**
Berardet, Corentin RC10.4
Bereczki, Kristóf P341
Beretta, Virginia OC8.5, P112
Bergh, Per-Olof RC11.6
Bergman, Idan P129
Bergoglio, Beatrice RC9.6
Beridze, Iela EP1537
Beridze, Meri EP1537, EP832
Berigoi, Andra EP248, EP996, EP1337
Berinder, Katarina P38
Berkeley, Rhiannon P105
Bermejo, Sheila EP1735
bernabeu, ignacio P267
Bernaczyk, Piotr RC4.5
Bernard, Daniel EP1076
Bernard, David P403
Bernard, Stefan RC8.2
Bernardi, Sara RC1.2
Bernardi, Stella **EP491**
Berner, Todd EP526
Bernini, Andrea P506
Bernoy González, Maria del Puerto EP1195
Berr, Christina **P85**
Berrocal, Carlos **EP1898**
Berruti, Alfredo P223, RC12.5
Berry, Lindsay EP526
Berta, Eszter EP1507
Berta, Eszter **P389**
Bertagna, Xavier P285
Bertasso, Iala Milene P235
Bertherat, Jérôme RC9.3, P272, EP1075, P285, P55, EP138, OC6.5, P280, RC12.4
Berthon, Annabel RC9.3, P55
Berti, Sabrina EP459, EP394, EP512
Bertocchio, Jean-Philippe RC10.2
Bertoli, Maria **EP850**, **P182**
Bertolino, Philippe P403
Berton, Alessandro Maria EP1029, EP1186, P315, P278
Berton, Alessandro Maria **EP1030**
Bertrand, Noemie EP1393
Besir, Viktória P147
Besisik Terzioglu, Mehves EP53
Besrour, Chayma **EP202**, **EP1099**, **EP1652**
Betea, Daniela EP1482
Betsi, Grigoria P100, P94
Bettaieb, Hiba EP202, EP1099, EP1652
Betts, Marissa EP260
Beuschlein, Felix EP100, OC7.2, OC6.4, EP1108, P42, P10, P5, EP30, P19, P30, EP55, P452
Bezhentseva, Elena EP1244
Bhandari, Shweta EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Bhaskar, Amit EP689, EP639, EP403, EP509, EP565, EP640
Bhaskaran, Gayathri **EP523**, **EP1799**
Bhaskaran, Gayathri EP1791
Bhatnagar, Anish RC2.5, P142
Bhatt, Bhavini EP1281, EP937
Bhatt, Shuchi P131, EP396
Bhatta, Laxmi P432
Bhattarai, Binaya **EP433**
Bhuiyan, Abdullah P448
Biagetti, Betina EP1735, **P267**, **P307**
Biagini, Francesco EP1030
Bianchi, Antonio EP1055, EP1060, EP1146, P298, EP1151, EP1057, EP1139, EP1069
Bianchi, Antonio EP1032
Bianchi, Laura P311
Bianco, Antonio RC1.6, P449
Bibik, Ekaterina EP256
Bicho, Manuel P366
Biddanda, Aiyappa EP1865
Bidlingmaier, Martin RC5.5, OC5.5, P28, OC6.1, P294, OC9.6, RC8.2, P457
Biehl, Michael RC7.1
Bieniek, Ewa EP57
Biermasz, Nienke P293, **EP1067**
Bignardi, Paulo EP529
Bignotti, Bianca P271
Bilariki, Kalliopi **EP1393**
Bilbao Garay, Ismene **EP978**
Bilbao Garay, Ismene P305
Bilezikian, John OC12.4
Bilgili, Elif P390
Bilha, Stefana EP1641, EP248, **EP354**, EP262, EP996, EP1491, EP1292, EP1337, EP159
Bilharinho de Mendonça, Berenice EP137
Bilik Oyman, Gamze EP258
Biliou, Eirini EP1869, **P196**
Biller, Beverly M.K. P266, RC3.4, EP1063, P306, P274
Bilo, Grzegorz EP51
Biloglav, Zrinka EP1466
Bin Osman, Ismail OC6.4, OC6.3
Binderup, Marie Louise P8
Bingul, Ilknur EP585
Bini, Luca P311
Binnebösel, Marc EP1479
Binowski, Grzegorz P306
Binti Nordin, Nini Nagyha **EP1545**
Bioletto, Fabio **EP1029**, P285, EP14, EP1186, EP1030
Bioletto, Fabio OC6.5
Biondo, Mattia P462
Bird, Lynne P142
Birolo, Giovanni EP497
Birtolo, Maria Francesca P285, OC6.5, EP1048, **P466**
Bisceglia, Nicolò **P104**, P80
Bischler, Thorsten RC11.1, EP423
Bislev, Lise Sofie P22
Bisschop, Peter EP64, EP92
Bissi, Valentina EP80, EP98
Bistika, Margarita **EP911**
Bistolfi, Federica **P123**, EP1019, P154, P509
Bitan, Michal EP486, EP742
Bitovska, Iskra EP1895
Bitri, Sonila EP854
Biviano Rosenkilde, Marie P372
Bıyıklı, Ziya Mithat P314, EP943, P504, P486
Bizuneh, Asmamaw P320, EP637
Bjekic Macut, Jelica P324, P343, P360, EP563
Bjerre Knudsen, Lotte **6**
Björnsdottir, Sigridur P74
Björnson, Elias RC11.6
Blacked, John P417
Blanca, Elena Sofia EP1001, P258, EP152, P311, **EP1229**
Blanchard, Anne EP1017, P452
Blanchet, Benoît RC9.3
Blanco Carrera, Concepcion P227
Blasco, Miquel EP1096
Blaser, Martin EP1368
Błasiak, Anna EP1322
Blasszauer, Celia **P428**
Bley, Thorsten P11
Bliznuks, Dmitrijs EP518
Blois, Quitterie P200
Bloise, Flavia EP1308
Blomqvist, Maria RC11.6
Blondel, Juliette RC9.3
Bloomfield, Anna RC1.6
Boanta, Roxana EP1460
Boboc, Aura Madalina EP1779
Bobrowicz, Malgorzata EP906, **EP1416**, EP183, EP928
Bobrowicz, Malgorzata EP63
Bobryk, Maryna EP714
Bocchiotti, Maria Alessandra P154
Bodoque-Cubas, Javier EP1480
Bodor, Miklos P389
Bodor, Miklós EP1507
Boehm, Ulrich EP1076
Boerboom, Derek EP1076
Boesen, Victor Brun P22
Boezennec, Robin P285
Bogazzi, Fausto RC3.3, EP216
Bognar, Zoltan P480
Bogusławska, Anna P264, EP1093, **P262**, EP1814
Böhm, Pauline EP30
Bohonowych, Jessica P142
Bohus, Peter P50
Boi, Francesco RC1.2, OC12.3, EP1709
Boido, Marina P509
Bojic, Mirjana **EP1441**, **EP1235**
Bojic, Mirjana EP1177
Bojoga, Irina **EP1358**
Bojunga, Jörg P345
Bolamperti, Simona EP280
Bolanowski, Marek EP21, EP1192, EP1889, EP1197, EP1323, EP651
Bolek, Tomáš P363
Bolek, Tomáš EP1121
Bolelli, Federico P358
Bollerslev, Jens **7**
Bologna, Chiara EP1291
Bolshova, Olena EP1211
Bolusani, Praneet P435
Bolzan, Chiara EP1182
Bona, Chiara EP219
Bonadies, Enzo EP265
Bonaventura, Ilaria EP966, P253
Bonenkamp, Han J. P95
Bonera, Claudia P223
Boniakos, Anastasios P192
BONIAKOS, ANASTASIOS P445
Bonifacino, Tiziana P509
Bonnet-Serrano, Fidéline RC9.3, P285, P55, OC6.5
Bonomi, Marco EP1127, EP1347, P501
Bonroy, Carolien EP1344
Boonsripitayanon, Mongkol EP315
Bordacs, Barbara **EP1563**

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Bordeianu, Cristina Andreea EP619
Borel, Anne-Laure EP1002
Borén, Jan RC11.6
Borg, Anouk EP1137, EP1791, EP1700
Borg, Jade EP136
Borg, Jasmine EP136
Borgeraas, Heidi P75
Borges, Teresa EP1326, EP525
Borges Canha, Marta P77, EP1450, P400
Borges Duarte, Diana EP245, EP386
Borjini, Nozha P346
Borkowska, Anna P211
Bornstein, Stefan OC9.3, OC7.6, OC9.1
Børøsund, Elin **EP1136**
Borovets, Myroslava P158
Borowska, Wiktoria EP99
Borozan, Sanja **EP146**, **EP182**
Borresen, Stina Willemoes P22, EP60
Borroto, Marelis Triana EP1717
Borsa, Melissa **OC12.1**
Borson-Chazot, Francoise P403
Borysowicz, Maria EP114
Boschetti, Mara P271
Boschiero, Dario P90
Bosdou, Julia EP1340
Boseley, Rhiannon P495
Boskovski, Bojan EP314
Bosnjak, Anja EP1351
Bosoni, Luca RC7.5
Bossi, Francesca P112
Bossoni, Simonetta EP280
Bossowska, Magdalena EP1721
Bossowski, Filip EP1721
Bostan, Hayri EP1346, **P194**, EP1131
Botezatu, Anca P230
Botha, Tanita EP222
Bottici, Valeria RC7.6
Botusan, Ileana R. **P38**
Bou Nader, Myriam P280
Bouba, Ioanna EP1796
Boubziz, Fatima P9
Boudina, Maria EP1459, **EP1859**, P426, **EP1766**
Boudokhane, Manel EP202, EP1099, EP1652
Bouillet, Elise P4
Boujelben, Khouloud EP608
Bouklas, Dimitrios EP113, EP192
Boulkroun, Sheerazed P31, OC6.2
Bouloux, Peirre EP1791
Bourgeois, Soline P19
Bourguiba, Rim EP202, EP1099, EP1652
Boutsikos, Ioannis EP1219
Boutzios, Georgios **EP1546**, **EP1568**
Bouvard, Francois OC6.5
Bouys, Lucas RC9.3
Bouys, Lucas EP138
Bovo, Giulia **EP190**, EP1086, P56, EP1094, P289
Bovo, Giulia RC9.4
Boyer, Alexandre EP1076
Boz, Aslı EP1212
Boz, Oğulcan EP1457
Boz Aksoy, Senem RC5.4, P314, EP943, P486
Boz Öncel, Eda EP1068
Bozan, Gürkan EP733
Bozic-Antic, Ivana EP563
Bozkur, Evin P110
Bradac, Ondrej EP1141
Bradley, Meghan Norris EP1374
Braha, Elena EP1013, EP318, EP757, EP1779
Braha, Elena Emanuela EP241
Brahma, Anupam P243
Brainovich, Valentina EP1182
Braithwaite, William EP1095
Bralić Lang, Valerija P156
Brambilla, Maria Maddalena OC8.2
Bramis, Konstantinos EP1733
Brand, Harrison EP1343
Brandão Neves, Diogo **EP1027**
Brandi, Maria Luisa OC10.1, **OC12.4**, P97, EP973
Brant, Jason EP1474
Brantley, Scott EP116
Bratcikoviene, Nomeda RC8.1
Bratu, Gratiela **P382**
Braukyliene, Rugile **EP20**
Braun, Kelly EP1676
Braun, Leah EP1049
Bravis, Vassiliki P427
Brčić, Klara EP1526
Breasail, Mícheál Ó EP269, EP303
Brehar, Andreea Cristiana EP1779
Brempou, Dimitria OC7.6, RC6.1
Briand, Marine EP1860
Briand, Marine P458
Bricaire, Léopoldine RC9.3
Brigante, Giulia P391
Brindle, Rachel EP1222
Brînzan, Andreea Anne-Marie EP1672
Brito, Patrícia **EP245**, **EP386**, EP1589, **EP286**, EP632
Brizzi, Maria Felice P123
Brizzi, Mariapia OC7.4
Brkic, Milena **EP1586**, EP1177
Brkljačić, Jelena EP563
Brødbæk, Kasper EP60
Brodowicz, Justyna P226
Brogioni, Sandra RC7.6
Brokkelkamp, Rona **EP92**
Brol, Maximilian EP1059
Broman, Elin **EP1064**
Bromińska, Barbara **EP377**
Brona, Anna EP21, EP1192, EP1889, EP1323
Brona, Anna **EP1197**
Bronec, Matej **EP1122**
Broughton, Sophie EP1325
Brown, Hannah **EP1119**
Brown, Jennie **P23**
Brue, Thierry P280
Bruggi, Francesco EP590
Brügmann, Petra P293, EP973
Brugnoni, Duilio P223
Brumpton, Ben P432
Brunetti, Antonio P159, OC2.1
Brunetti, Francesco Saverio OC2.1
Bruno, Lapauw EP1344
Bruno, Stefania P123
Brunová, Jana **EP252**
Brusgaard, Klaus **EP934**
Brutvan, Tomas EP1113
Bruun, Niels Henrik EP1134
Brzeska, Anna EP1024
Brzica, Hrvoje EP426
Bubanja, Dragana EP1422
Bubbear, Judith EP224
Bubenikova, Adela EP1141
Bubnov, Rostyslav **EP369**, **EP586**
Bucci, Ines P431
Buchalska, Barbara **EP1232**, **EP1150**, P309
Buchfelder, Michael OC3.1
Buchschuster, Henrike P85
Buck, Andreas P11
Bucur, Paula EP218
Buczyńska-Górna, Maria EP612
Budzulak, Joanna EP612
Budzynowska, Barbara P218
Budzyńska, Anna P211
Bueno, Marta OC11.1
Buffolo, Fabrizio P452
Bugianesi, Elisabetta EP497
Buha, Aleksandra **EP1748**
Bui, Quang EP1122
Builes Montaño, Carlos EP82
Bujanova, Jana EP1153
Bujawansa, Sumudu EP1376
Bujko, Mateusz EP1232
Bukała, Adrian EP99
Bukelytė, Erika **EP339**
Bukh Madsen, Emilie EP1360
Bukhari, Hassan EP160
Buklioska Ilievska, Daniela EP207, EP693, EP824, EP200
Bukva, Mátyás P341
Bulanova, Barbora EP1453, EP1521, P419, P375
Bulashvili, Mariam **EP1624**, EP141, **EP1295**, EP173
Bulikaite, Virginija EP439
Bulugahapitiya, Uditha EP1221, EP361
Bulugahapitiya, Uditha EP277
Bulut, Asiye Şafak EP1484
Bulut, Yeliz EP1058, P265
Bulut, Yeliz **EP1334**
Bunceanu, Stefania EP1515, EP1503
Bunceanu, Stefania-Alexandra **EP1657**, **EP194**, **EP1263**, EP507, EP834
Burakgazi, Gulen RC12.2
Burčak, Matej EP1466
Burcea, Iulia Florentina **EP903**, EP961, EP1115, **EP1672**, **EP241**, EP1190, **EP1683**, EP757, **EP1062**
Burel, Adrien P458
Burhan, Sebnem **EP1034**, **EP270**, EP1163
Burián, Katalin EP1370
Burley, Connor EP269
Burnier, Alberth EP30
Burri, Sushma **EP1470**
Burton, Mark EP1364
Busche, Tobias P145
Büscher, Sebastian P145
Buse, John EP526
Busioc, Roxana-Elena EP1894
Busteros Moraza, Jose Ignacio P227
Buti, Simona EP150
Butler, Javed EP94
Butt, Allison P338, P372
Büyükdag, Sarah P145
Buzanakov, Dmitrii **P470**
Bychkov, Mykola EP603
Bylok, Krzysztof EP99
Bystrova, Anna EP1749
Cabello-Rivera, Daniel **EP259**
Cabral da Cunha Araujo, Layanne EP424
Cabrera García, Patricia EP1478
Cabrera García, Patricia EP1304, EP553
Caccin, Vanessa EP1130, **EP1066**
Caçola, Rute EP992

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Caetano, Francisco RC4.6
Cagoroska, Zaklina EP1611
Caiazzo, Robert P4
Caimari Palou, Francisca EP1191
Cairns, Ross EP554
Cairoli, Elisa P96
Caixás, Assumpta OC11.1
Cajka, Tomas EP399
Cakal, Erman EP1457, P489, EP1745
Cakir, Bekir EP1711, P410, EP84, EP1484, EP726, EP641, EP249, EP1015
Çakir, İlkay EP1092, P110
Calado, Rodrigo P457
Calañas Continente, Alfonso Jesús EP630
Calandrelli, Rosalinda EP1146, P298, EP1057
Calapkulu, Murat **P489**, **EP1745**
Caldeira, Camille P148, EP393
Calheiros, Raquel **EP947**
Calheno, Carlos Lucas EP386
Caligo, Maria Adelaide EP226, EP216
Calikoglu, Bedia Fulya EP585
Calikoglu, Fulya P279, P291
Calissendorf, Jan P6
Calissendorff, Jan P89
Calla, Daniella OC4.3
Calugaru, Valentin P285
Camacho Martel, Laura EP467
Camara-Gómez, Rosa P267, P307
Camargo Camero, Raquel EP467
Camenzuli, Christian EP225
Camerin, Sara-Jessica OC3.4, EP991
Camolas, José EP731
Camozzi, Valentina P97
Camozzi, Valentina EP282, P289, EP233
Campana, Claudia P69, **EP1024**
Campana, Claudia P271
Campanella, Vania EP394
Campaniolo, Marco EP280
Campbell, Rebecca RC4.3
Camper, Sally P301
Campi, Irene EP1127
Camporez, João Paulo OC11.5, EP424
Campos Barros, Angel P329
Campos Peris, Andreu **EP1191**
Campos Varela, Teresa EP845
Camussi, Giovanni P123
Can, Aylin EP1281
Canbay, Erhan EP1204
Candela, Pol EP1096
Cander, Soner EP1774
Cangiano, Biagio EP1127, EP51, **P501**
Cangiano, Biagio EP1347
Cankaya, Hazım P385
Cankaya, Revah EP1745
Cannavò, Salvatore EP1001, P258, EP152, P311
Cannavò, Salvatore EP1229
Cano Gonzales, David EP1213, EP1102
Cano González, David EP1145
Cano Oncala, Guadalupe EP1305
Canovetti, Silvia P312
Cansız Ersöz, Cevriye EP1042
Cantini, Giulia P506, P464
Canton Blanco, Ana EP669
Cantone, Cristiana EP394, P80
Cantone, Cristiana P104
Cantrell, Dror P121
Canu, Gianluigi OC12.3
Canu, Giulia EP62, P13
Canu, Letizia P464
Canudas Costa, Mafalda EP696, EP1450, P400
Canudas Costa, Mafalda **P414**, **EP494**
Cao, Xiaopei **OC2.3**
Cap, Jan EP849
Capatina, Cristina EP893
Capitão, Ricardo EP323, EP1621
Capobianco, Emmanuele EP394
Capozzi, Francesco EP98
Cappa, Marco RC3.3
Cappagli, Virginia RC7.6
Capparelli, Emma **EP106**, **EP1291**, **P312**
Capra, Sara P104, **P80**, EP512
Capraru, Oana-Maria **EP218**
Caprio, Massimiliano P154
Capristán Díaz, Vanessa EP1730
Caputo, Marina EP1138, EP1215, EP1048
Caragheorgheopol, Andra EP241
Carbonara, Francesca P305
Carbonari, Maurizio EP106, EP1291, P312
Carbone, Erika RC8.3
CARDENAS, JERSY EP562
Cardona, Andres OC11.1
Cardona Attard, Carol EP166
Cardona-Arias, Andres EP1735, P267
Carén, Helena P296
Carette, Claire EP1002
Caric, Bojana P120, EP1142, EP1177
Carini, Mattia P223
Carkova, Jitka EP1453, EP1521, P419, P375
Carleo, Alfonso P311
Carlomagno, Francesco P444
Carneiro, Everardo EP478
Carosi, Giulia **EP957**, P286, EP1014, EP246
Carosi, Giulia **EP1044**
Carotenuto, Raffaela P334
Carpentier, André EP408
Carpio Salmerón, Manuel **P402**
Carranza-Mamane, Belina RC11.2
Carrara, Silvia P96, P73, P97, P84
Carreira, Ana OC7.2, EP974
Carretti, Anna RC1.4, **P270**
Carrilho-Candeias, Sofia EP698
Carrillo Lopez, Elena EP1535
Carroll, Paul EP96, OC7.6, RC6.1
Carroll, Paul RC5.6
Carthy, Claire P283, P259
Carvajal, Cristian EP30
Carvalho, Carolina EP1678
Carvalho, Francisco Simões de EP483
Carvalho, Liliana P77
Carvalho, Lina EP1285
Carvalho, Tânia EP974, EP1168, EP206, EP611
Casals, Eudald P195
Casals, Gregori EP821, **P195**, EP1205
Casarini, Livio RC4.1, P391, EP936, EP1314
Casas Marcos, Ana EP1306
Casas Miras, Ana P402
Casas-Maldonado, Francisco EP253
Casella, Giovanni EP429
Casey, Edel EP1300
Casey, Ruth RC6.5
Casi, Massimo RC3.3, EP94
Casiraghi, Alice **EP1127**
Casiraghi, Alice P501
Casoria, Michele OC8.5
Cassar, Jacob EP78
Cassar, Matthew EP225
Castano, Pablo EP82
Castaño, Luis EP496
Castell, Maria EP44
Castellana, Giampiero OC1.6
Castellano, Elena P96, **EP219**, P97
Castellanos, Alejandro EP1804
Castenetto, Alice **EP946**, RC7.2
Casteràs Roman, Anna **EP1735**
Castiglione, Anna EP1030
Castinetti, Frederic P272, EP1075, **P280**, EP1025, EP973
castro, Ana P267
Castro, Ana I. P188
Castro, Cindhy EP899
Castro, Margaret P457
Castro Mesa, Carlos EP851
Castro Tomé, Marta EP1123, EP483, EP238
Catalano, Rosa **OC12.5**, RC7.5
Catarino, Diana EP974
Catellani, Cecilia OC8.2
Catherine, Cardot P4, P72
Catsburg, Chelsea EP1157
Cattaneo, Marco P150
Cavallo Aita, Fred EP1171
Caviedes Sanchez, Edinson P227
Caviglia, Gianpaolo EP497
Ceausu, Amalia Raluca EP1115
Ceballos, Diego EP1073
Cebotari, Serghei P447
Cebrecos, Jesus P280
Ceccato, Filippo P280
Ceccato, Filippo EP1086, P56, EP1094, RC9.4, P289, P452
Ceccato, Filippo EP190
Cecchetti, Carolina OC4.6, P323, EP1048
Cecere, Francesco EP470
Cee, Pavel EP1498, **EP849**, EP1533
Cegla, Paulina P221
Cekic, Ivana EP1464, P297, P120
Celano, Stefano EP590
Celik, Ali EP1797
Celik, Aykut P394
Celik, Selin **EP121**, EP1079, **EP935**, **P394**, P110
Celo, Eni EP366
Cemel, Marianna EP1056, EP402
Cennet, Omer P16
Cennet, Ömer EP1755
Centanni, Marco **EP1315**, RC1.4
Cera, Gianluca EP347, **EP1451**, EP1179
Cerezo, Clara EP978
Čerim-Aldobašić, Amila EP1101
Cerit, Ethem Turgay EP41, EP656, EP1797, P440, EP1886
Cerit, Mahinur EP41, P440
Çerma, Adishah **EP1875**
Cerrato, Sara **EP62**, P13
Cerroni, Lorenzo EP1026
Cesur, Mustafa **EP1100**
Cetani, Filomena OC10.2, EP227, P96, EP1291, EP226, EP216, P97, P84
Cetani, Filomena **OC10.1**
Cetin, Sena **P500**
Çetin, Deniz P390
Cetinalp, Eralp EP1212
Cetinkalp, Sevki EP1189
Cevikdizici, Melike P279
Cha, Wonjae P373
Chaari, Inass **EP1437**

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Chachati, Anne-Sophie EP1482
Chacon, Melissa EP1804
Chadli, Asma **EP1603**, **EP392**, **EP1155**
Chahal, Harvinder EP430
Chaikali, Fani EP1541
Chakarova, Nevena EP1820
Chaker, Layal EP994
Chalewska, Wioletta P211
Chaliasou, Anna Louisa EP453, EP237, EP115
Chalmantzi, Varvava EP1045, EP1496, EP1262, EP25, P141
Chalopin, Sarah EP1002
Chamakioti, Myrsini EP39, EP1230, P90
Chamoun, Rita OC6.2
Chan, Alex EP85
Chan, Alice Yi-Yun EP416
Chan, Carmela Therese EP677
Chan, Jean OC9.5, P21
Chan, Wai-Chi P378
Chanal, Marie P403
Chandran, Alexander RC5.1
Chandran, Kurumbian OC6.3
Chandrasekaran, Mahisha EP277
Chang, Shao-Chiang EP895
Chang, Wei Chuan P177
Chang, Wei-Chuan **EP416**
Chang, You Jin **EP558**
Channon, Sue P340
Chanopoulos, Konstantinos P426
Chansavang, Albain EP138, RC12.4
Chansavang, Albain RC10.2
Chanson, Philippe EP1017, P242, P304
Chanturishvili, Ketevan EP353
Chantzichristos, Dimitrios **RC11.6**, EP1759
Chapple, Paul OC7.6
Chapurlat, Roland EP224
Charalambous, Marika OC5.6
charfi, nadia EP608
Charlier, Corinne RC8.3
Charoenngam, Nipith EP260
Chasan, Onour P279, **EP53**
Chasseloup, Fanny P242, P304
Chatchomchuan, Waralee EP1659
Chatee, Paul **EP1881**, **EP1772**
Chatterjee, Debajyoti EP1084, P453
Chatys, Jakub **EP1405**
Chatzi, Sofia P166
Chatzi, Sofia EP145, EP139, EP115
Chatzigeorgiou, Antonios P138
Chatziioannou, Sofia P59
Chatzinikolaou, Anastasios EP108, EP1265
Chatzis, Dimitrios G. P208
Chatzivasileiou, Panagiota EP1363
Chatzopoulos, Kyriakos EP1855
Chaudhary, Aparna **EP564**
Chaudhury, Nadia P449
Chaussain, Catherine **8**, RC10.2
Chaves, Carolina EP325
Chaves, Catarina EP1816
Chavez, Sonia EP1804
Chayani, Nirupama P152
Che, Xiangguo EP210
Cheetham, tim EP34
Cheliadinova, Uliana P361
Chen, Chuanjiang P63
Chen, Danlei OC7.5
Chen, Guan-Ho **EP1601**
Chen, Huiling EP1035
Chen, Jessica P72
Chen, Jie EP1676
Chen, Juan EP1035
Chen, Judy EP634, EP697
Chen, Juliana EP697
Chen, Junjie OC7.5
Chen, Nan OC2.3
Chen, Pei-Lung P216
Chen, Peiyun EP370
Chen, Shiwei OC9.2
Chen, Suet Ching P228
Chen, Yann-Jang P379
Chen, Yanyan P493
Chen, Yun-Ru P379
Chen, Yu-Tang **EP897**
Cheng, Chih-Ya P379
Cheng, Haixia RC3.2
Cheng, Shih-Ping EP895
Cherenko, Mariya EP224, EP973
Chertok Shacham, Elena **EP406**, **RC2.2**
Chetan, Daniela EP218
Cheung, Ching-Lung EP1488, P378
Cheung, Cynthia EP621
Cheung, Elaine Yun-Ning EP1488, P378
Chevailler, Jil OC11.3
Chevais, Anastasia EP1675, P215
Chevalier, Nicolas P272, RC12.4
Chhabra, Rajesh EP1084
Chia, Jia P395
Chiefari, Eusebio OC2.1
Chifu, Irina **RC9.5**, P5, P45
Chik, Constance EP1684
Chilà, Alessandro P501
Chillotti, Stefano OC1.6
Chiloiro, Sabrina **EP1055**, **EP1146**, EP1151, EP1057, **EP1139**, **EP1069**
Chiloiro, Sabrina EP1032
Chiloiro, Sabrina **EP1060**, P298
Chinnì, Anna EP946, RC7.2
Chiodini, Iacopo EP1117, EP1152, EP27, EP51, EP163, P288
Chionh, Siok Bee P107
Chirila, Veronica **EP953**
Chiu, Tzu-En EP945
CHIU, WEI-YIH EP892
Chkholaria, Mariam **EP16**
Chmelová, Renata P81
Cho, Dong Hyeok **EP735**
Cho, Eun Ju P57
Cho, Jung-Hwan EP484
Cho, Sanda EP1095, EP1180
Cho, Yoon young EP437, EP438
Choi, Inho EP692
Choi, Je-Yong EP210
Choi, Jiyoung P443
Choi, June Young P373
Choi, Man Ho P44, P57
Choi, Sang Il P373
Choi, Seung Joon EP645
Choi, Suji EP418, EP427
Choi, Sung-E EP385, EP418, EP427
Chojnacki, Marceli OC3.2
Chokhonelidze, Ana **EP191**
Cholidou, Kyriaki EP560, EP670
Chondrogianni, Maria Eleni P213
Chondrogianni, Maria-Eleni **EP231**, **EP239**, **EP589**, RC10.3, P138
Chorell, Elin EP1905
Chortis, Vasileios OC6.6, RC7.1
Choudhury, Sirazum OC9.4
Choudhury, Sirazum EP430
Chouraki, Vincent P9
Choustoulakis, Emmanouil P445
Chovanec, Martin EP1521, P419, P375
Chowdhury, Prodipta P473
Chowdhury, Ritoo EP222
Chrisogonidis, Ioannis P401
Chrisoulidou, Alexandra EP1459, EP1859, P426, EP1766, RC10.3
Christ, Emanuel **9**, OC3.4, P203
Christakou, Charikleia P213
Christantoniou, Georgios EP1459, EP1859, P426, EP1766
Christ-Crain, Mirjam OC3.4, OC5.1, EP1081, EP991, P292, OC3.3, OC5.2, EP1064, P273, EP1126, EP1109, P275
Christesen, Henrik RC11.3, P371, EP135
Christiansen, Christian OC12.2
Christine, Do Cao P4
Christoffersen, Christina EP60
Christou, Eleni EP729
Christou, Maria **EP729**
Christou, Panagiota EP729
Chrousos, George EP39, EP1230, P25, EP306, P90
Chtioui, Haithem P1
Chua, Aldons P67
Chuah, Matthew OC6.3
Chudek, Anna EP197
Chudek, Jerzy EP197
Chukov, Andrii EP1159
Chumbiauca, Estefanía EP602
Chung, Dong Jin EP735
Chung, Ho Yeon EP517
Chung, Jin Ook EP735
Chung, Ying Ki P228
Chuthapisith, Suebwong EP315
Chwialkowska, Karolina EP468
Chylíková, Blanka OC10.5, P132
Cianfarani, Stefano EP559, EP465
Ciarleglio, Francesco Antonio EP265
Cicchinelli, MIchela EP1151
Cicchinelli, Michela EP1060
Ciccone, Giovannino EP1030
Cidade Rodrigues, Catarina **EP1816**
Ciekot-Sołtysiak, Monika EP561
Cieślewicz, Maja **P106**
Cieszykowska, Izabela P211
Ciftci, Sema **EP1092**, EP121, **EP1079**, EP935, RC5.4, P394, EP1070, P110
Ciftci, Turkmen Turan P321
Cihan, Hüseyin EP140
Cillikova, Olivia EP1453, **EP1521**, P419, P375, P81
Cima, Luminita EP1894
Cimmino, Maria P29
Cimpean, Anisoara EP1615, EP730
Cindil, Emetullah EP1797
Cindro Kostelec, Ema EP1342
Cinpolat, Havva P194
Cinzia, Aurilia EP973
Cipriani, Cristiana P96
Cirello, Valentina RC8.3
Ciric, Jasmina EP1651
Ciric, Luka EP1651
Ćirić, Vojislav EP668

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Ciszek, Karol **EP242**
Citterio, Valeria OC11.6, P330
Ciudin, Andreea OC11.1
Civiletti, Roberta EP1117
Claire, Douillard P9
Clark, T P151
Clarke, Bart L. OC10.2
Clarke, Sophie P351
Clarke, William A. EP228, EP1374
Clayton, Peter P228
Clément, Karine EP1002
Clifton-Bligh, Roderick OC10.1, P72
Clotilde, Vincent EP1002
Clunie, Gavin EP224
Cob, Alejandro EP1804
Cobelo-Gómez, Silvia P188
Cobo, Amparo P83
Coca, Bibiana EP1073, EP899
Cocchini, Claudia P334
Cocoloș, Andra EP307
Codegoni, Marta EP1044
Coelho, Mariana EP291, EP974, EP1168, EP206, EP1120
Cohen, Arnon P91
Cohen-Solal, Martine EP224
Colao, Annamaria EP400, EP470, P169, P253, EP1025, P29
Cole, Christian P452
Coles, Diana Felicia **EP250**
Collado Solé, Alejandro **P346**
Collamati, Francesco EP1182
Collantes Alcalá, Virginia EP924
Collares-Buzato, Carla **EP1678**
Colleo, Alessandro RC1.2
Collet, François P4
Collet, Sarah EP1344
Collini, Valentina OC11.6, P330
Collins, Michael OC10.1
Colman, Ellen P74
Colombero, Simone **OC1.6**
Colombin, Giacomo EP98
Columbu, Carla **EP337**
Colzani, Raffaella **P261**
Coman, Cristina EP68
Comaneshter, Doron P91
Comberiati, Pasquale P97
Comninos, Alexander **10**, P349, OC4.1, EP217, P351, OC4.2, P322, P325
Comninos, Alexander EP363
Comune, Irene EP219
Concepción, Luís EP1011
Concha, Javiera EP602
Conflitti, Anna Chiara P12
Coniac, Simona EP969
Conlon, Peter EP10, EP38
Consoli, Clara **EP1109**
Constantin, Teodor EP903, EP977, EP919
Constantinescu, Andreea Georgiana EP1790
Constantinescu, Georgiana EP1292, EP1641, P10, **P30**, P45, **EP55**
Constantinescu, Stefan Matei **EP1046**
Constantoulakis, Pantelis P426
Contarino, Andrea RC6.2
Contini, Giacomo EP233, **EP282**
Contreras- Bolívar, Victoria EP253
Contreras Pascual, Cristina EP975, EP360
Conway, Ann RC4.2
Cooksley, Tim RC5.2
Coope, Helen RC9.5
Çorapçıoğlu, Demet P204
Corbetta, Sabrina **P73**, **P97**
Corbetta, Sabrina P96, P84
Corda, Claudia EP1709
Cordeiro, Maria Carlos EP1188, EP1098, EP1267, EP323, EP1621
Cordero, Esteban P307
Cordovez, Simone **EP1073**
Corica, Domenico OC8.5, P112
Corica, Giuliana EP1024
Corlan, Ana-Silvia EP1570, **EP920**
Cornec, Marie EP72
Cornejo-Pareja, Isabel EP869
Corpe, Christopher EP1674
Corrias, Silvia RC1.2
Corrias, Silvia OC12.3, EP1709
Corsello, Andrea EP1451
Cortez, Alexander OC7.1, EP905
Coscia, Kimberly EP98
Cosentini, Deborah P223, RC12.5
Cosentino, Alessia EP1352
Cosentino, Teresa P452
Coskun, Meric EP1015
Coşkun, Aylin RC5.4
Cosma, Daniel-Tudor **EP798**
Cosma, Diandra Carmen **EP1779**
Cosottini, Mirco P312
Cosseddù, Domenico P223
Cosson, Emmanuel P458
Costa, Anabela EP494
Costa, Carla Paola EP1001, **P258**, EP152, P311, EP1229
Costa, Francisca EP261
Costa, Gracinda EP974
Costantino, Francesco **EP1329**
Costanza, Flavia **EP1032**, EP1055
Costea, Mirona EP122
Costinescu, Ruxandra EP771, **EP122**, EP1897, EP1887, EP1522
Cotoi, Laura EP1039, EP1105, EP1248
Cotta, Oana Ruxandra **EP1001**, P311
Coulden, Amy **P277**, **EP1164**
Coulman, Elinor P340
Coulon, Anne-Laure EP1860
Couto, Joana EP1501
Couto, Luísa P77
Couto, Rosa EP1098
Cove-Smith, Laura RC5.2
Cowen, Neil RC2.5
Cowie, Louise EP1374
Cox, Jeremy EP363
Cozzi, Renato Cesare EP1152, P288
Craggs, Matthew EP1199
Craig, Sonya EP1199
Craparo, Andrea EP219
Crasan, Ioana-Maria EP1615, **EP730**
Crasta, Beatrice EP1057
Crastin, Ana OC6.6, P27
Credi, Giacomo OC1.6
Cremaschi, Arianna EP957, P286, EP1014, P278, EP1044
Crescenzo, Erminio M. EP470, P169, **P29**, P12
Crescenzo, Raffaella EP470, P169
Criminelli, Diego EP1024
Criollo Posso, Alejandra Salomé EP1730
Crispino, Laura EP1451
Cristante, Justine P272, EP1002
Cristea, Beatrice EP1258, EP1460, EP23, **EP7**, EP112, EP1149
Cristiana, Calin EP903
Cristina, Căpăţînă EP1062
Cristofolini, Giacomo OC12.5
Croce, Alessandro EP51
Crocetti, Giorgio P506
Crona, Joakim OC7.2, RC6.5
Crowhurst, Elliot EP160
Crown, Anna EP73
Crowne, Liz EP34
Cruces Párraga, Jerónimo EP390
Crutcher, Kimberly OC2.2
Cruz, Stefania EP82
Cruz-Iglesias, Elena OC10.3
Csabai- Tanics, Timea Judith P480
Csitári, Gergő EP1000, **EP148**, **EP593**, **P147**
Cuboni, Daniela EP1029, EP1186, **EP189**
Cui, Ying EP210
Cui, Yunying OC7.2
Cunningham, Ameera EP1400
Cuny, Thomas P508
Curcio, Martina **P342**, **P352**
curreli, mariaignazia EP429
Cusini, Claudio EP894
Cuthbertson, Daniel EP1199
Cutilla Muñoz, María Ángeles EP382
Čužić, Snježana EP426
Cvetkovic, Vesna EP699, EP762
Cylke-Falkowska, Karolina **EP1143**, **EP1172**
Cypaite, Gabriele **OC11.3**
Cyran, Clemens P28
Cyrany, Jiří EP849
Cysewski, Dominik EP1721
Czajka - Oraniec, Izabella EP1169
Czékus, Csilla **EP1006**
Czepczyński, Rafał P106
Czerwiec, Frank **EP526**
Czupińska, Michalina EP912
da Silva, Silvano **EP495**, EP388, **EP371**, EP376
Da Silva Xavier, Gabriela P277, EP397, EP1164
Dabadghao, Preeti EP1091, EP215
Dadej, Daniela **EP1056**, EP402
Dagdelen, Selcuk P317, EP1239, EP1111, P295, EP1384
Dahal, Puspa EP1280, EP205, EP1428
Dahia, Patricia **11**
Dahlqvist, Per P26
Dahmani, Doha **EP1391**, **EP1812**
Dakic, Zoran EP1586
Dal, Jakob **EP1134**, **P249**, EP1147
Dal, Jakob P244
Dal Lago, Anna EP227, P96
Dal Lago, Anna **EP226**, EP216, **P84**
Dalamaga, Maria P207, EP589
Dalili, Muhammad EP1581, **EP1606**
Dalla Valentina, Leonardo EP575
Dall'Asta, Andrea OC8.5, P112
Dalvie, Deepak P36
Daly, Adrian P252
Daly, Adrian **12**, **P305**
D'Amati, Antonio P298
Damiani, Stefania OC1.6
Damm, Mathilde EP1058, P265
Dan, Ioana Claudia EP17, EP969, **EP977**
Dana, Stoian EP1039, EP1105, EP1248, EP1657, EP194, EP1263, EP507, EP834, EP1515, EP1503

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

DANAIS, Antoine P237
Danda, Vijay Sheker EP391, EP1041
Danevych, Olena EP1159, EP1902
D'Angelo, Salvatore EP224
Daniel, Christoph EP423
Daniela, Dinu Draganescu P230
d'Aniello, Francesco EP559, EP465
Daniels, Colton EP1611
Daniels, Elisabeth OC4.1, P351, P322
Daniels, Elisabeth OC4.2
Danielyan, Meri EP544
Daoud, Lina EP1046
Daoussis, Dmitirios EP224
Daraki, Vasiliki P100, P94
Daria, Dinu Draganescu P230
Daroszewski, Jacek EP651
Darsa, Daniella OC5.3
Das, Bharat EP596, EP636, EP788
Das, Urmi EP34
Dasari, Mani EP596, EP636, EP788
Daskalakis, George EP654
Daskalakis, Kosmas **RC10.1**, **P213**
Datta, Ritwik OC2.2, EP739, P172
Dattani, Mehul EP34, P255, P256
Dautbegovic Stevanovic, Davorka EP1078
Davanellos, Nikolaos **EP1864**
Davidov, Georgi EP1708
Davids, Mark EP563
Davies, Eleanor OC6.2
Davies, Emily **EP1008**
Davies, Justin EP34
Davies, Sarah EP42
Davison, Andrew EP42
D'Ávola, Delia EP372
Davolio, Emanuela OC8.2
Dawid, Monika EP1324
Dayan, Colin RC1.6, P449
De Alcubierre, Dario EP966, **P303**, **EP1026**
De Alessandris, Quintino Giorgio EP1060
De Angelis, Cristina EP470, P169
De Biase, Dario OC1.6, RC6.4
De Block, Christophe P134
de Carvalho, Mariana P148
de Damas Medina, María EP830
De Fanti, Alessandro OC8.2
De Ferrari, Gaetano Maria P123
de Freitas, Declan EP10, EP38
De Graaf, Johan P293
De Graaff, Laura P260
de Gracia Valero, Ana EP851
De Griné Severino, Mariana EP261, EP1534
de Griné Severino, Mariana EP856
De Griné Severino, Mariana **EP1449**
de Herder, Wouter Willem P305
de Krijger, Ronald EP1790
De la Cruz Bonilla, Alejandro EP1191
De la Higuera, Magdalena EP487
De la Iglesia Arnaez, Raquel EP674
De La Rosa-Herencia, Ana **EP1185**, EP1213
De La Torre, Eduardo P36, EP116, EP36
De Leo, Antonio RC6.4, P464
De Leo, Giacomo EP226, EP216, P84
de Leon-Durango, Ricardo Jose EP1703, EP1833, P497, EP1841, EP1835, EP1707, EP1773, EP1706, P498
De Luca, Arnaud EP1002
De Luis Román, Daniel EP1306
DE LUIS ROMAN, DANIEL EP1195
De Marinis, Laura EP1055, EP1146, EP1151, EP1057, EP1139
De Marinis, Laura EP1060, P298
De Marinis, Laura EP1032
De Marinis, Laura EP1069
de Murat, Daniel P285
De Napoli, Luigi EP226
de Paiva, Camilly EP388, EP371
de Paula, Francisco P457
De Salvo, Rossana P311
De Sanctis, Simone Antonio **P298**
de Santana, Maria Eduarda EP376
De Santis, Maria Cristina EP62, P13
De Santis, Pascual EP938
De Simone, Andrea EP1179
De Sousa, Sunita **13**
de Sousa Lages, Adriana EP245, EP1589, EP286
De Stefano, Valerio EP960
De Vincentis, Sara EP1130, EP1066, EP1329
De Vincentis, Sara EP62, P13
De Waal, Tom EP228
De Wilt, Johannes H.W. P95
De Wit, Victoria **EP138**
Dearden, Laura EP1400
Debeljak, Željko EP1680
Debono, Miguel EP1493
DeBono, Miguel EP124
Decallonne, Brigitte P72
Decaroli, Maria Chiara EP1130, EP1066
Decaussin-Petrucci, Myriam P403
Decaux, Karine EP1002
Dechend, Ralf EP135
Deckers, Nynke EP12
Decoudier, Benedicte P272
Decouvelaere, Anne-Valérie EP1366
Dede, Monika EP1787
Dedecjus, Marek P211
Dedecjus, Marek P411
Dedecjus, Marek EP964, P221
Dedonno, Anna Aurora OC6.5, P464
Defreyne, Justine EP1344
Degirmenci, Ali EP1131
Degmečić, Dunja EP793
Degradi, Chiara P73
Deinum, Jaap P452
Dekanski, Anja **EP1905**
Dekkers, Olaf 14, P5, P249, EP224
del Arco Romualdo, Belen EP971, **EP1286**
Del Duca, Nicoletta P501
Del Nogal Avila, Maria EP259
Del Sindaco, Giulia EP957, P286, EP1014, EP1044
Del Sindaco, Giulia **EP246**
Del Vecchio, Guendalina EP400
Delaney, Angela P228
Delannoy, Pauline EP1482
Delaporta, Polyxeni EP1365
Delgado, Elías EP1677
Delgado Castro, Liseth Gabriela **EP1171**, EP1746
Delgado Garcia, Esther EP1306
Delgado Moya, Pablo EP924
Delia, Corina EP1615, EP730
Delic, Neda EP444
Deligeorgakis, Dimitrios EP1508
Delivanis, Danae P445
Della Valentina, Simone **EP227**, **P96**, EP226, P97, P84
Dellal Kahramanca, Fatma Dilek EP1711
Delle Donne, Elisa EP1127, EP51, EP1347
Demarchis, Luigi **EP1151**
Demarchis, Luigi EP1060, **EP1057**
Demeke, Belene EP157
Demeocq, Vianney EP1002
Demerouti, Eftychia P208
Demir, Özgür EP1542, EP1042
Demir, Özgür EP1154
Demirci, Ibrahim EP1743
Demirel, Ali Haydar P321
Demirkıran, Oktay EP1231
Demirtas, Sena Nur P291
den Elzen, Wendy EP64
Deng, Tuo P153
Denichelis, Veronica Maria EP1329
deniz, muzaffer serdar P410, EP84
Deniz Yücel, Hatice RC5.4
Dennedy, Michael RC7.1
Denos, Marion **P432**
Denton, Mark EP10, EP38
Derakhshan, Arash RC1.1, OC8.6
Dermitzaki, Eleni EP378, P179
Deroux, Flore P403
Derrien, Christèle P17
Dervishi, Orsela **OC9.6**
Derwich-Rudowicz, Aleksandra EP561, **EP1187**
Desailloud, Rachel RC12.4
Desevic, Enra EP1856
Deshmukh, Harshal EP1485
Deshpande, Shrikant EP596, EP636, EP788
D'Este, Francesca EP946
Detomas, Mario OC3.1, OC3.4, OC12.5
DEUTSCHBEIN, Timo OC3.1
Deutschbein, Timo P266, RC3.4, OC3.4, P269, EP1025
Dey, Uttam Kumar **EP1751**
Dhage, Shaishav RC5.2
Dhamale, Rutuja **OC8.6**
Dhesi, Balraj RC6.4
Dhillo, Waljit P349, OC4.1, EP217, P351, OC4.2, P322, P325
Di, Ying EP1164
Di Bari, Sonia RC7.5
Di Carlo, Maria Chiara RC9.6
Di Dalmazi, Giulia P431
Di Dalmazi, Guido EP459, EP394, RC6.4, RC7.5, **EP80**, EP512, **EP98**, P2, P464
Di Filippo, Luigi **EP280**
Di Giulio, Francesca P303
Di Iasi, Gianfranco RC6.2
Di Iorgi, Natascia P97
Di Muro, Genesio EP1173, RC7.5
Di Paola, Nicola P253, P29
Diah, Mohd Idris **EP577**
Diana, Federica **RC1.2**, OC12.3, EP1709
Diana, Renato **EP894**
Diaz, Nestor EP82
Díaz, Yesika EP496
Díaz Gorrín, Kevin David **EP1304**, **EP553**, EP492, EP493, EP1478, EP199, EP784
Diaz Perdigones, Cristina Mª EP1161
Díaz-López, Everardo J. **P188**
Diazzi, Chiara EP1130, EP1066
Dichtel, Laura EP1075
Didbaridze, Tamar EP1524
Dițescu, Bogdan Radu EP241
Diez, Nerea EP978
Díez Fernández, Natalia EP1730
Digitale Selvaggio, Lucia P334, P97

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Dijoud, Frédérique EP1366
Dikaiakou, Eirini EP231
Diker Cohen, Talia EP473, **P129**, **P109**, P268
Dimassi, Oumaima EP1632
Dimitriadis, Georgios K. P342, P352
Dimitriadis, Georgios K. EP1348
Dimitrova, Radina EP1040, **EP1708**, EP1301
Dinca, Mirona EP771, EP1897, EP1887, **EP1522**
Dionese, Paola OC4.6, P323
Dios, Elena RC11.4, P180
Dios-Fuentes, Elena EP1145
D'Ippolito, Enrico EP1182
Dirinck, Eveline P134
Dischinger, Ulrich P71, P239, EP500, RC11.1, EP423, P241, EP463
Disko, Ulrike EP1108
Ditsiou, Angeliki RC7.2
Divaris, Efstathios P102
Djajic, Olga EP1464
Djinic Krasavcevic, Ana P120
Djordjevic, Ana EP563
Dmitrienko, Alex OC10.1
do Vale, Sónia EP856
Dobiasovska, Karolina EP1453, EP1521, P419, P375
Doblas Ráez, Pablo EP390
Dobler, Stefanie P150
Dobre, Ramona EP1683, EP757
Dobre, Ramona EP961, EP1190
Dobre, Ramona EP903
Dobruch-Sobczak, Katarzyna P411
Doelle, Michael P293
Doga, Mauro EP280
Doglietto, Francesco EP1055, EP1146, P298, EP1151, EP1179, EP1057, EP1139, EP1069
Doglietto, Francesco EP1060
Doğrul, Ahmet Bülent EP1755
Dohan, Anthony P285
Doi, Yuji P174, P185
Dojcinovic, Boris EP193
Dojcinovic, Tamara **EP193**, **EP1142**, EP1441, EP1235, EP1246, EP1177
Doknic, Mirjana EP1464, P297, P120
Dolacinska, olga EP940
Dolen Burak, Duygu EP53
Dolev, Lilach P91
Dolezal, Jiri EP1338
Doman, Eleanor EP1759
Domańska-Czajka, Agnieszka EP212
Domański, Jan **EP906**, **EP1404**, EP1218, EP756, P103, EP1408
Domenig, Oliver EP1017, OC6.2, EP54, EP131
Domin, Remigiusz P49
Domingue, Marie-Eve EP1684
Donado, Jorge EP82
Donath, Marc P150
Doneda, Paola EP1152
Donegan, Diane EP1144
Donini, Lorenzo EP966
Dönmez, Mehmet P504, P486
Donnarumma, Francesca EP80, P2
Donner, Davide EP1754
D'Onofrio, Valentino EP1344
Dophidze, Elene **EP1244**
Dorato, Emma EP1347
Dorogi, Carmen EP289
Dorrington, Ian EP42
Dorta-Bouza, Valentina OC4.4
Dorward, Neil EP1137
Dosedelova, Vera RC7.1, **EP1359**
Dotan, Idit P316, P129, P109
Dotan, Idit RC3.5
Dottermusch, Matthias OC3.1
Doucet, Laurent EP72
Doudakmanis, Christos EP1568
Dourmap, Caroline EP14
Doyle, Georgina EP419
Draghici, Alexandru-Ioan EP1679
Dragicevic, Natalija EP1311, EP900, EP43, P344
Drąg-Kozak, Ewa EP1322
Dragula, Milan EP1121
Drake, William Martyn EP1865
Drakopoulou, Anna EP1541
Drakos, Panagiotis EP1700
Dram, Mariana EP937, EP940
Dreier, Tim P43
Drettwan, Diana **EP657**
Drincic, Andjela T. EP1676
Dronjak, Đurđina EP1074
Drosou, Aspasia EP1541
Drozdinsky, Genady EP1132
Drozenova, Jana EP1521, P419, P375
Drugda, Jan **EP1498**
Drui, Delphine P272
Drummond, Juliana OC3.4, EP1047
D'Souza, Chrisel P468
Du, Yunfeng EP32
Du Toit, Therina EP1760
Duan, lian **EP1035**
Duan, Lian P487
Duan, Shaowei EP490, EP370
Duan, Yale **EP490**, **EP370**
Duan, Yaqian EP370
Duarte, Adriana EP291, EP974, EP1168, EP206, **EP1120**
Duarte, Daniel EP1188, EP1098, EP323, EP1621
Duarte, Daniel **EP1267**
Duarte, Miguel EP856, EP1449
Duarte, Miguel António EP261, EP1534
Dubeikaite, Ruta EP1467
Dubeikaitė, Rūta EP339
Dubiel, Aleksandra EP1238
Dubois, Jasperina EP469
Dudonytė, Laura EP20
Dufour, Patrice RC8.3
Dugal, TABINDA **EP1778**, **EP1899**
Dughera, Francesca EP95
Đukić, Mirjana P222, **EP910**
Dulugiac, Alexandra **EP1460**
Duman, Azad **EP461**
Dumbadze, Mariam **EP1890**
Dumitrache, Sabina Maria **EP1894**
Dumitrașcu, Anda EP917, EP23, EP7, P299
Dumitrascu, Anda EP1247
Dumskyj, Martin EP523
Duncan, Colin **P332**, OC4.5
Dundua, Ketevan EP832
Dundua, Ketevan EP1890
Dunleavy, Therese EP456
Dunn, Warwick P277, EP1164
Dupeux, Margot P304
Duquenne, Alicja EP77
Duquenne, Alicja OC6.4
Duquenne, Alicja **EP1169**, **P51**
Durak, Hüseyin Mert EP434
Durantas, Halil EP1457
Durcan, Emre **EP1231**
duregon, Eleonora OC6.1
Durmanova, Aigul EP287, EP331, EP796
Durmek, Igor EP1269, EP1264
Duro, Bariola **EP366**
Durutovic, Lana EP444
Dusa, Ina EP1813
Dusceac, Roxana EP214, EP68
Dusek, Tina P222, EP910
Duskin-Bitan, Hadar **P429**, **P91**
Dutta, Arshiya **EP208**
Dutta, Pinaki EP1084, EP208, **P453**
Dwyer, Andrew EP1349
Dydyshka, Yuliya EP838, EP1372, EP1373
Dyrmishi, Blertina **EP1798**
Džepina, Martiana P156
Dzialach, Lukasz **EP1160**, EP928, EP1238
Džijan, Snježana EP1466
Dzubanova, Martina EP399
Earnest, Arul P320, EP637
Ebeling, Peter EP269, EP303
Ebid, Mahmoud EP1376
Edholm, Adam **RC6.5**
Edouard, Thomas RC10.2
Edward, Fomekong EP1046
Edwards, Erin **EP1413**
Effraimidis, Grigoris **EP5**, **EP1596**, EP1476, EP327, **P461**
Efstathiadou, Zoe EP1005, RC10.3, EP9, EP1508
Efstathopoulos, Efstathios EP589
Efthymiadis, Agathoklis **EP217**
Efthymiadis, Agathoklis P349, OC4.2, P322, P325
Efthymiou, Christoforos EP850
Efthymiou, Kleanthia P50
Egaña Zunzunegui, Nerea EP978
Ege Gül, Aylin EP943
Eggermann, Thomas **15**
Egli, Adrian EP638
Einsele, Hermann OC7.3
Eisenhofer, Graeme EP100, P42, P10, P19
Eisenhofer, Graeme P30, EP55
Eken, Yagmur **EP1797**
Ekici Duman, Julide EP461
El Azime, Zineb EP255
El aziz, Siham EP1603, EP392, EP1155
El Cadhi, Youssef EP1393
El Fekih, HAMZA EP75, EP1499
El Hadi, Hamza **EP1059**, **EP1135**
El Jadi, Hamza EP1437
El Moudden, sanae EP1808
EL YOUNSI, Sarra EP153
El Younsi, Sarra EP1393
Elabasy, Ahmed P99
Eladla, Meryem **EP255**, **EP1808**
Elamin, Nazik P162
Elamo, Heidi P357
Elawwa, Ahmed EP546, EP987, EP667
Elbelt, Ulf OC3.4
Elbuken, Gulsah EP1829
Eldar, Dor **P397**
Elena Domínguez-López, Marta EP420
Elenkova, Atanaska EP1386, EP1380
Elezovic Kovacevic, Valentina **EP1311**, EP900, EP43, P344
Elfekih, Hamza EP835
Elford, Sue EP125
Elhadri-Egea, Aida **EP443**, **EP890**, **EP535**

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Elhadri-Egea, Aida EP609, EP826, EP884, EP601, EP550
Elhariry, Maiar P339
Elhasnaoui, Mohamed Amine EP101
Elias, Ann EP391, EP1041
Elisei, Rossella OC1.5
Elisei, Rossella P383, RC7.6
Elkan, Matan EP741
Eller Vainicher, Cristina P96, P97, EP27
Eller Vainicher, Cristina EP1044
Elleuch, Mouna EP608
Elston, Marianne EP1610
Eltayieb, Lina EP940
El-Toukhy, Sarah EP1606
Elüstü Belten, Zeynep EP1092, EP121, P394, EP1070, P110
Elvas, Ana Rita EP1501
Emanuel, Anna **EP503**
Emery, Blaise EP1573
Emral, Rifat EP1154, P176, P204
Emral, Rıfat EP1542, EP1042
Enache, Ana-Teodora EP619
Enachescu, Roxana **EP1423**
Enachescu, Roxana EP68
Endo, Takaaki EP1063
Ene, Cristina **EP1261**
Eng, Pei P351
Eng, Pei Chia P107
Engelhardt, Annika RC11.1
Engelhardt, Julien P508
Eon, Solène **EP1860**, P458
Epstein, Michael OC11.3
Eraslan Aydemir, Esra EP1154, EP1042
Erbas, Tomris EP1239
Erbaş, Tomris P317, EP1111, P295
Ercan, Polat EP1239
Ercolino, Tonino P464
Erdogan, Mehmet EP1189
Erdogan, Murat EP1154, EP1542, EP1042
Erdogan, Seyda EP1212
Erdoğan, Tuğba P460
ERDOĞAN KABLAN, Sevilay P463
Eremkina, Anna EP1544, EP256
Erickson, Dana **EP1144**
Eriksson, Daniel P384
Eriksson, Gustaw EP1905, EP1906
Erini, Marco EP1754
Erkan, Buruc EP1201, EP1163, EP1079
Erlic, Zoran **P452**
Erman, Hande P314
Ersoy, Canan EP1774, EP1743
Ersoy, Reyhan P410, EP84, EP1484, EP726, EP641, EP249, EP1015
Ersoy, Reyhan EP1711
Ertuna, Gokcen EP1015
Erturk, Erdinc EP1774
Ertürk, Banu EP1755
Erzik, Can EP934
Escalada, Javier EP372, EP487
Escalada, Javier EP602
Escalante, Miriam EP1158
Escobar Gómez, Jorge EP151
Escribano, Arancha P305
Eshkoli, Tamar OC1.1
Espada, Filipa RC5.3
Espejo-Cordero, Azahara OC4.4
Espiard, Stéphanie **EP1075**, P4, P9
Espiga Alzola, Javier P79, OC10.3
Esposito, Daniela **P296**, P484, P485
Esposito, Emanuela RC7.5
Esquivel Vargas, Jose Edmond EP1171, EP1746
Essafi, Mohammed Amine EP255
Esteves Ferreira, Sara EP245, EP286
Estevez, Jose carlos EP630
Estévez Asensio, Lucía EP1306, **EP1195**
Esvant, Annabelle P17
Etxeberria, Eider P79, OC10.3
Eubler, Katja EP1421
Evangelatou, Anastasia P25
EVANGELISTA, LISA ANGELICA EP1436
Evans, Mia EP1413
Evirgen, Oya P194
Evliati, Loukia EP139, EP115, EP1387
Evranos Ogmen, Berna P410, **EP641**, **EP249**, **EP1015**
Exposito, Amaya OC10.3
Eyüpoğlu, Erol EP934
Eyüpoğlu, Havva EP934
Ezzahoum, Zaynab EP1603
Faa, Giulia OC12.3
Fabris, Bruno EP491
Fabris, Luca EP265
Faccini, Riccardo EP1182
Faccioli, Giacomo EP265
Faedda, Nicolo P31, OC6.2
Faggiano, Antongiulio OC7.4, EP1182, RC6.2, EP1224
Fagher, Katarina P137
Fagherazzi, Guy P458
Fahmi, Helena EP1851, EP1836
Fahmi, Helena **EP1811**, **EP1803**
Faisal Al Aqarbeh, Shatha EP1679
Fajardo-Montañana, Carmen P267
Fakhreldin, Marwa EP1908
Fakiolas, Stefanos EP1869
Falcetta, Pierpaolo EP150
Falhammar, Henrik **16**, OC7.2, P6, P8
Falvey, Heather EP260
Fammler, Heidrun OC8.1
Fan, Christina EP228
Fanadka, Feda EP916
Fanelli, Flaminia EP394, EP80, EP98
Fano, Martina RC6.2
Fanos, Vassilios OC8.2
Fantini Trinca, Bruna Maria OC11.5
Faouzi, Mohamed RC10.6
Farahani, Pendar **EP702**, **EP695**, **EP822**
Faranda, Alessio P383
FARAOUN, Khadra **EP1085**, **EP1259**
Fardella, Carlos EP30
Farhat, Abdullatif EP211
Faria, Nuno EP386, **EP1589**, **EP632**
Faria, Teresa P77
Farida, Chentli EP1259
Farigon, Nicolas EP1002
Fariselli, Piero EP497
Faron-Górecka, Agata EP1093
Farsetti, Antonella OC12.1
Fasanella, Silvia EP1754
Fasano, Tommaso EP62, P13
Fasciglione, Elsa EP1002
Fassnacht, Martin OC7.3, P71, OC3.1, OC3.4, OC7.2, P239, EP500, RC11.1, EP423, OC6.5, RC7.1, OC12.5, P241, EP463, P11, P30, EP55
Fath, Anne-Sophie P345
Fatima, Aziouaz EP1391, EP1812, EP128
Fatima, Neha **EP1865**
Fatima, Sereen **EP941**
Fatma, Ayadi EP608
Faubert, Joanie EP408
Faucher, Pauline **EP1002**
Faul, Clare P283, P259
Favaro, Federico EP491
Favero, Vittoria P27, EP1117, EP1152, **EP27**, EP51, EP163, P288
Fayad, May **P31**, **OC6.2**
Fedeli, Francesco EP911
Federici, Silvia EP1347
Fedorczak, Anna EP212
Feelders, Richard EP1075, P280
Feeny, Claire P427
Fekih, hamza EP1156
Fekih, Hamza EP1487, EP571
Feldkamp, Jasper EP1479
Feldkamp, Joachim EP1479, P145
Feldt-Rasmussen, Ulla P22, EP60
Felicani, Cristina EP575
Felker, Jasmin P71, P239, P241
Fell, Vanessa OC6.4
Fellinger, Paul EP1017, P43, EP54, EP131, P455
Feltoft, Claus P249, EP60
Fendt, Sarah-Maria P210
Fenger Dreyer, Anja RC11.3, P22
Feola, Tiziana EP966, P303, EP1026
Ferdousi, Tahmina P473
Ferencakova, Michaela EP399
Ferjan, Petra **P328**
Fernandes, Ana P77
Fernandes, Cristina EP1450
Fernandes, Tânia EP1123, EP483, **EP238**
Fernandes, Vera EP286, EP632
Fernandes, Vítor EP1450
Fernandes-Rosa, Fabio P31, OC6.2
Fernandez, Cornelius EP89
Fernandez, Eva EP821
Fernandez, Herve EP1908
Fernandez Castañer, Alejandra EP467
Fernandez James, Cornelius EP1252, EP986, EP1216, EP1427, EP774
Fernández Jiménez, Rocío EP405
Fernandez Lopez, Maria del Carmen EP244
Fernandez Sanchez, Alvaro EP562
Fernández Velasco, Pablo EP1195
Fernandez-Escabias, Manuel EP698
Fernandez-Escabias, Rodrigo EP698
Fernandez-Jimenez, Juan P450, EP1742, EP1776, EP1777
Fernández-Pombo, Antia P188
Fernández-Ramírez, Víctor J. EP909
Fernandez-Trujillo-Comenge, Paula Maria EP1707
Fernandez-Twinn, Denise S. EP1400
Fernández-Varo, Guillermo P195
Fernando, Minuri **EP401**
Fernandois, Daniela **17**
Ferone, Diego P266, RC3.4, P274, P69, P271, P484, P485
Ferone, Diego EP1024, P253
Ferrante, Emanuele EP957, OC3.4, P280, P286, EP1014, P315, RC7.5, P253, **P278**, EP1044
Ferrarese, Michela P97
Ferrarese, Michela EP282
Ferrarese, Michela EP233
Ferrari, Davide P253, **P12**

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Ferrari, Dora EP526
Ferraù, Francesco P253, EP1229, P258, **P311**, EP1001, EP152
Ferreira, Ana Gonçalves EP1188
Ferreira, Joana P366
Ferreira, Lia EP1326
Ferreira, Patricia EP494, EP1450
Ferreira, Sofia RC5.3, RC4.6
Ferrero, Alice EP1215
Ferrero, Alice EP1138
Ferriere, Amandine EP1075
Ferrulli, Anna EP1665
Ferruzza, Giuseppe EP95
Feve, Bruno P31
Fialho, Christhiane EP989
Fibigr, David 20
Fiedorowicz, Joanna **P140**
Fierro-Milla, Evigeni EP1805
Fiévet, Manon **P234**
Figueiredo, Ana EP325
Figueiredo, Arnaldo EP944
Figueiredo, Catarina EP1326, EP525
Figueiredo, Suzana RC4.6
Figurova, Jana EP447
Filice, Alessia **EP966**
Filipovic, Aleksandar EP146
Filipowicz, Dorota EP1056, **EP402**
Filipowicz, Dorota P106
Filippidou, Anastasia EP108, EP1265
Filippone, Melissa RC11.2
Filipsson Nyström, Helena **18**, P89
Fintini, Danilo EP559, EP465, P97
Fiore, Emilio EP150, P24
Firat, Sevde Nur OC11.2
Firfilioni, Katerina EP306, P90
Fischer, Alessa OC7.2
Fischer, Justus P150
Fischetti, Fabio EP491
Fisher, David **EP1497**
Fiszer, Jowita **P309**
Fiszer, Jowita P39, P62
Fitzgerald, Robert EP1374
Fitzpatrick, David P283, P259
Flack, Sarah EP464
Flamigni, Sara EP459, EP512
Flavia, Costi EP920
Fleseriu, Maria P266, **RC3.4**, OC3.4, P306, P268, P316, P274, RC3.5, P228, EP1170
Fleseriu, Maria EP1032
Flessa, Christina-Maria EP589, **P138**
Flitsch, Jörg OC3.1
Flood, John **EP1350**
Florakis, Dimos RC10.3
Florakis, Dimos P445
Florence, Roucher EP1366
Flores Rios, Leyla Vivana EP899
Florescu, Alexandru EP1641, EP248, EP354, EP262, **EP996**, EP1491, EP1292, **EP1337**, EP159
Flores-Martínez, Álvaro EP1185, EP1213, EP1161, **EP1102**
Fogarty, Michael EP222
Fogel, Olivier EP224
Foglarová, Tereza **EP1113**
Folden Flensburg, Mimi P8
Folgueira, Cintia P346
Foligno, Nadia P97
Fong, Carol Ho Yi EP8
Fonseca, Ana Margarida EP1450
Fonseca, Beatriz P77
Fonseca, Vivian EP526
Fontana, Marta OC8.2
Fontana, Natalia EP224
Foo, Roger OC6.3
Forte, Dalia EP1220
Fota, Roxana EP23, EP7, EP112
Foti, Daniela P159, OC2.1
Fountas, Athanasios **EP113**, EP192, EP1594, **EP1082**, **P59**, EP1879
Fountoulakis, Stylianos P445
Fowkes, Rob **EP85**
Fowler, Paul P332
Fraenkel, Emil EP447
Fraenkel, Merav EP1497, OC1.1
Frampton, James EP260
Frances, Jorge EP1167, P263
Frances, Jorge EP1022
Francis, Ann EP1252, EP1427, EP774
Franco, Cristina EP44
Franco, Giorgio P444
Franco, Patricia **EP1474**
Franco, Sara EP1267
François, Pattou P4
Francque, Sven P134
Franek, Edward EP1404, EP1218
Franek, Edward EP756, P103, P388, EP1408, P425
Franke, Adrian EP1368
Franke, Martin P252
Frankel, meir P397
Frankel, Meir **EP102**
Franks, Stephen P332
Frau, Annica P234
Frederiksen, Anja EP1364
Freitas, Izabella EP1047
Freitas, Joana EP1326, EP525, RC5.3, RC4.6
Freitas, Lucas EP1047
Freitas, Paula P77
Freud, Tamar EP1497
Friedman, Zachary EP711
Frimat, Coralie P31
Frolinger, Tal P361
Frouget, Thierry EP14
Fruhbeck, Gema EP602
Frustaci, Gianluca EP227, EP226
Frystyk, Jan P327, OC5.5, EP1360, EP1364, P457
Fu, Antony P228
Fu, Jack EP1343
Fu, Wei EP633
Fuentes, Antonio J. EP1185
Fuentes-Fayos, Antonio C. EP1213, EP951, EP1102
Fuentes-Fayos, Antonio Carlos EP1185, EP1161
Fuertes Rioja, Lidia P143
Fugazzola, Laura **19**, RC8.3
Fuhrberg, Konstantin EP50
Fujio, Shingo EP1063, EP1104, **EP1184**, EP1088
Fujisawa, Haruki EP1129, EP1200
Fukuoka, Hidenori EP1063
Fuld, Sybille EP100
Fuld, Sybille P30, EP55
Fung, Matrix P82
Furer, Victoria EP224
Furmanek, Mariusz EP1218
Furrer, Jan EP1374
Furth, Christian P284
Furukawa, Shinya EP684
Fuss, Carmina Teresa EP100, P42, P10, P19
Fuster, David P83
Fux, Elie EP228, EP1374
Fyda, Rafał **EP954**
G. Martins, Raquel EP1501
G. Santamaria, Patricia P346
Gabalec, Filip EP1498, EP849, EP1533
Gabalec, Filip 20
Gabidzashvili, Nino EP1244
Gabreska Kebakoska, Aksinja EP876
Gabrielli, Filippo EP575
Gaćina, Petar EP1526
Gadelha, Mônica EP989, P266, RC3.4, **P306**, **P274**
Gadelha, Mônica EP1185
Gadelho, Luís EP992
Gadus, Lukas P224
Gafni, Rachel OC10.1
Gagliano, Teresa EP946, RC7.2
Gagliardi, Arianna EP966
Gago Da Câmara Dias Pereira, Bernardo EP325
Gahete, Manuel D. EP1077, EP909, EP425, EP1213, P219, EP951, P210, EP698
Gaidytė, Saiva EP999
Gaillard, Martin OC6.5
Gaillard, Stephan P285
Gala-Bladzinska, Agnieszka EP1463
Galac, Sara **EP12**
Galani, Maria EP5, EP1596, EP327
Galante, Greta EP80, EP98
Galcheva, Sonya EP1040
Gałczyński, Jacek P411
Gales, Cristina **P491**
Gales, Daniel Costel P491
Gálfi, Márta EP985
Gallach Martínez, Marta **P116**
Galletta, Federica EP152
Gallone, Guglielmo P123
Gallova, Johana **EP263**
Galmiche, Mathieu EP80
Galo, Elisa RC5.3, RC4.6
Galoiu, Simona EP68, EP757, EP1062
Galvagno, Lea **EP1126**
Galvez Moreno, Maria Angeles EP630, EP1185, EP1213, EP1161
Gama, Catarina EP1458
Gamallo, Ignace Claire **EP783**
Gambale, Carla **OC1.5**, P383, RC7.6
Gambera, Francesco EP946, **RC7.2**
Gambineri, Alessandra P320, EP637, OC4.6, P323
Gambineri, Alessandra EP1048
Gamertsfelder, Elise EP464
Gamrat-Żmuda, Aleksandra EP114, EP1083, **EP932**, **P247**, EP1093, P246, **EP1814**
Gan, Hoong-Wei P293
Ganeb, Elshimaa EP759
Ganz, Anna-Lena P396
Gao, Hongwei EP1671
Gao, Yixin EP1671
Garai, Jon P79, OC10.3
Garavaglia, Ilinka P501
Garay, Karla EP1804
Garberoglio, Sara EP1455
Garbicz, Filip EP1137
Garcia, Andres EP1898

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Garcia, Cyril P285
García, Elena EP1167, EP1124, P263
García, Elena EP1158
García, Miguel EP1677
García Centeno, Rogelio P267
García de Yébenes, Manuel EP372
Garcia Delgado, Cristina EP978
García Feijoo, Pablo EP1125
García Gómez, Irene EP845
Garcia Gonzalez, Maria del Mar **EP1535**
García Gonzalez, Diego EP924
García Izquierdo, Belén **EP372**
García Izquierdo, Belén EP487
García López, Abraham EP1125
García Moreno, Rosa **P329**
Garcia Olivares, María EP405
García Pérez, Rosa Natalia EP609, EP826, EP884, EP443, EP890, EP535, **EP601**, **EP550**
García Piorno, Alberto EP46, EP1535
García Vilela, Celia P346
Garcia-Almeida, Jose Manuel EP869, EP405
García-Amores, Manuel EP253
García-Calzón, Sonia P137
Garcia-Centeno, Rogelio P280
García-Estrada, Antonio **EP1077**
García-Fuentes, Eduardo **EP467**
Garcia-Garrigos, Elena EP1022
Garcia-Sanchez, Cristian EP698
GARCIA-VALDECASAS VAZQUEZ, LEOPOLDO EP1730
Gardella, Thomas P78
Garfinkel, Benjamin RC4.3
Gargasz, Krzysztof EP1463
gargouri, Fatma EP608
Garibbo, Cristina P466
Garifulina, Lilya EP1749
Garner, Terence EP1759
Garnuszek, Piotr P211
Garrido-Sánchez, Lourdes **EP405**
Gasco, Valentina EP1029, EP1186, EP189, P315
Gašić, Uroš EP563
Gąsior-Perczak, Danuta EP1591, P211
Gasmi, Ayoub EP75
Gaspar de Moura, Egberto P235
Gaspar Monteiro, Helena EP424
Gatta-Cherifi, Blandine EP1002, **P508**
Gatto, Federico P69, EP1024, P253, P271
Gatto, Federico P485
Gauchat-Bouchardy, Isabelle P1
Gaudino, Simona EP1146, P298, EP1057
Gaume, Xavier P78, RC10.4
Gauthier, Camille **EP1907**
Gauvin, Rachel EP153
Gavazova, Valentina **EP600**
Gavriilidis, Stylianos EP237
Gawlik, Katarzyna P226
Gawlik, Tomasz EP905
Gayane, Bayburdyan EP1411
Gayen, Sampriti EP502
Gebauer, Judith **P228**
Gebhart, Johanna P43
Geer, Eliza EP1075, EP1676
Gegeshidze, Basa EP328, EP345, EP365, EP1609
Gegia, George EP1244
Geiger, Niklas P71, **P239**, **EP500**, **RC11.1**
Gemoets, Darren OC2.4
Genard, Oriane P55
Genc, Birgul EP249, EP1015
Gendler, Sami P128
Genesi, Fabianna EP1773, EP1706
Geneviève, Rondeau EP283
Gennai, Alessia EP80
Gentile, Ilaria EP51
Gentile, Ilaria P501
Genzić, Zvjezdana EP1526
Georgakopoulou, Danai EP1262, EP1594, EP1082, EP1879
Georgescu, Carmen Emanuela EP1336, EP1744, P95
Georgescu, Medeea EP893
Georgescu, Oana Maria Teodora EP336
Georgiadi, Sofia EP145, EP453, EP237, EP139
Georgiadou, Nektaria EP1459
Georgievska Ismail, Ljubica EP647
Georgiou, Eleni EP5, EP1596, EP327
Georgiou, Ioannis EP1796
Georgopoulos, Neoklis P207
Geraki, Tina P495
Gerbracht, Christiana P494
Gereben, Balázs **21**
Gerges, Andrew **EP1243**
Gerke, Heidi EP1421
Gerner, Jana RC11.1
Gesmundo, Iacopo P123, EP1019, **P154**, P509
Gessi, Marco EP1146, P298, EP1057
Gevers, Evelien EP34, **RC2.5**, **P142**
G-Garcia, Miguel E. EP1185, EP1213, P219, EP1161, EP951, EP1102
Ghadge, Pravin EP596, EP689, EP636, EP788, EP639, EP403, **EP509**, **EP565**, **EP640**
Ghalmi, Ikram EP1187
Ghanekar, Gayatri EP596, EP636, EP788
Ghannadi, Fatemeh EP956
Ghannadi, Kiana **EP956**
Ghemigian, Adina EP307
Gheorghe Milea, Ana **EP1336**, **P95**
Gheorghiu, Monica Livia EP23, P382, EP7, EP112, **P299**
Gherghe, Ionela-Madalina **EP893**
Gherlan, Iuliana EP757, EP1779
Ghibradze, Ketevan EP1244
Ghigo, Ezio EP1029, EP189, EP1030, P278, P154
Ghisleni, Lucrezia EP246
Ghossan, Roba EP224
Giacobini, Paolo **22**
Giagourta, Irini EP113, RC10.3
Gialouris, Joshua **EP1357**, **RC4.2**
Giambo', Penelope EP1151
Giambò, Penelope EP1139
Giampietro, Antonella EP1055, EP1060, EP1146, P298, EP1057, EP1139, EP1069
Giampietro, Antonella EP1032
Giampietro, Antonella EP1151
Giandalia, Annalisa EP152
Giandalia, Annalisa EP1001
Gianfrilli, Daniele P444, P12, EP429, EP501
Giani, Carlotta RC7.6
Giannaccare, Giuseppe RC1.2, OC12.3, EP1709
Giannas, Rafail EP1864
Giannattasio, Cristina EP163
Giannetta, Elisa EP966, OC7.4, RC6.2
Gianni, Nicoletta EP559, EP465
Giannini, Sandro P97
Giannou, Alexandra RC10.3
Gianotti, Laura P96
Gianotti, Laura P97
Giavoli, Claudia OC11.6, P330
Gibson, Martin EP441
Gifoon, Nasreldin EP1791
Gifuni, Licia EP280
Gil, Jesus OC5.4
Gil, Pedro EP435
Gil, Robert EP756
Gil Boix, José Vicente **EP1480**
Gil Korilis, Adrián EP602
Gil-Duque, Ignacio **EP1213**, P219, EP951, P210
Gilis-Januszewska, Aleksandra P266, RC3.4, EP1814
Gilis-Januszewska, Aleksandra EP114, EP1083, EP932, P247, EP79, P264, EP1093, P246, P262
Gill, Tiara EP224
Gillard, Steve EP1349
Gimbert, Edouard P508
Gimenez-Roig, Judit P361
Ginghina, Octav EP619
Giordano, Roberta EP189, P253, RC9.6
Giorgadze, Elen EP1225
Giorgadze, Elene EP881
Gioxaris, Vasilis P445, EP239
Girardi, Paola **P367**, **EP960**
Giri, Richa EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Giri, Richa EP596
Giri, Somdatta EP502
Girschick, Hermann EP224
Giscos-Douriez, Isabelle P31, OC6.2
Gissi, Clarissa EP946, RC7.2
Gittoes, Neil **23**, **24**
Giusti, Francesca EP973
Giusti, Massimo **EP922**
Giustina, Andrea OC10.1, EP280
Gjersdal, Erlend EP1134
Gkaniatsa, Eleftheria P14
Gkeli, Myrsini EP1541
Gkinis, Alexandros P208, EP850, P182
Gkolemis, Christos EP1082
Gkoufa, Kyriaki **EP1733**
Gkounta, Anastasia EP1796
Gkountios, Ioannis EP5, EP1596, EP327
Gkousis, Pyrros EP1541
Gladkova, Anastasiia EP521
Gładysz, Aleksandra EP984
Glaser, Krzysztof **EP868**
Glegj, Mirna EP1680
Glinicki, Piotr OC6.4, EP77, P51
Glintborg, Dorte **OC4.3**, P327, RC11.3, P22, P371, EP1360, EP1364, EP135, **EP1316**
Glojnarić, Ines EP426
Gluvic, Zoran **EP1560**, EP1422
Gnann, Alexandra EP638
Gnessi, Lucio EP501
Go, Cara OC9.4
Göçmen, Rahşan P317, EP1384
Godfrey, Sean EP281
Gogas, Helen EP1045, P141
Gogitidze, Teona EP1890
Gogola-Mruk, Justyna P354
Goh, Wei Rui OC6.3
Goindoo, Ryan EP65
Gojda, Jan EP263
Gojny, Łukasz EP1323
Gökçay Canpolat, Asena EP1542, EP1042, EP1154

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Gokkaya, Naile P314, EP943, P504, P486
Gola, Zgjim EP170
Golan, Gil P301, OC5.3
Gold, Lukas RC9.1, EP97
Goldstein, Ido **25**
Golemi, Arber OC1.6
Golisano, Bianca **RC6.2**
Golu, Ioana EP1039, EP1105, EP1248, EP1570, EP1148
Gomes, Ana EP261, EP1534
Gomes, Larissa EP137, EP1348
Gomes, Leonor EP291, EP974, EP1168, EP206, EP1120
Gomes, Leonor EP944, EP1285, EP611
Gomes, Olavo EP731
Gomes Porras, Mariana Jesús **EP420**, **EP1305**, **EP1713**
Gomez, Lourdes OC11.1
Gomez García, Ines EP582
Gomez Hoyos, Emilia **EP1306**, EP1195
Gómez Ramírez, Joaquín EP151
Gomez Sanz, Remedios P227
Gomez Vazquez, Eva EP669
Gomez-Peralta, Fernando **EP496**
Gönç, E. Nazlı P317
Gonçalves, Beatriz EP731
Gonçalves, Juliana EP696, P414, EP494, EP1450
Gonçalves, Margarida EP457
Gonçalves, Margarida **EP992**
Gonçalves, Maria Fernanda EP376
Gonçalves da Cruz, Alessandra **OC11.5**, EP424
Gonen, Mustafa Sait EP1231
Gong, Jing RC2.5, P142
Gonul Iremli, Burcin P317
Gonzalez, Josefina EP1804
González Casado, Isabel P329
González Casaus, María Luisa EP1125, EP151
Gonzalez Collantes, Ruth EP1306
González de la Presa, Bernardino **EP821**
Gonzalez Fernandez, Laura P267
González Gutierrez, Jaime EP1195
Gonzalez Lazaro, Paloma **EP582**, **EP975**, **EP360**
González Lizán, Fausto EP275
González Prieto, Jorge **EP1717**
González Suárez, Eva **26**, P346
González-Pacheco, María EP841
Gonzalvo Díaz, César P116
Goodchild, Emily EP1865, P479
Goos, Jacqueline P260
Gopalakrishnan, Prethivan Pillai **EP42**
Gopalkrishnan, Unnikrishnan EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Goralska, Magdalena **EP480**, **EP1795**
Góralski, Piotr P411
Gordeladze, Marine P424
Gordon, Julia EP634
Gordon, Julia EP697
Górecki, Mateusz RC8.5
Goretzki, Peter P470
Görgülü, Murat P489
Gornik Kljaić, Olga P156
Gorsek Sparovec, Tina EP1905, EP1906
Gorshtein, Alexander P109
Gortazar, Arancha R EP259
Gorun, Andreea EP1190
Gorwa, Joanna EP561
Gosmanov, Aidar **OC2.4**
Goswami, Kalyan EP502
Goto, Hiromasa EP1129
Goulis, Dimitrios P401
Goulis, Dimitrios EP654, P207
Gourdy, Pierre P458
Gowaid, Ahmed Awad EP759
Gowda, Ambana EP689, EP639, EP403, EP509, EP565, EP640
Gowda, Ambanna EP596, EP636, EP788
Gowda, Sucheeth EP211
Gracia-Herencia, Belén EP425
Graczyk, Szymon OC8.1
Grada, Mirel EP1278
Gräfenhan, Tom OC3.1
Grajkowska, Wiesława P309
Grammatiki, Maria EP1704, EP1855, EP1796
Grana, Costantino P358
Granata, Antonio P358, EP575
Granata, Antonio Raffaele Michele RC4.1
Granata, Riccarda P123, EP1019, P154, P509
Granato, Giuseppina P154
Grandone, Anna P97
Grange, Cristina P123
Grant, Russell P. EP228, EP1374
Gras-Ozimek, Jordi EP905
Grasselli, Chiara OC6.4
Grassi, Federica OC8.5, P112
Grassi, Giorgia P97, EP1044
Grasso, Alexia P252
Grasso, Vincenzo EP347
Grasu, Cristian Mugur EP619
Graungaard, Signe EP1134
Gravrand, Victor P285, OC6.5
Gravvanis, Miltiadis EP1262
Graziadei, Giovanna EP1044
Graziadio, Chiara EP400
Graziani, Giulia EP922
Greben, Natalia EP389
Grech, Brett EP136
Greco, Marta P159
Grecu, Beatrice EP771, EP122, EP1897, EP1887
Grecu, Beatrice EP1522
Greenman, Yona EP1183, EP147, EP1107
Greere, Daniela EP771, EP122
Greere, Daniela Ioana Iulia EP1522
Gregoric, Pavle EP779
Gregova, Juliana EP88
Greulich, Franziska **EP15**
Griffiths, Alexander P495
Grifoni, Giacomo Fabio Antonio **EP1152**, P288
Grigore, Iulia EP757
Grigorie, Daniel **EP304**, **EP1013**
Grigorie, Daniel EP250
Grigoryan, Karen EP1524
Grigoryan, Shogher EP544
Grijó, Carlos EP1450
Grill, Vivian **EP222**
Grimbizis, Grigorios EP1340
Grimmichova, Tereza 20, **27**
Grisanti, Salvatore RC12.5
Griseta, Valentina **RC4.1**
Grivea, Ioanna EP378, P179
Grochowska, Anna P32
Groesgen, Sven EP228, EP1374
Grøntved, Anders RC11.3, P371
Gross, Naftali P397
Grossman, Ashley B. EP1108, P23
Grossrubatscher, Erika OC7.4
Grosu, Andreea-Alexandra **EP1258**, **EP17**, EP977
Groti Antonic, Kristina **EP1342**
Grottoli, Silvia EP1029, EP1186, EP1030, P315, P278
Group, TEMD Study EP1743
Groussin, Lionel RC9.3, P285, EP138
Grove-Laugesen, Diana OC12.2
Gruber, Hadas P301
Gruber, Sven EP100, OC6.4, P19, P30, EP55
Gruden, Gabriella EP1019
Grümme, Lea RC8.4
Gruppetta, Mark EP209, EP225
Gruppetta, Mark EP136
Grytaas, Marianne P38
Grzelak, Olga RC7.3
Grzesiak, Małgorzata EP1322
Gu, Yingqi P74
Guadalix, Sonsoles EP372, EP487
Guarnieri, Vito EP337
Guarnotta, Valentina **P462**
Gubbi, Sriram OC7.2
Gudnason, Vilmundur EP49
Guduk Sirvan, Naciye **EP1239**, **P16**, **EP1384**
Guelho, Daniela EP1285, EP1168, EP1120
Guelho, Daniela EP291, EP974
GUENEGO, Agathe P17, P458
Gueron, Beatrice EP1075, P306
Guerrero, Fernando P267
Guerrero-Kesselman, Facundo Marcelo P450, EP1742, EP1776, EP1777
Guglielmotto, Michela EP1019
Guibourdenche, Jean RC9.3
Guignat, Laurence RC9.3, P285, EP138
Guillen, Cristina EP1011, **EP1167**, **EP1124**, **P263**
Guillén, Cristina EP1158
Guillotin, Julie P508
Guimarães, Luís P414
Guirar, ilef EP1632
Güiza, Fabian EP469
Guk, Mykola EP1159, EP1902
Gul, Ayse Nur P467, RC12.2, EP1724
Gul, Nurdan P279, EP53, P460
Gul, Nurdan P291
Gullì, Consolato EP1055
Güllü, Sevim EP1154, EP1542, EP1042
Gülpınar, F. Kübra EP140
Guma, Muna **EP160**
Gumerova, Anisa P361
Gündoğan, Suna Nur EP1070
Gunes, Sevkican **EP258**
Güney, Engin P390
Güngör, Hilal EP1542
Güngör Semİz, Gökçen OC11.2
Guni, Mirjeta **EP1787**, **EP1806**
Gunjic, Ilija EP444
Gunnarsdottir, Harpa **EP49**
Gunst, Jan EP469
Guo, Irene EP430
Gupta, Rahul EP1084
Gupta, Vishal **EP1532**
Gurianov, Vitalii P167
Gurlek, Alper P16
Gurlek, Alper EP1755
Gurnell, Mark RC6.5
Gurnell, Mark P254, EP56
Gut, Paweł EP912
Gutierrez, Teresa P79

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Gutierrez Restrepo, Johnayro EP1804, EP82
Gutierrez Vilchez, Elena EP420
Gutierrez-Medina, Sonsoles EP372, **EP487**
Gutiérrez-Repiso, Carolina EP405
Gutiérrrez-Martínez, Fernando EP467
Guzek, Magdalena P309
Guzmán, Rocío P210
Guzzi, Fabio EP911
Gvajaia, Nino EP908, EP1524
Gyllenberg, Frida OC4.3
H., Francisca EP1267, EP323, EP1621
Ha, Kyounghwa EP450
Haagensen, Ellen EP1187
Haberbosch, Linus P284, EP1818
Habete-Asres, Hellena EP441
Habisch, Hansjörg EP54, EP131
Hacisahinogullari, Hulya P279, P291, EP53, P460, EP1743, EP258
Had, Khadija EP1499
Hadoux, Julien OC7.2
Haeberer, Mariana EP496
Haenelt, Michael OC5.5, EP1036
Haffner-Luntzer, Melanie P71
Hagen, Mina EP444, **EP1351**
Hagen, Mina EP1748
Hagog Natour, Hitam EP486, EP742, **EP916**
Hahner, Stefanie P42, P10, P5, P45, P19
Haidar, Vera **EP860**
Haidautu, Mirela Daniela EP1615
Haissaguerre, Magalie RC7.1
Haj Kacem Akid, Faten EP608
Hajdini, Ursina EP1237
Hajji, Ekram EP1632
Hakim, Florian P237
Häkkinen, Merja P350
Hakobyan, Sona EP544
Halil, Meltem Gülhan EP1755
Hallén, Tobias P276
Hallett-Morley, Chris P254
Halloul, Imen EP1156, EP571
Halloul, Imen EP75, EP1499, EP835
Halloul, Imen EP1487
Hallqvist Everhov, Åsa EP11
Halperin, Reut P305
Halsall, David RC1.6, P449
Halsall, Ian RC1.6, P449
Halupczok-Żyła, Jowita EP21, EP1197, EP1323
Halupczok-Żyła, Jowita **EP1889**
Hamarat, Gaye EP1204
Hamati, Julia **EP1108**
Hamdi, Hiba OC5.4
Hamdy, Neveen A. T. EP224
Hamed, Noor EP546, EP987, EP667, EP142, P369, EP1214, EP653, EP1371, EP576, EP432, EP749
Hameed, Saira EP430
Hamidi, Oksana EP94, OC9.5, P21
Hamilton, Jill P255, P256
Hamrahian, Amir EP94
Han, Ashley **EP1020**
Han, Ji Min EP484
Han, Seung Jin **EP48**, EP450
Han, Seung jin EP385, EP418, EP427
Hana, Vaclav EP1122
Hána Jr, Václav EP1113, EP70, EP1122
Hanada, Tomoko EP1184, EP1088
Hanassab, Simon P351
Hanaya, Ryosuke EP1104, EP1184, EP1088
Handa, Priya OC2.2, EP739, P172
Handelsman, David EP1357, RC4.2
Handkiewicz-Junak, Daria OC7.1, EP905
Handzlik, Gabriela **EP197**
Hannan, Fadil RC10.2
Hannon, Anne Marie EP456, P377
Hansen, Cathrin E. P293
Hansen, Karl EP1908
Hansen, Simon Bøggild P22
Hantel, Constanze EP1108
Hanyaloglu, Aylin P478
Hanzu, Felicia Alexandra OC6.5, P267, P83, EP1205
Hao, Wenzhen EP1782
Haraj, Nassim Essabah EP1603, EP392, EP1155
Harangi, Mariann P389
Harbeck, Birgit RC9.5
Harbeck, Birgit P45
Hardy, Rowan P27
Harizopoulou, Vikentia P207
Haroon Riasat, Muhammad EP2, EP1279, EP1490
Harrie, Maria P266, RC3.4
harris, alan EP911
Harris, Aliana EP15
Harris, Robert EP1909
Harrold, Christopher EP257
Harsløf, Torben P108
Hartzell, Andrea OC9.5, P21
Harwood, Matire EP1610
Hasan, Mashfiqul P448
Hasanat, Muhammad P448, P473
Hascoet, Juliette EP14, P17
Hasinger, Julia EP463
Hasni, Yosra **EP1156**, **EP835**
Hasni, Yosra **EP75**, **EP1499**
Hasni, Yosra **EP1487**, **EP571**
Hassa, Julia P145
Hassan, Nomaira EP1720
Hasse-Lazar, Kornelia EP905
Hatazaki, Masahiro P185
Hatipoglu, Esra P52, P33
Hatipoglu, Esra EP1034, EP1201, EP1133, EP24, EP270, EP1163, RC3.6, RC5.4
Hauge, Jostein Wågen **P75**
Hauser, Barbara EP224
Havlinova, Barbora **EP1338**
Havryliak, Iryna **EP389**
Hawkins, Anna **EP686**, EP768, EP677
Hawley, Christina EP1908
Hawley, James M. **RC7.1**, EP1359, EP1348
Hay Mele, Bruno EP470
Hayashida, Tomoko OC1.3
Hayem, Gilles EP224
Haymana, Cem EP1743
He, Minzhi EP31
Heald, Adrian **RC1.6**, **P449**
Heald, Adrian **EP441**
Heaney, Anthony EP1676
Hee, Daryl OC6.3
Hegde, Pallavi EP42
Hegedus, Agnes RC6.5
Hegele, Robert EP1843
Heger, Laura **P45**
Heijboer, Annemieke C EP64, EP1374
Heilbronn, Leonie EP558
Hein, Aung Kaung Sett EP1545
Heinze, Stefanie RC8.4
Helali, Wiem EP202, EP1099, EP1652
Hélène, Lasolle P272, P403
Helliwell, Philip EP224
Hellman, Per RC6.5
Hemmati, Iman EP956
Hempenstall, Jonathan EP1153
Henry, Michelle EP157
Heo, Yu Jung EP385
Heok, Cheow RC6.5
Heper, Aylin EP1154
Hepprich, Matthias **P150**
Hepprich, Matthias P203
Hepşen, Emre EP434
Hepşen, Sema **EP434**, **EP1457**
Heracek, Jiri P224
Herghea, Ioana **EP318**, **EP619**
Hermann, Pernille EP1360
Hermán-Sánchez, Natalia EP425
Hermosilla, Raquel RC4.2
Hernandez, Cristina P143, EP435
Hernández Lucas, María Carmen EP1125
Hernández- Terciado, Fernando EP372
Hernandez-Hernandez, Irene P450, EP1703, EP1742, EP1776, EP1777, P498
Hernandez-Lazaro, Alba P497, EP1841, EP1835, EP1707, EP1773, EP1706, P498
Hernández-Munive, Abigail **EP613**
Hernando, Iñigo P79, OC10.3
Herold, Zoltan OC6.4
Herr, Caroline RC8.4
Herr, Felix P28, EP33, EP29, RC9.1, EP97
Herrador, Luis EP44
Herraiz-Vilela, Marina EP467
Herrera-Martínez, Aura D. EP1213, EP1161, EP1102
Herrmann, Eva P345
Herrou, Anne Flore P17
Hertel, Jens Kristoffer P75
Herterich, Sabine OC3.1, OC12.5
Herzig, David P150
Heshmati, Hassan **EP805**, **EP711**, EP959
Heshof, Eva P250
Hesse, Linus **P284**, EP1818
Hessman, Eva P485
Heuberger, Joachim EP1064
Heuten, Hilde P134
Hidalgo Molina, Bruno EP529
Hidalgo-Llorca, María EP995
Higuchi, Takahiro RC11.1
Higuera, Isabel EP487
Hildebrandt, Talitha **OC5.2**
Hilger, Anton EP228
Hill, Martin P161, EP1210
Hillas, Georgios EP850
Hillebrand, Jacquelien EP64
Hilliard, Nicholas EP56
Hilpert, Jan P151
Hilsted, Linda EP60
Himathongkam, Thep EP745, EP1572
Hińcza-Nowak, Kinga EP1591
Hind, Karen P75
Hindges, Robert P495
Hippolyte, DUPUIS P4, **P200**, **P237**
Hirani, Shashi P23, P68
Hirata, Kiyotaka EP37
Hiriart, Marcia EP613
Hirner, Raphael EP97
Hirschfeldová, Kateřina EP273

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Hislop, Colin OC2.2, EP739, P172
Hitman, Graham EP441
Hiwot, Tarekegn EP397
Hjelmesæth, Jøran P75
Hjortebjerg, Rikke P327, EP1360
Hline, Aye EP976
Hlozek, Jiri P419
Ho, Kelvin EP1488
Hochberg, Irit **EP1317**
Hodgkinson, Victoria EP1684
Hodzic, Mubina **EP1078**, EP1101
Hofbauer, Lorenz OC10.2, OC12.4
Hoffman, Andrew P228
Hoffmann, Michal OC6.4
Hofman, Joanna EP1452
Hofmans, Mattias EP1344
Hofsø, Dag P75
Hogstrand, Christer P495
Højby, Michael EP1063
Højlund, Kurt EP1360
Holá, Barbora **EP70**
Holland, David P449
Holland, Paula P146
Holle, Rolf EP1049
Holm, Frida EP1909
Holm Egebæk, Christine **P108**, P98
Holmberg, Mats P89
Honegger, Jürgen OC3.4
Honegger, Jürgen OC3.1
Hong, A Ram EP1597, EP1670, P34
Hong, Jae Won RC11.5
Hong, Namki P405
Hong, Sang Mo EP754
Hong, Tianpei EP1328, EP1671, EP633, P365
Hoogkamer, Anouk EP638
Hoogmoed, Jantien P250
Hoong Ho, Jan RC5.2, EP941
Hooper, Sarah EP526
Hoorn, Ewout **28**, OC5.1
Hopkins, Thomas P325, P468
Horiike, Norio EP684
Horvath, Andrea P42, P10, P19
Horzelski, Wojciech EP57
Hossain, Belayet EP937
Hossain, Solaiman P473
Hoste, Eric EP469
Hou, Wanxin EP1357, RC4.2
Hounsome, Juliet P340
Hovorková, Klára P81
Howarth, Sophie P254
Howe, David EP257
Hoxha, Edlira **EP1631**
Hoxha, Elion EP423
Hoxha, Violeta **EP1053**, EP1514, EP1667, EP1237, EP364
Hoyer, Annika EP1479, P145
Hranov, Yuri EP1386
Hrckulakova, Karolina EP1453, P381
Hristova, Diana EP1386
Hristozov, Kiril EP1301
Hrychyniuk, Daryna EP417
Hrynyshyn, Daniil EP518
HSIAO, CHUN-JEN **EP892**
Hsu, Ren-Jun EP897
Hsu, Yi-Chiung EP895
Htet, Thaw **EP823**, **EP634**, **EP697**
Htut, Zin OC9.4
Hu, Shuang P256
Hu, Yingying P493
Hu, Zhizhen EP490, EP370
Huang, Chen-Che EP468
Huang, Hu **P135**
Huang, Huei-Kai P177, EP416
Huang, Jianping EP1010
Huang, Jie P493
Huang, Michael RC2.5, P142
Huang, Rui (Rachel) EP458
Huang, Wan-Ting **P177**, EP416
HUANG, WEI-LIN **EP1236**
Hubalewska-Dydejczyk, Alicja P6, P15, EP932, P247, P211, EP242, **EP79**, P32, EP1814
Hubalewska-Dydejczyk, Alicja EP954, EP114, EP1083, P226
Hubalewska-Dydejczyk, Alicja P3, P376, P264, EP1093, P246, P262
Hubballi, Prashant **EP1638**
Hubbard, Johnathan EP96
Hubertus, Vanessa P284
Hudson, Amy EP10, EP38
Huerta, Ana EP372
Huertas Cabrera, Hugo **EP1161**
Huffman, Alexandra RC4.4
Hughes, Brooke EP634, EP697
Huguet, Isabel EP46, P116
Huguet, Isabel EP1535
Huh, Joo Young **EP436**
Huhtala, Heini EP61
Huhtaniemi, Ilpo EP468, RC4.5
Hui, Hannah **P212**, P153, **P133**, **EP415**
Hui, Pratisruti EP502
HUI, Pui Sze Grace EP621
Huillard, Olivier P285
Hullur, Kiran **EP855**
Hungbauer, Maximilian EP1108
Hurjui-Jarnet, Daniela EP1860
Hurni, Lisa EP638
Hurskainen, Elisa P350
Husebye, Eystein Sverre P38
Huseynov, Rasim EP1605
Hussain, Hafsah EP1281, EP937
Hussain, Zarish EP1674
Hussein, Furhana EP976
Hussein, Furhana EP1281, **EP1300**, **EP937**, **EP940**
Hutchison, Amy EP558
Hüttl, Martina P132
Hwang, Jeeyeun **EP324**
Hwang, Mei-Ju P105
Hwang, Su Jung **EP1747**
Hwang, Yoon-a RC11.5
Hwang, You-Cheol **EP517**
Hyer, Stephen EP1318
Hyotylainen, Tuulia EP497
Hysenbelli, Bledar EP610
Iakovou, Ioannis P401
Iavarone, Federica EP1151
Iavarone, Federica EP1060
Ibragimov, Marlen EP777
Ibrahim, Hassan P423, EP1644
Ibrahim, Ilias EP1281
Ibrahim, Mohsen EP1182
Ichihara, Atsuhiro EP37
Ichijo, Takamasa P53
Ichim, Alexandra EP1615
Idampitiya, Chandima EP1583, EP319
Idan, Amanda RC4.2
İdiz, Cemile P291
Idkowiak, Jan OC6.6, EP1317
Idrissi, Ayoub EP1437
Iftimie, Mădălina Elena EP1683
Igaz, Peter OC7.2
Igaz, Peter OC6.4
Igbelina, Chukwuebuka Dominic EP260
Iggar, Malak EP1603, EP392, EP1155
Iglesias, Carmela EP1735
Iglesias, Pedro P267, P307
Iglesias Hernandez, Natalia Covadonga P79
Iglesias-Lozano, Irene EP995
Ignatius, Anita P71
Ignjatovic, Aleksandra EP668
Ignjatović, Milica EP699, EP762
Ignjatović, Sofija EP563
Igrutinovic, Nebojsa EP1422
Ijaz, Azheem RC5.1
IJzerman, Richard EP503
Ikehata, Masami OC11.6
Ikram, Fareeha **EP1720**
Ilangaratne, Charmaine EP1811
Iliakopoulos, Konstantinos EP1733
Ilias, Ioannis **EP1592**, **EP123**, **EP1394**, EP685, EP1241, **29**
Ilic, Dusan EP1311, **EP900**, EP43, P344
Ilkiv, Yeva **P167**, EP714, EP866
Illangasekera, Yasitha EP441
Ilmberger, Sarah OC3.2
Im, Seung-Soon **EP614**
Imamovic, Marcus **P26**
Imdahl, Fabian OC3.1
Imel, Erik OC10.1, P72
Imran, Syed **EP1684**
Imruetaicharoenchoke, Waraporn EP315
Ince, Erdem EP1212, EP1815
ince, nurcan EP641
Inchiappa, Danilo P254
Inci, Tarik EP1204
Inês Alexandre, Maria EP1449
Infante, Amato EP1055
Ing, Steven OC10.1, OC12.4, P72
Inglesi, Alessia P223, RC12.5
Ingwersen, Jan-Peter P151
Inoue, Momoka EP1200
Insalaco, Antonella EP224
Inui, Ryoko P174, P185
Ioachim, Dumitru EP17, EP919
Ioachim, Dumitru EP1460
Ioana, Julia EP474
Ioannidou, Katerina EP231
Ionesco, Oana EP1860
Ionica, Elena EP1615, EP730
Iorashvili, Nana EP1244
Iordachescu, Carmen P299
Iordanishvili, Tina EP1244
Iorgulescu, Radu EP68
Iotova, Violeta EP1040, P228
Ioutsi, Vitalii P451
Iqbal, Ahmed RC5.1
Iqbal, Fizzah **P435**
Iqbal, Maliha EP302
Irfan, Hira EP925, EP300
Irie, Yoko P174
Irigaray, Ana P267
Irshad, Zehra **EP76**, **EP254**
Isabela, Banu P458
Isaeva, Elena RC3.4

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Isand, Kristina OC3.4
Isasa Rodriguez, Leire EP244
Ischuk, Vadym EP404
Isenovic, Esma R. EP1560
Ishibashi, Kenichi EP1294
Ishtiaq, Shahina **EP1435**, **EP673**
Isidori, Andrea EP966, P358, P444, P253, P303, EP1026, P12, EP429, EP501
Işıklar, Özben EP1523
Islam, Md. Rafayel P475
Islam, Quazi Tamjidul EP1791
Islam, Zaynah EP677
Işler, Alperen Onur EP1239, EP1384
Isojärvi, Juhani P35, EP61
Issa, Fatumo EP940
issa, vrej EP544
Issabayeva, Assel EP796
Ito, Nobuaki OC10.1, P72
Iturregui Guevara, Marta EP1713
Iulia-Ştefania, Plotuna EP1570, EP1148
Ivanishchak, Mariana **EP1307**
Ivić, Anesa EP426
Ivo, Catarina EP1220, EP267, EP69, EP351
Ivosevic, Zeljko EP1422
Ivovic, Miomira EP444, P67
Iwata, Naoko EP1129, **EP1200**
Iyen, Barbara EP1413
Iyer, Rishi EP523, EP1799
Izatt, Louise OC7.6, RC6.1
Izawa, Shoichiro **P53**
Izuzquiza, Ana P79, OC10.3
Izzi-Engbeaya, Chioma OC4.2, P322, EP430
Jackuliak, Peter EP701
Jacob, Julian P285
Jacobs, An P346
Jacobs, Kerstin P345
Jácome de Castro, João EP1220, EP267, EP69, EP351
Jacome Torres M Mesquita, Deciara EP938
Jaddoe, Vincent RC1.1
Jafar-Mohammadi, Bahram EP109, EP949
Jafar-Mohammadi, Bahram EP1181, EP1313
Jafar-Mohommadi, Bahram EP933
Jafery, Oraizi EP1545
Jaffrain-Rea, Marie-Lise P305, P303, EP1026
Jagodić- Ejubovic, Amira EP1078
Jain, Gunjan P162
Jain, Rajesh OC10.2
Jaiswal, Awadhesh EP1091
Jajah, Bilal EP855, EP1454
Jäkel, René P10
Jakhtanidze, Ketevani EP1244
Jakovljevic, Milica **EP699**, **EP762**
Jakuc, Natalia **EP1076**
Jallo, Mahir Khalil Ibrahim EP1679
jalouli, dana EP608
James, K Lynette **EP125**
James, Lisa RC6.4
James, Nathan EP526
Jamjoom, Hasan **EP725**
Janas, Ksenia **EP963**, **EP99**, **EP955**, **RC7.3**
Janez, Andrej EP1342
Jang, Han Na **EP221**
Jangid, Sanjay EP596, EP636, EP788
Janic, Tamara EP172, EP1651
Janjgava, Shota EP1225, EP881
Janjić, Mirela EP426
Jankovic, Dijana EP444, **P67**, EP149
JANNIN, ARNAUD P4, P9
Jansson, Per-Anders EP1759
Januszkiewicz-Caulier, Joanna P211
Januszkiewicz-Caulier, Joanna P221
Januszkiewicz-Caulier, Joanna **EP964**
Jara Vidal, Marina P116
Järås, Jacob RC9.2
Jariene, Kristina EP1379
Jarząb, Barbara EP905
Jashi, Liana **EP1537**, **EP832**
Jaskeviciute, Vika EP439
Jaume, Juan Carlos P445
Javadpour, Mohsen P283, P259
Javed, Hafiz Awais **P243**, **EP1584**, **P356**
Javorsky, Martin P50
Jawiarczyk-Przybyłowska, Aleksandra EP21, **EP1192**, EP1197, EP1323
Jayadev, Veena RC4.2
Jayaprakasan, Kanna EP1908
Jayasena, Channa P351, EP1349, EP1348
Jayatilleke, Aruni EP224
Jayaweera, Jayamalee P243, EP1584
jaziri, rawen EP1632
Jean, De Schepper RC3.3
jean francois, emile P285
Jean-Christophe, LIFANTE P403
Jean-Denis, Farrah RC11.2
Jedliński, Jędrzej **P103**, EP1408
Jędrzejuk, Diana EP651
Jefferson, Emily P452
Jegaden, Margaux EP1908
Jemuovic, Zvezdana P297
Jemuovic, Zvezdana EP1464, P120
Jenkinson, Carl RC7.1
Jensen, Boye Lagerbon EP135
Jensen, Richard Christian EP135
Jensen, Tina Kold RC11.3, EP135
Jensterle, Mojca EP1342
Jeon, Ja Young EP48, **EP450**, EP418, EP427
Jeon, Ja Young EP385
Jeong, In-Kyung P127, EP517
Jeong, Jae Seok EP1673
Jeong, Jong Ju EP1701
Jeong, Se Yun EP1747
Jeong, Woo-Jin P373
Jercalau, Simona Georgeta P299
Jeremic, Danka EP779
Jeremic, Danka EP1074
Jerez Arzola, Maria Elena **EP924**
Jesus, Bárbara EP1168, **EP206**
Jesus, Bárbara EP1285, EP291, EP974, EP611, EP1120
Jesus, Nuno EP457
Jesus, Nuno EP992
Jevtic, Ivan EP1464, P297, P120
Jewuła, Oliwia EP99
Jezkova, Jana EP1122
Jezková, Jana EP1113
Ji, Jeong-Yeon P373
Ji, Yongli EP31
Jia, Minyue EP31
Jiang, Jingjing OC7.2, OC7.5
Jimenez, Camilo OC7.2
Jiménez, Wladimiro P195
Jiménez Aceituno, Maria EP851
Jiménez Sánchez, Andrés EP1145
Jimenez-Pacheco, Lara EP430
JIn, Heung Yong **EP1673**, EP476
Jin, Xian EP210
Jin, Zi **EP658**
Jing, Changying EP6
Jiskra, Jan EP1113, 20
Joachim, Michael P121
Job, Anais EP1046
Joergensen, Niels P357
Joham, Anju P320, **EP637**
Johannsson, Gudmundur **EP1063**, **P8**, P276, P296, EP1759, P228, P484, P485
Johnson, Hadley **EP1400**
Jojua, Natalia EP1793
Jokela, Heli **EP1421**
Jokharidze, Tedo EP355
Jokiniitty, Antti **EP3**
Joksimovic, Bojan EP1560
Joksimovic, Nata EP172, EP1651
Jonas, Kim P325, P468
Jonas, Kim P495
Jones, Charlotte EP1720
Jørgensen, Anders EP1136
Jørgensen, Emma Linnea **EP1364**
Jørgensen, Jan RC11.3, EP135
Jørgensen, Jens Otto EP1134, P249, P244
Jørgensen, Nanna Thurmann P22, **EP60**
Jørgensen, Niklas EP60
joseph, Robin EP1181
Joshi, Ameya EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Joshi, Ansumali **EP1280**, **EP205**, **EP1428**
Jouanneau, Emmanuel P270
Jouinot, Anne RC9.3, P285, EP138, **OC6.5**, RC6.4
Joulin, Vincent EP72
Journiac, Nathalie P346
Jovanovic, Milan EP149
Jovanovska Mishevska, Sasha EP1895
Jovanovska Mishevska, Sasha EP368
Juhlin, C Christofer P6
Jun, Ji Eun **P127**, EP517
Jung, Bowon EP1747
Jung, Chan-Hee **EP437**, EP438
Jung, Hye Seung RC2.4
Jung, Jin Woo EP1597, EP1673
Jung, Kyong Yeun P34
Junior, Joel EP478
Jurecka-Lubieniecka, Beata OC7.1
Jurica, Jakub EP1121
Juskiene, Martyna **EP1175**
Juškienė, Martyna EP999
Just, Ivica EP54, EP131
Justinien, Etienne EP153, EP1393
Justus, Weber OC7.3
Jusufovic, Selma EP1856
Jyothinagaram, Sathya P436, EP1418
K, Venu Gopal Reddy EP391, EP1041
Kacperski, Krzysztof P211
Kaczmarska-Turek, Dorota **EP1028**
Kadah, Muhammad EP406
Kadian, Kavita P305
Kadioglu, Pinar RC3.4
Kadowaki, Kanako P53
Kadusauskiene, Agne EP20
Kafetzi, Maria EP1723
Kafley, Pragya EP215
kagansky, Dana **EP741**, **EP486**, **EP742**
Kahaly, George **OC1.3**, **P396**
Kahraman Çetin, Nesibe P390

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

KAIBI, Imene EP1627, EP787
Kakargia, Eleftheria EP1879
Kakkavas, Apostolos P208
Kakutani, Miki P53
Kalandadze, Salome **EP355**, EP1443, EP1582, EP1250
Kałas, Maria EP939
Kalava, Bhanusree EP391, EP1041
Kalayci, Tugba EP258
Kaldani, Salome EP1524
Kaliakatsou, Eirini EP192
Kalika, Lev EP369
Kalinauskaite, Goda P284
Kalkana, Chrysa EP139, EP115, EP1387
Kallah, Jaspal EP1606
Kallio, Markus P35
Kalliopi, BILARIKI **EP153**
Kallistrou, Efthymia EP1592, EP123, EP1394, EP685, EP1241
Kalogeris, Nikolaos EP1335, RC10.3
Kalogeropoulos, Athanasios P25
Kalogeropoulos, Charalampos P25
Kalra, Philip EP441
Kaltsas, Gregory EP918, RC10.1, EP927, EP25, EP589, P196, P213
Kaltsas, Gregory P471
Kaltzidou, Victoria EP1541
Kałuża, Bernadetta EP1404, **EP1218**, **EP756**, P103, P388, EP1408, P425
Kamal, Sumaiya EP1581
Kamalak, Sercan EP140
Kamand, Emmanuelle **P4**
Kamashidze, Koba EP1537
Kamenicky, Peter EP1017, P242, P304, OC10.1
Kaminer, Keren **EP473**, **P268**, P316, P109
Kaminska, Liudmyla **P417**
Kamińska, Kinga EP1322
Kaminskas, Vakaris **EP1556**
Kamiński, Grzegorz P211
Kammerlander, Andreas EP54
Kamp Nørlund, Mathilde EP1360
Kämpe, Olle P384, P38
Kanamoto, Naotetsu **EP1294**
Kanbur, Busra EP943, P486
Kanbur, Büşra P504
Kancheva, Ludmila EP1210
Kancheva, Radmila **EP1210**
Kandemir, Zuhal EP1711
Kandinashvili, Teona **EP816**
Kang, Ho-Cheol **EP1597**, EP476, EP1670
Kang, Yang Ho P168
Kangasniemi, Marika P350
Kaniuka-Jakubowska, Sonia P93, P309
Kankava, ketevan EP355
Kanouta, Fotini EP654
Kansara, Abishek OC10.1
Kantar, Rümeysa EP1774
Kantreva, Kanella P166
KANTREVA, KANELLA EP1387
Kapama, Aikaterini EP139, EP115, EP1387
Kaparos, George EP1363
Kapczuk, Karina EP1390
Kapiris, Stylianos EP145
Kara, Oğuzhan **P130**
Karabulut, Benay P500
Karaca, Meryem EP258
Karaçalık Ünver, Ceren EP1457
Karachalios, Kostis EP192
Karadağ, Hülya EP1569
Karademir, Nevra P314
Karaduman, Didem EP1755
Karaflou, Maria P445
Karageorgiou, Panagiotis EP649, EP591
Karagiannakis, Dimitrios S. EP479
Karagkiozakis, Paschalis EP729
Karagkouni, Iliana EP1363
Karagulle, Mehmet EP1163
Karagyozov, Petko EP1820
karahmetli, Gulsum EP1015
Karakilic, Ersen **EP1346**, P194, EP1131
Karakoc, Ayhan EP41, EP656, EP1797, P440, EP1886
Karakoç, Ayhan EP1743
Karakozis, Lampros EP237
Karakozis, Stavros EP237
Karakullukcu, Mina P130
Karakullukçuoğlu, Eda RC5.4
Karaliolios, Georgios EP1796
Karaman, Tayyip P442
Karanxha, Juliana EP1787, EP1806
Karaosmanoglu, Ali Devrim P16
Karapanagioti, Aggeliki EP927
Karapanou, Olga EP1476
Karastathi, Christina EP1872
Karataş, Hakan Ömer EP1569, EP1642
Karatas Kiliccioglu, Gizem EP1133, P52
Karatay, Huseyin EP1201
Karatoprak, Kadircan EP1774
Karavitaki, Niki **30**, P277, OC3.4, EP1164
Karban, Yonatan EP499
Karbownik-Lewińska, Małgorzata EP984, EP1162, EP1590, EP57
Karges, Wolfram P269
Karim, Rehmat EP2, EP1279, EP1490
Karkampouna, Agapi EP1230
Karki, Akriti **EP1388**
Karkın, Zeynep EP733, EP1523
Karlovich, Natalia EP1031
Karmacharya, Srijana EP1280, EP205, EP1428
Karosiene, Dovile RC8.1
Karoumpalis, Ioannis P59
Karov, Ruth **EP1183**
Karpenko, Olena EP714
Karra, Efthimia EP942, EP1791
KARRAS, SPYRIDON P207
Kartal, Yigitcan EP270
Karuppagounder, Vengadeshprabhu OC2.2, EP739, P172
Kasapic, Dusanka **EP228**, **EP1374**
Kasarla, Ramesh P154
Kasemi, Donika EP1514, EP1667
Kaser, Susanne EP1033
Kasher Meron, Michal EP916
Kasko, Martin **EP447**
Kasotas, Athanasios EP5, EP1596, EP327
Kassem, Sameer RC1.5, EP1176
Kassi, Eva P445, EP231, EP239, EP1365, EP589, RC10.3, P138
Kassi, Evanthia EP479, RC10.1, P102, EP560, EP670, EP1869, P207, P196, P213
Kastelan, Darko RC6.6, OC6.5, P222, EP910
Kastelan, Darko RC7.1
Kasuki, Leandro EP1185
Kasuki, Leandro EP989
Kaszewska-Perka, Dominika EP212
Kaszubkiewicz-Wardęga, Dorota EP651
Katabami, Takuyuki P53
Katafigiotis, Sokratis P415
Katalinić, Darko EP1466
Katariya, Kabeer EP1427, EP774
Katchakhidze, Giorgi EP1244
Katcharava, Lia **EP1582**
Katkó, Mónika P389
Kato, Shigeaki EP210
Kato, Yusuke EP1200
Katra, Rami EP350, P375
Katra, Rami EP1521, P419
Katrapas, Panagiotis P208
Katsafyloudi, Maria EP1255
Katsika, Evangelia EP1340
Katsiki, Evangelia EP1508
Kattamis, Antonis EP1365
Katuchova, Jana P50
Katulanda, Prasad EP401
Katz, David A. EP526
Kaufman-Cook, James **RC5.6**, OC5.6, OC7.6, OC3.6, OC5.4
Kaur, Esha P339
Kaur, Gavita EP686, EP768
Kaur, Vaishali EP1084, P453
Kautzky-Willer, Alexandra **31**, EP1017, P43, EP54, EP131, P455
Kaván, Jan EP1113
KAVARIC, SRETEN EP146
Kavaz, Aslı EP733
Kavrakis, Nikolaos EP729
Kavtiashvili, Ia EP1624, EP1249, **EP353**, **EP173**, **EP174**
Kavvadias, Georgios Alexandros P94
Kavvoura, Foteini EP564
Kawade, Shigeru EP1104
Kawaji, Tomohiro EP37
Kaya Terzi, Neslihan P194
Kazakou, Paraskevi EP479, EP1219
Kaziakhmedova, Samira **P65**
Kearney, Tara EP1119
Keating, Aileen **32**
Kebakoska, Mihaela **EP876**
Kedikova, Sesil EP1386
Kędzia, Andrzej P248, P290, EP612
Keelawat, Somboon EP1659
Keevil, Brian P364, P479, EP34
Kek, Peng Chin OC6.3, EP133
Keklikkiran, Caglayan P467, RC12.2
Kekutia, Data **EP1225**
Kelestimur, Fahrettin EP1231
Kelly, Lorraine EP419
Kelt, Amy EP940
Kemboi, Douglas P238
Kemkem, Yasmine RC5.6, OC5.6, **OC7.6**, OC3.6, OC5.4
Kemmotsu, Ryosuke P174, **P185**
Kemp, Robert P449
Kempegowda, Punith RC5.1, P151, P339, EP1325
Kenkre, Julia EP430
Kentaoui-Bousellam, Imane EP467
Kerkau, Katharina **P11**
Kermaj, Marjeta EP1053, EP1514, EP1667, **EP170**, **EP1237**, EP364
Kerxhaliu, Jetmira EP1278
Keser, Sevinç P314
Keshav, Phadke EP689, EP639, EP403, EP509, EP565, EP640

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Keskin, Caglar EP1484
Keskin, Ismail P467
Keskin, Müge EP1100
Keskin, Onur EP1384
Keskin, Özcan P314
Keswani, Sanjay OC9.5, P21
Khachaturyan, Sofiya EP1275, EP1283
Khadka, Smriti EP1280, EP205, EP1428
Khalid, Neelam EP1552
Khalifa, Hussam EP1606
Khalil, Ahmed EP1371
Khalimov, Yuri EP1749
Khalisadar, Naeemah EP658
khamisi, selwan P89
Khan, Aliya OC10.2, P74, OC10.1, OC12.4, P72
Khan, Dilawar EP1720
Khan, Hamza EP42
Khan, Huma Humayun **EP676**
Khan, Muhammad Athar Iqbal EP311
Khan, Muhammad Waqar EP1881, EP1772
Khan, Shahab EP109
Khanam, Amina EP52
Khang, Ah Reum P168
Khanoyan, Yeranuhi EP1888
Khiewvan, Benjapa EP315
Khilko, Alena EP334
Khine, Aye Aye EP1728, EP1729
Khochtali, Rihab EP835
Khochteli, Inès EP1632
Khong, Pek-Lan OC6.3
Khoo, Bernard EP1799
Khoo, Chin Meng P107
Khoo, Chin Meng OC6.3
Khoperia, Ana EP355
Khoruzha Aleksandrovych, Sofiya P227
Khurodze, Tea EP328, EP345, **EP365**, EP1609
Khvedelidze, Ana EP908, EP1524
Khyzhnyak, Oksana **EP1012**
Kibel, Aleksandar EP794
Kickuth, Ralph EP100
Kiconco, Sylvia P320
Kiefer, Florian EP54, OC9.5
Kienitz, Tina EP1049
Kievišienė, Lina EP4
Kifer, Domagoj P156
Kikhtiak, Taras **EP646**
Kikhtyak, Olesya EP646
Kikodze, Nino P424
Kilian, Larissa P284
Kılıç, İlhan EP1131
Kilinc, Faruk EP1743
Kılınç Candemir, Dilek EP1298
Kim, Bo-Yeon EP437, EP438
Kim, Chan Jong **EP1362**
KIM, Chul Sik EP411
Kim, Chul-Hee EP437, EP438
Kim, Dae Jung EP385, EP48, EP450, EP418, EP427
Kim, Daham **P407**
Kim, Dong Hee P168
kim, doohwa EP545
Kim, Hae Jin **EP385**, EP48, EP450, EP418, EP427
Kim, Hanbin P201
Kim, Hayoung P34
Kim, Hee Ju OC2.2, EP739, P172
Kim, Hee Kyung **EP1670**
Kim, Hee Kyung EP1597, EP476
Kim, Hye Jeong **EP1564**
Kim, Hyo-Jeong P34
Kim, Hyun Ah RC2.4
Kim, Hyun-Ju **EP210**
Kim, Jae Hyeon P127
Kim, Jaehyun P201
Kim, Jeong kyu EP374
Kim, Jin Ju P320, EP637
kim, jinmi EP545
Kim, Jong Seung EP1673
Kim, Joo Yeon **P168**
Kim, Jung Hee P44, P34, P57
Kim, Jung Ho P405
Kim, Jungmin EP1673, EP476
Kim, Ki Hyun EP1747
Kim, Kwangsoon P409
Kim, Kyoung Min **EP431**
Kim, Kyung-Hwa EP210
Kim, Mikyung EP324
Kim, Min Joo P373
Kim, Sang Soo EP545
Kim, Seohyun P127
Kim, Su-Jin EP1701, P44
Kim, Sungrae EP748
Kim, Tae Ho **EP418**, **EP427**
Kim, Woochul P44
Kim, Youngha EP418, EP427
Kimpel, Otilia RC6.6, OC6.5, OC12.5, P11
Kindmark, Andreas RC11.6
King, Kylie EP1312
King, Seth EP103
Kiose, Kokkoni EP1340
Kip, Elodie RC4.3
Kıpık, Samet EP434
Kircher, Stefan OC12.5
Kirel, Birgul **EP733**, **EP1523**, **EP1068**
Kirigin Biloš, Lora EP313, EP511
Kirilenko, Roman EP156
Kirilenko, Zhanna EP310
Kirk, Edwin P252
Kirty, Kaushiki **EP1454**, **P186**
Kishor Mehta, Saumya EP395
Kislach, Eleonora P355
Kiss, Alpar P490
Kiss, Boglarka P490
Kiss, Peter EP985
Kissel, Nina EP1860
Kistkins, Svjatoslavs EP518
Kistorp, Caroline EP1334, EP1058, P265
Kitayama, Saori EP37
Kiyani, Emmon EP211
Kızartıcı, Baver P486
Kjær, Anne **P371**
Kjems, Lise P36, EP116
Klimaite, Raimonda **EP1467**, EP1556
Klit, Frederik EP1147
Kloock, Simon **P71**, P239, EP500, RC11.1, EP423, **P241**, **EP463**, P11
Klose, Marianne P22, P249, EP60
Klotz, Camille **EP283**
Kluczyński, Łukasz EP905
Klymenko, Oksana EP866
Kmieć, Piotr OC6.4, **P39**, **EP203**, **P62**
Knoesel, Thomas EP1108, OC6.1
Knudsen, Oliver EP1364
Knyazeva, Polina P470
Knysak, Alicja **EP1153**
Ko, Junghae EP324
Kobayashi, Hiroki P53
Kober, Nicole EP50
Kobrynska, Nataliia EP1159
Kobuladze, Maia EP832
Kobuladze, Mariam **EP881**
Kobyliak, Nazarii EP1650, P167, EP714, EP866
Koca, Irfan P502
Kocaturk, Evin EP1523
Kocevski, Ivica EP314
Kocherzhynska-Halis, Yana **EP1668**
Kochhar, Rupinder P449
Koci, Marsel **P14**
Kocjan, Tomaz OC7.2, EP1342
Kocjan, Tomaz OC6.4, P76
Koda, Mariusz EP468
Kodetova, Daniela EP1521, P419, P375
Kogut, Dmytro EP404
Kohlhaas, Michael RC11.1
Kohli, Harit RC6.1
Kohlmeier, Lynn OC12.4
Koike, Naoki **P174**, P185
Kojic, Lidija EP1560
Kok Seng Lee, Melvin **EP1050**
Kokkinos, Alexander EP560, EP670
Kokko, Eeva P20, P35, EP61
Kokkorou, Marika EP39, EP1230
Kokorina, Tatiana **EP1544**, **EP256**, **P451**
Kokoszka, Joanna EP79
Koky, Tomas EP447
Kolačkov, Katarzyna EP21, EP1192
Kolasa, Magdalena EP79
Kolatorova, Lucie EP1165, **EP1141**, EP86, P224, EP445
Kolcsar, Melinda **EP1764**
Koldyka, Oliver EP131
Koletsa, Triantafyllia EP1704
Kolibianakis, Efstratios EP1340
Kolodziej, Maciej P211
Kolomodi, Dionysia EP1733
Kołos, Małgorzata P388, P425
Koloutsou, Maria Evangelia EP927, **EP560**, **EP670**, **EP1365**, RC10.3
Kolsuz Türker, irem EP1815
Komaç, Ömer **P390**
Komai, Alexander EP638
Komal, Zain **EP1848**
Komarnicki, Paweł **EP912**, P106
Komisarenko, Iuliia EP1650, P167, EP714
Komisarenko, Kateryna **EP583**
Komisarz-Calik, Maria Aleksandra **P264**, **EP1093**
Komshilova, Kseniya P451
Kondracka, Agnieszka EP63
Kondrotiene, Aiste EP20
Kondrotienė, Aistė EP339
Kong, Linghui P31, OC6.2
Kong, Ying **P74**, RC10.4
Koniari, Eleni EP306
Koniari, Kalliopi EP145
Konidaki, Myrto P100
Konidari, Anastasia EP1872
Konidaris, Alexandros EP1255
Konieczny, Jacek EP651
Konstadoulakis, Manousos EP1733
KONSTANTAKOU, PANAGIOTA EP1733
Konstantinidis, Athanasios EP729
Kontitsi, Marina EP1872
Kontogianni, Stavroula EP378

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Kontou, Elisavet P166
Kontsas, Konstantinos P208
Konturek, Aleksander EP242
Konukoglu, Dildar EP1231
Kooistra, Hans S. EP12
Koopman, Miou P250
Koops, Karlijn EP64
Kopanos, Stylianos **EP1479**, **P145**
Kopczyński, Janusz EP1591
Kopecky, Jan EP399
Koperski, Lukasz EP906, EP63
Koppolou, Agnieszka EP1137
Koprivova, Katerina EP1338
Korakovouni, Areti P445
Koranne, Ashil OC2.2, EP739, P172
Koray Fedai, Neslihan EP434, EP1457, EP1745
Korbonits, Marta EP1377, EP1137, P244, EP1700
Koren, Ronit **EP147**
Koren, Shlomit EP1132
Korevaar, Tim RC1.1, OC8.6
Korkmaz, Fatma Nur **EP301**
Korkmaz, Funda P361
Korkmaz, Merve EP24
Korkmaz Yilmaz, Merve **P52**, **P33**
Körmöczi, Konrad EP54
Köroğlu, Ekin Yiğit **P410**, **EP1484**
Korosidou, Hlianna EP1796
Kosak, Mikulas EP1122
Koschker, Ann-Cathrin EP463
Köse, Mustafa EP434
Köse Hamidi, Ece Gül EP292, EP1481, P173
KÖŞGER, Pelin EP733
Koskenkari, Noona OC4.3
Kos-Kudła, Beata EP955, RC7.3
Kosmidou, Maria EP1116
Kosovsky, Gleb EP413
Kostadinov, Nikolay EP732
Kostaki, Evangelia-Georgia P25
Koster, Linus P276
Kosteria, Ioanna EP1872
Kostik, Mikhail EP224
Kostikas, Konstantinos EP729, P182
Kostitska, Iryna EP417, EP712, EP1307
Kostopoulos, Georgios EP1527, EP1005, **EP9**, **EP1508**, EP332, **P415**, EP1877
Kostopoulou, Akrivi EP1594, P59, EP1879
Kostoulas, Charilaos EP1796
Kotarska, Katarzyna EP1354
Kotecka-Blicharz, Agnieszka OC7.1
Kotecka-Blicharz, Agnieszka **EP905**
Kotlyarevska, Nadejda EP281
Kotnik, Primož EP1342
Kotsa, Kalliopi EP1704, EP1855, EP1796
Kotsi, Eleni EP1541
Kotsini, Vasiliki EP891
Kotsis, Vasileios EP1116
Kotzeva, Elina OC3.2
Kou, Qunhuan **EP1010**
Koual, Ourida OC6.2
Koukoula, Chrysoula EP145, EP453
Koumantakis, Emanuele EP95
Kouris, Nikolaos EP1864
Kouroglou, Eleni EP1241
Koutrouli, Mina EP1230, P90
Koutsompina, Maria-Loukia EP589
Kovaci, Franceska RC10.2
Kover, Bence RC5.6, OC5.6, OC7.6, OC5.4
Kövér, Bence **OC3.6**
Kowalczyk, Tomasz EP1721
Kowalik, Artur EP1591
Kowalik-Zakrzewska, Dorota P240, EP1629
Kowalka, Anna P322, EP430
Kowalska, Aldona EP1591, EP1574, P211
Kowalski, Konrad P51
Kowaltowski, Alicia P148, EP393
Koysombat, Kanyada P349, OC4.1, P351, OC4.2, P325
Koysombat, Kanyada **P322**
Kozarzewski, Leonard P284, **EP1818**
Kozhemzharova, Malika EP1288, EP293
Kozinszky, Zoltán P341
Krabbe, Hans OC8.6
Krabbe Schie, Line Cecilie EP1136
Král, Adam OC10.5
Králik, Roman **P114**
Kraljevic, Ivana EP320, P222, EP910, **EP635**
Kramer, Achim EP1402
Krasnenkov, Dmytro RC2.1, EP156
Krátká, Zuzana EP70
Kratky, jan 20
Kratochvílová, Simona EP252
Krausova, Adela EP1113
Kravchuk, Stanislav **EP603**
Kravvariti, Evrydiki EP560
Krawczyk-Rusiecka, Kinga EP1452, EP57
Krążek, Małgorzata P140
Krebs, Michael EP1017, P43, EP54, EP131, P455
Kreitschmann-Andermahr, Ilonka **P269**
Krenig, Esther-Marie P11
Krętowski, Adam EP1721
Kroiss, Markus OC6.4, RC9.1, EP97
Krone, Nils EP125, EP34
Krone, Ruth EP34
Krotowski, Łukasz EP212
Krsek, Michal EP1122
Krsek, Michal EP1113, EP70
Krssak, Martin EP54, EP131
Krstic, Katarina EP1311, EP900, EP43, P344
Krüger, Lucia P28
Kruk, Ian OC3.6
Kruse, Pia OC3.2
Krygier, Aleksandra EP377
Krzempek, Marcela OC7.1
Krzesiński, Paweł EP756
Krzyścin, Mariola **P503**
Ku, Cheol Ryong **RC11.5**
Ku, Eu Jeong P34
Kubala Havrdová, Eva EP1210
Kubat Uzum, Ayse P291, EP53, P460, EP258
kubat Uzum, Ayse P279
Kubik, Agata P211
Kucharczyk, Karolina **P3**
Kudlova, Anna EP352
Kudugunti, Neelaveni EP1780, EP1198
Kuerzinger, Lydia EP100, P30, EP55
Kuhle, Jens EP1109
Kühn, Jens-Peter EP1790
Kuja-Halkola, Ralf P384
Kuklikova, Vlasta **EP1453**, EP1521, P419, P375
Kukoricza, Krisztina **RC2.3**
Kula, Sylwia EP1324
Kuliczkowska-Płaksej, Justyna EP21, EP1192, EP1197, **EP1323**
Kuliczkowska-Płaksej, Justyna P324, P343, P360
Kumar, Ankitesh **P131**
Kumar, Chirag EP1084
Kumar, Harish EP689, EP639, EP403, EP509, EP565, EP640
Kumar, Nitya **EP1674**, EP1350
Kumbhar, Avinash EP596, EP636, EP788
Kundu, Adrija EP1368
Kunicki, Jacek EP1232, EP1150, P309, EP1093
Kunori, Takao **EP1613**
Kunstmann, Anke EP15
Kunz, Sonja OC9.6, RC8.2
Kunz, Wolfgang RC9.1, EP97
Kuo, Chi-Yu **EP895**
Kupai, Krisztina EP1563
Küppers, Sarah OC12.5
Kurcubic, Boris EP1464, P297, P120
Kurenkoviene, Marija EP1379
Kurgambekova, Diana EP287
Kurlbaum, Max P239, EP423, P241, EP463
Kurmi, Prakash EP596, EP636, EP788
Kurowska, Patrycja EP1405
Kurt, Can Ebru EP1384
Kurt Ömürlü, İmran P390
Kurunthachalam, Kannan P241
Kurzyńska, Anna P226
Kus, Aleksander **33**
Kushnir, Shiri P268, P316, EP1170
Kusushita, Moe P185
Kusushita, Moe P174
Kusy, Krzysztof EP561
Kutchava, Tatia **EP1793**
Kutchukhidze, Tinatin **P336**, **P454**, **P333**
Kuzina, Liliya **EP362**
Kuzior, Agnieszka P450, EP1703, EP1833, P497, EP1742, EP1805, EP1776, EP1777, EP1841, EP1835, EP1707, EP1773, **EP1706**, **P498**
Kuzma, Martin P114
Kužma, Martin EP701
Kuzmenko, Elena EP1108
Kuzmina, Vera EP1749
Kuzu Kumcu, Muge EP1842
Kvanchakhadze, Rusudan EP1537
Kvaratskhelia, Tamar **EP1234**
Kvist, Annika EP1147
Kwak, Soo Heon **34**
Kwek, Kevin **P406**, **P434**
Kwok, Anna EP222
Kwok, Chak Yan Isaac EP621
Kwon, Obin **P201**
Kwon, Su Jin EP431
Kyatham, Vivek EP391, EP1041
Kyaw, Zambu EP1494
Kyaw Kyaw, Naychi EP677
Kydonaki, Konstantina P94
Kyithar, Ma Pyeh EP1, EP419, EP1848
Kypraiou, Maria P207
Kyriakidou, Artemis **EP1704**, **EP1855**, **EP1796**
Kyriakopoulos, Christos EP729
Kyriakopoulos, Georgios EP918, EP145, EP927, EP519, EP108, EP1476, P471, P461, EP1733
Kyriakos, Georgios P402
Kyriakou, Aggeliki EP519, EP453, EP591, **EP237**, **EP1387**, **EP952**
Kyrou, Ioannis EP589, P138
Kyryliuk, Mykhailo **EP1293**
Kyung Kim, Min EP374
Kyungdo, Han EP754
La Rocca, Federica P509

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

La Vista, Monica P150
Labazanova, Shuainat EP256
Laçej, Doris EP1278
Lacerda, Ema EP856, EP1449
Lacerda Nobre, Ema EP261, EP1534
Lacharme, Mélanie-Clothilde **EP1366**
Lackovic, Milena EP1560
Laço, Mário EP1816
Laetitia, Martinerie RC3.3
Lafage-Proust, Marie-Helene **35**
Lafaurie-Noriega, Rubel **EP1465**, EP1511
Laffaire, Julien OC12.4
Lafioniatis, Alexandros EP1045, EP1496, EP1262, **EP25**, P141
Lagana, Marta RC12.5
Lagana, Martina P97
Laganà, Marta RC6.6, P223
Lagoa, Andre EP1308
Lagopodi, Elina P426
Lagou, Vasiliki EP495, EP388, EP371, EP376
Lahlou, Soukaina EP392, EP1155
Lahoda, Daria EP1821, EP1767
Lai, Fenghua OC2.3
Lai, Silvia P97
Lai, Yi-Hsuan **EP1271**
Laina, Angeliki P445
Lajeunesse-Trempe, Fannie P342, P352, EP1348
Lakhel, Anne-Laure RC10.2
Lalanda, Raquel EP731
Lalli, Enzo **36**
Lamas, Cristina P116
Lamback, Elisa EP989
Lambadiari, Vaia P324, P343, P360
Lambrinoudaki, Irene EP1363
Lameirão, Diogo EP974
Lamine, Faiza P1
Lampropoulou, Pinelopi P59
Land, Christof P269
Landi, Alberto EP1296
Landin, Andreas RC2.3
Landolfi, Alessandro P303
Landwehr, Laura Sophie OC7.3, RC7.5
Lang, Brian P82
Lang, Liv-Helen **EP991**
Langdahl, Bente **37**
Langlois, Fabienne EP1684
Langlois, Marie-France RC11.2
Lania, Andrea P252, OC7.4, EP1048, P466
Lania, Andrea Gerardo Antonio P96
Lania, Tommaso P466
Laniush, Fedir **EP1446**, **P158**
Lankes, Erwin P269
Lanzi, Roberto P96
Lanzi, Valeria P278
Lanzolla, Giulia RC1.2, **OC12.3**, **EP1709**
Łapa, Alicja EP1405
Lapshina, Anastasia EP1080
Lapuente, Fernando EP487
Lara Barea, Almudena EP841
Larocca, Angelica P29
Larrabeiti, Sara EP978
Larsen, Klaus Groes P8
Lašaitė, Lina EP439
Lasio, Giovanni Battista EP1152
Laskowski, Gustaw **EP928**
Lasorella, Claudia Angela **EP1179**
Laspa, Eleni P445
Lastivka, Iryna **EP1588**
Lastuvka, Petr EP1521, P375
Laszlo, Anna EP985
Latia, Monica EP1263
Latocha, Julia EP77
Latronico, Ana Claudia EP137
Laubender, Ruediger EP1374
Laura, Iconaru EP93, EP129
Laura-Semonia, Stanescu **EP919**
Laure, Cécilia **P242**, **P304**
Lauretti, Liverana EP1146, EP1151, EP1139, EP1069
Lauretti, Liverana P298
Lauri, Chiara EP1182
Laviv, Amir P121
Lavoie, Hélène RC11.2
Lavrador, Mariana EP1285, EP291, EP974, EP1168, EP1120
Lavrador, Mariana EP206
Law, Lawrence P107
Lay, Abigail EP441
lay, incilay EP1755
Lazar, Elena **EP969**
Lázár, Krisztina EP1764
Lazaratos, Michail P494
Lazarevski, Danilo EP779, EP1074
Lazaridou, Eleni EP145
Lazarus, Katharine OC9.4
Lazarus, Katharine **OC9.4**
Lazarus, Syndia OC10.1
Lazurova, Zora **P50**
Lazúrová, Ivica EP447, EP91
Lazúrová, Zora EP91
Lazzaretti, Clara P391, EP936, **EP1314**
Le Guennec, Adrien P325
Le Mouhaër, Jeannie EP1075
Le Scouiller, Stéphanie EP14
Leal, Angela OC5.5, EP1047, **P457**
Leão Matos, Sandro OC11.5
Leão Matos, Sandro EP424
Lebada, Codruta EP1277, EP196
Lebanova, Hristina EP1320
Lebib, Inès P285
Lebiedzinska, Weronika EP468
Lecoq, Anne-Lise P304
Lecube, Albert EP435, OC11.1
Ledieu, Guillaume P4
Ledinsky, Lea EP511
Lee, Alan Chun Hong EP8
Lee, Brian **EP1468**
Lee, Dae Ho EP645
Lee, Dong-Kyo EP210
Lee, Eun Jig P407
Lee, Eun Ju **EP692**
Lee, Hyo-Jong EP1747, P499
Lee, Hyun-ju EP437, EP438
Lee, I-Te **EP713**, **EP682**
Lee, Ja Kyung P373
Lee, Jack P283, P259
Lee, Jaekyung P7
Lee, Jee-Soo RC2.4
Lee, Jeongmin P34
Lee, Jin Hee EP692
Lee, Ju Hee **P34**
Lee, Junho P507
Lee, Kwan-Woo EP385, EP48, EP450, EP418, EP427
lee, kyeongjun EP545
Lee, Min Jin P168
Lee, Nami EP385, EP418, EP427
Lee, Paul Chi-Ho P82, EP8
Lee, SeongSu EP748
Lee, Seulah EP1747
Lee, Seung Hun P34
Lee, Seungho P44
Lee, Sihoon EP210
Lee, So Hee **EP1701**
Lee, So Jeong P407
Lee, Sung Ok RC2.4
Lee, Vickie P427
Lee, Ying-Ray **EP945**
Lee, Yoojin P201
Lee, Yu-mi EP1701
Leena, Jayalekshmi EP1606
Leerling, Anne EP224
Lefebvre, Hervé P272
Legro, Richard P353
Lehmann Christensen, Louise P327, P22, **EP1360**, EP1364, EP1316
Lehun, Myroslav EP417
Leijon, Helena P35, EP61
Leikam, Lena-Marie OC2.5
Leitão H., Francisca **EP1188**, **EP1098**, **EP989**
Leite, Ana **RC5.3**, **RC4.6**
Leite, Ana Rita EP696, P77, P414, EP494
Leite, Gabriel EP1047
Leite, Gustavo **EP1047**
Leiva-Hidalgo, Natalio **EP951**
Leiwy, Joelle EP85
Leka-Emiri, Sofia EP1869
Lekbello, Megi EP1053, **EP1514**, **EP1667**, **EP364**
Lekbello, Megi EP170
Lekić, Ivan **EP793**, **EP794**
LEKKA, SOFIA EP1723
Lembo, Giuseppe P303
Lems, Willem EP224
Lenda-Tracz, Wioletta P211
Lenders, Jacques EP100, P42, P30, EP55
Lener, Luisa EP1451
Lenzini, Livia P452
Leon del Campo, Marta EP46
Leon del Campo, Marta EP1535
León González, Patricia EP553, EP493
León Mengíbar, Josep **EP435**, **OC11.1**
Leon Ocando, Ana Paola EP1304, EP492, EP493, EP1478, EP199, EP784
Leong, Annie P228
Leoni, Laura P58, EP497
Lepage, Marie P458
Leporati, Marta P223
Lepri, Chiara **P506**, P464
Lerakis, Vasilis P25
Lerouge, Jennifer EP1393
Leskova, Jana EP1269, EP1264
Lešková, Jana P114
Lešková, Jana **EP88**
Lesniewska, Monika RC4.5
Lestari, Dewi EP1398
Leszczynska, Dorota **EP77**
Leszczynska, Dorota P51
Letourneur, Franck P285
Leuker-Cozma, Diana **OC9.3**
Leuker-Cozma, Diana OC9.1
Leung, Joseph EP458
Leung, Lydia EP621

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Leutner, Michael P43, EP54, EP131, P455
Levek, Noah P163
Levek, Noah P128
Levi, Noa EP742
Levi, Riccardo P466
Levin, Malin RC11.6
Levine, Michael A. OC10.1
Levran, Neriya P128, P163
Lev-Shalem, Liat P163
Levy, Miles OC3.4
Lewandowski, Krzysztof **EP57**
Lewandowsky, Lidia EP1127
Lewczuk, Anna P309
Lewczuk-Myślicka, Anna EP939
Lewicki, Marcin **RC8.5**
Lewiński, Andrzej EP1162
Lewiński, Andrzej P240, EP1629
Leyes, Pere EP1096
Lezaron, Katrina P254
Li, Congru EP1906
Li, Danting RC2.6
Li, Gloria Hoi-Yee **EP1488**, **P378**
Li, Kaige RC12.3
Li, Ke EP370
Li, Lanlan P82
Li, Linna P494
Li, Minghao **OC7.5**
Li, Nong RC2.6
Li, Ping EP1035
Li, Ping P63, EP32
Li, Ruyi **P48**
Li, Shengbing EP370
Li, Shiman **P63**
Li, tianke **EP477**
Li, Xiangdong RC4.5
Li, Xiaomin P31
Li, Xingnan EP1368
Li, Xinjun EP1479
Li, Yanbing EP1035, OC2.3
Li, Ying-Syuan EP895
Li, Zhihua OC2.2, EP739, P172
Li, Zhong-Min P241
LI VOON CHONG, Jimmy EP143
Liang, Guo OC6.3
Liang, Sheng-Bin P379
Liang, Shuhui OC2.3
Lianidou, Evi P426
Lianou, Maria P138
Libánský, Petr **EP350**, EP243, P81
Libe, Rossella RC9.3, P285, RC6.6, OC6.5
Libertínová, Jana EP1210
Lichewitz, Gavriel EP102, P397
Licitri, Laura P311
Lidia, Radomir EP1779
Liechti, Matthias EP1081, EP991, OC3.3
Lightman, Stafford P38
Likharad, Natalia EP1646, EP334
Lilja-Fischer, Jacob P108, P98
Lim, Dong Jun P7
Lim, Hunjong P373
Lim, Jungah **P373**
Lim, Shao Ting EP133
Lima da Costa, Eduardo P77
Limbert, Catarina RC5.3, RC4.6
Lin, Andrew EP1676
Lin, Chia-Hung EP179, **RC1.3**, P412, EP1236
Lin, E P396
Lin, Gloria EP805
Lin, Songbai EP1782
Lin, Vivian OC9.5, P21
Lin, Wanchang P277
Linardaki, Emmanouela EP1476, P461
Lindberg, Morten P75
Lindén Hirschberg, Angelica EP1905, EP1906
Lindgren, Eva EP1907
Lindström, Axel P137
Ling, Charlotte P137
Ling Jie Yee, Amanda **RC5.1**
Linglart, Agnès RC3.3, RC10.2, P72
Linhartová, Marcela P81
Linkeviciute Dumce, Ausra RC8.1
Linkohr, Birgit EP1049
Lin-Marq, Nathalie P1
Lipscomb, Victoria EP85
Lisa, Zanetti OC11.3
Lisboa, Patricia Cristina **P235**
Lisbona Catalán, Arturo EP1125
Lishchuk, Orysia **EP1492**
Lisi, Giulia OC1.5
Lisi, Giulia **P383**
Lithgow, Kirstie EP1684
Litscher, Hanna **OC2.5**
Liu, Aihua **EP1671**, P365
Liu, Bin OC1.2
Liu, Chenghang **OC1.2**
Liu, Dai-Wei EP897
Liu, Dongfang EP370
Liu, Jianping EP32
Liu, Jinghua OC9.2
Liu, Jun OC7.2
Liu, Lianyong EP490
Liu, Libin EP32
Liu, Longfei OC7.2, OC7.5
Liu, Sheng P493
Liu, Xiaodong **P82**
Liu, Ye **EP1328**
Liu, Ye P365
Liu, Zhenjie EP31
Livadas, Sarantis P192, P445
Livadas, Sarantis P324, P343, P360
Lixi, Filippo RC1.2, OC12.3
Lizano Sanchez Villacañas, María EP582
Lizarraga, Aitzol P79, OC10.3
ljunggren, östen P89
Llahana, Sofia EP157, EP125, EP1349
Llahana, Sofia P66, P23, P68
Llavero Valero, Maria EP46, EP1535
Llewellyn, David EP52
Lo, Nicholas **EP907**
Lo Preiato, Valentina EP394
Lobanovs, Sergejs EP518
Locantore, Pietro EP1179
Locantore, Pietro EP347, EP1451
Locantore, Pietro OC12.1
Locatelli, Alessandro EP1073
Locatelli, Marco EP1173
Lochnan, Heather EP1684
Lodge, Emily OC5.6
Lodi Rizzini, Elisa OC1.6
Loforte, Antonino P123
Logan, Monica P228
Loh, Ching-Hui P177
Loh, Ching-Hui EP416
Loh, Lih Ming EP133
Loh, Zhi Wen EP907
Löhr, Phillip P85
Loi, Hoi Yin OC6.3
Lombard, Margot OC6.5
Lombardi, Giovanni P73
Lomidze, Ketevan **P424**
Longoni, Mauro **EP1106**
Loo, Helen **P437**
Lopes, Catarina Isabel EP261, EP1534, EP856, EP1449
Lopes, Joana EP1450
Lopes, Luis EP1220, EP267, EP69, EP351
Lopes, Marta EP731
Lopes, Sofia EP291, EP974
Lopesino, José María EP487
Lopes-Pinto, Mariana EP1449
Lopez, Ascension EP69, EP351
Lopez, Jonathan P270
Lopez, Laura **38**
Lopez, Maureen P304
Lopez, Nestor EP82
Lopez, Victor P346
López de la Torre Casares, Martín EP601
López de la Torre-Casares, Martín EP884, EP535
Lopez Gomez, Juan Jose EP1195
López Jiménez, Verónica EP420
Lopez Lopez, Franco Nicolas **EP669**
López Montalbán, Ángel EP845
López Pérez, Carmen María EP830
Lopez Sarmiento, Carlos EP924
López-Cánovas, Juan Luis EP909, EP425, **EP698**
López-Cánovas, Juan Luis EP1077
López-Fernández, Judith EP1185
Lopez-Gomez, Carlos EP467
Lopez-Lazaro, David EP89, EP986, EP1216
López-Pereira, Carlos EP841, EP382
Lorenz, Kristina RC11.1
Lores, Juliana EP1804
Lőrincz, Hajnalka P389
Lorusso, Loredana RC7.6
Lottspeich, Christian EP1108
Lou, Yuxing P63, EP32
Loughrey, Paul OC3.4
Louie, Sharon OC2.2
Lovovic, Djurdjina EP779
Lovric, Karmelo **EP320**
Low, Eric EP464
Lozano de la Haba, Samanta EP909
Lozano-Aida, Claudia P267
Lu, Haojiang EP1907
Lu, Hui-Chun OC3.6
Lu, Jianglong EP1035
Lu, Jiawen P378
Lu, Lin OC3.5, OC9.2, P487
Lu, Yung-Hsiu P379
Lubrano, Carla EP429, EP501
Luca, Thatiane EP1308
Lucchiari, Manuela EP1352
Lucena Morales, Cristian Jesús EP382
Luciano, Tommaso P431
Luconi, Michaela OC6.5, P506
Luconi, Michaela **P464**
Łuczak, Janusz EP212
Ludwig, Christian EP1164
Luengo Alvarez de Buergo, Cristina EP562
Luethi, Dino EP1081
Luffy, Maximilian P396
Luganceva, Anastasija **EP518**

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Lugaresi, Marina **RC8.3**
Lugari, Simonetta EP575
Luger, Anton EP1017, EP54, EP131
Lui, David P82, EP8
Luigi, Aloj RC6.5
Luís, Carla P77
Luk, Yan P82
Lukasova, Petra P161
Lukić, Vera EP1748
Luna-González, María EP1511
Lundberg, Elena P228
Lunde Jorgensen, Jens Otto P22
Lundgaard Riis, Malene P338, P372
Lunkwitz, Tom RC11.1
Luo, Rosa P36, EP116
Lupi, Isabella EP1296, EP106, EP1291, P312
Lupinska, Aleksandra **EP468**, RC4.5
Łupińska, Anna P240, EP1629
Lupp, Amelie EP1077
Lupu, Oana EP468, **RC4.5**
Luque, Raul M EP909, EP425, EP1213, EP951, P210
Luque, Raul M. EP1077, EP1185, P219, EP1161, EP1102
Lustenberger, Sven OC5.2
Lüthi, Dino OC3.3, EP1064
Luthman, Johan P8
Lutz, Mathias P85
Lutz, Thomas **39**
Luzi, Livio EP894
Luzi, Livio EP1665
Lygerou, Dimitra **P100**, **P94**
Lymniati, Christina **EP108**, **EP1265**, **EP1438**
Lymperopoulos, Kostas P59
Lyu, Young Sang EP1597
M Selva, David **P143**
M. El Zein, Rami OC6.2
M.C, Rekha EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Ma, Junjie EP1474
Ma, Nina S. OC10.1, P72
Maack, Christioph RC11.1
Maalouf, Eliane RC10.6
maaloul, kmar EP1627, EP787
Maaz, Shaheer P385
Mabulac, Marichu EP783
Maccario, Mauro EP1455, EP497
Maccio, Umberto EP1108
Macech, Magdalena **EP63**
Maçedo Krause †, Rui Werner P238
MacFarlane, James RC6.5
Macfarlane, James P254, EP56
Mach, Amy **EP1260**
Machado, Amanda Araújo EP1750
Machado, Catarina EP1589, EP286, EP632
Machann, Jürgen P494
Machtopoulou, Katerina P208
Macias, William P396
Macías, Manuel P195
Maciejczyk, Mateusz EP468
Maciejewski, Adam EP912
Maciel, Joana EP245
Macioniene, Ernesta RC8.1
Macionis, Aurimas EP1467
Mačionis, Aurimas EP339
Maćkowiak-Tadyszak, Maja EP561
MacRae, Caitlin **RC4.3**
Macut, Djuro EP1311, EP900, EP1425, EP43, P344, P324, P343, P360
mada, srikanth P186
Madeniyetova, Assem EP940
Madeo, Bruno EP1130, P96, EP1066, EP62, P13
Madhu, SV P131, EP396
Madhusudhan, C EP596, EP636, EP788
Madinelli, Alberto **EP1094**
Madl, Tobias EP54, EP131
Madonna, Elena EP559, EP465
Madureira, Guiomar EP137
Maffei, Pietro P266, P274
Magari, Hanae EP1199
Magee, Ciara N. EP10, EP38
Magee, Colm EP10, EP38
Maggio, Ettore EP1179
Maggiore, Riccardo P96
Maghakyan, Sona **EP1275**, **EP1283**
Magklis, Michail Savvas **EP306**, **P90**
Magklis, Michalis EP39, EP1230
Magkou, Stefania EP479, EP1219
Magla, Tatiana EP1813
Magliocca, Fabio P444
Magnacca, Nunzia EP400, **EP470**, P169
Magnani, Fabio EP1754
Magnezi, Racheli EP741
Magni, Elena EP1117
Magnoni, Cristina EP936
Magomedov, Khamzat P451
Maguolo, Alice P137
Maheshswari, Sanjiv EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Mahmood, Zain RC5.1
Mahzari, Moeber EP58
Mai, Knut P284, P494, EP1818
Mai, Stefania P501
Mai, Thach OC2.2, EP739, P172
Maia, Mafalda P77
Maillard, Alexis P9
Maillard, Arnaud P9
Maillard, Augustin **P9**
Main, Katharina M. **40**, P357
MAIONE, Luigi P242, P304
Mairinoja, Laura RC2.3
Maiter, Dominique EP127, EP1046
Majd, Nazanin K. EP1676
Majeed, Joohi P356
Majeed, Waseem EP1222, EP1119
Majewska, Katarzyna **P248**, **P290**, **EP612**
Majewski, Dominik EP612
Majic Tengg, Ana **EP1327**
Majka, Katarzyna EP1083
Májovský, Martin EP1113, EP1122
Majumder, Anirban EP752
Mak, Shermin OC5.4
Makarova, Maria EP1164
Makedou, Kali P207
Makhlina, Elena EP530
Makhmudova, Fotima **EP1309**, **EP1645**
Makino, Ryutaro **EP1104**, EP1184, EP1088
Mäkitie, Outi P72
Makras, Polyzois EP670, EP1365, RC10.3
Makri, Evangelia **EP1527**, **EP1005**, EP9, EP1508, EP332, P415, **EP1877**
Maksymowicz, Maria EP1232, EP1150, P309, EP1137, EP1103
Makunyte, Gabriela P403
Makwe, Christian P320, EP637
Malagon, Maria P210
Malagrinò, Matteo P104, OC4.6, P323, P80
Malaguti, Anna EP512
Malandrino, Pasqualino RC6.2
Malazonia, Zviad EP1250
Maldonado, Mario P272
Malek, Jerzy EP480
Maler, Bianca EP289
Malesevic, Gabrijela **EP803**, EP1425
Maleska, Aleksandra EP1109
Malik, Mohamed EP1485
Malik, Mohamed EP1490
Malinovic Pancic, Jelena EP193, EP1142, EP1246, EP1177
Malínská, Hana P132
Maliszewska, Katarzyna **EP1721**
Mallea, Marine P4, P9
Mallea-Gil, Susana EP1073, **EP899**
Mallet, Delphine EP1366
Mallik, Ritwika EP441
Mallorquín Castillo, Ainoa EP845
Maloberti, Alessandro EP163
Maloberti, Thais OC1.6
Malthankar, Gauri EP1106
Maltsev, Mikhail EP1540
Malyshko, Maryia **EP1031**
Mamlok Sherf, Rutie **P121**
Mammadov, Emin **EP1520**, **EP1504**
Mammadyarzada, Aysel EP140
Manaev, Almaz EP1540
Manaev, Almaz EP1675
Manaev, Almaz P215
Manakis, Andreas EP1082
Manara, Renzo EP1086
Manchaiah, Vinaya EP1474
Mancini, Antonio P367
Mancini, Camilla **OC7.4**, EP1182
Mancini, Massimiliano EP1182
Manco, Melania **EP559**, **EP465**
Manda, Dana EP318, P299
Mandal, Kausik EP215
Mandel, Hanna EP1317
Mandic, Ante OC6.5
Manethova, Monika EP1122
Manetti, Luca EP1296, EP106, EP1291, P312, P24
Manganaro, Lucia P444
Mangili, Federica **EP1173**
Mangion, Jessica **EP136**
Mangla, Lavanya **P422**
Mangone, Alessandra **EP1014**
Mangone, Alessandra P27
Mangone, Alessandra EP957, P286, EP1044
Mankovsky, Borys EP704, P197, EP488, RC2.1, EP156
Mankumare, Mohitraje EP1376
Mann, Alexander P269
Mannstadt, Michael OC10.4, OC10.1, OC12.4
Manoj, Aravind RC5.1
Manojlovic Gacic, Emilija P297
Manolakopoulou, Maria EP479
Manole, Tiberiu Gabriel **EP1247**
Manolopoulos, Konstantinos P445
Manova, Yuliya **EP96**
Manovich, Michal P397
Manshaei, Saba OC5.4
Mansour, Ahmed M. P154
Mansour, Nabeel P28, EP33, EP29, RC9.1, EP97

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Mansour, Shafik **EP785**, **EP642**
Manta, Aspasia RC5.1, **EP1325**
Mantovani, Giovanna EP957, OC12.5, P72, EP1173, OC11.6, P286, EP1014, P315, RC7.5, P253, P278, EP1044, EP246, P330
Manyalich, Martí P83
Manzano Valero, Lucía P267
Manzini, Chiara **EP1347**
Mao, Federico EP80
Mar, Htoo Htoo P434
Marangelo, Alessandro EP911
Maraşlı, Utku **P463**
Marath, Haris P243, EP1584
Maratos, Eleni EP1811
Maravall Royo, Francisco Javier EP1480
Maraver, Silvia EP1161
Marcelino, Mafalda EP1220, EP267, EP69, EP351
Marchesini, Kevin P358
Marchetti, Paula EP1243
Marciano, Maria Anna EP470, P169
Marciniak, Camille P4
Marcocci, Claudio EP216
Marconcini, Giulia EP106, EP1291, P312
Marcucci, Gemma P97
Marcus, Hani J EP1137
Marcus, Hani J EP1260
Marczi, Saška EP1680
Margalitadze, Eter EP832
Margara, Andrea P154
Margiotta, Gianluca EP1130
Margiotta, Gianluca EP1066
Mariani, Luigi OC3.4
Mariani, Stefania EP429, EP501
Marić, Đurđica EP1748
Marie Christine, VANTYGHEM P4, P9
Mariello, Noemi P431
Mariem, Benkacem EP1391, EP1812, EP128
Marín Bueno, Rebeca OC3.4
Marin Martinez, Luis P402
Marín Sospedra, Clara P402
Marina, Ljiljana EP444, P67, EP149, EP1351
Marini, Francesca EP973
Marinkovic, Milos EP1560
Marinkovic Radosevic, Jelena **EP313**, **EP511**
Marinou, Vasiliki EP891
Mariotti, Stefano RC1.2, EP1709
Mariotti, Stefano OC12.3
Markantes, Georgios **EP1343**
Markou, Athina EP1262, EP113, EP192, EP1594, EP1082, RC10.3, P59, P471, EP1879
Markou, Athina P426
Marková, Irena P132
Markovic, Aleksandra EP1142, EP1441, EP1235, **EP1246**, **EP1177**
Markovic, Aleksandra EP1586, EP1425
Markovic, Bojan EP172, EP1651
Markozannes, Georgios EP654
Markus, Efrat EP147
Markus, Efrat **EP1132**
Marmouch, Héla EP1632
Marques, Miguel EP1188, EP1098
Marques, Miguel EP1267, EP323, EP1621
Marques, Olinda EP245, EP386, EP1589, EP286, EP632
Marques, Pedro **EP1025**
Marques Jones, Renata EP295
Márquez De La Rosa, Juan Ignacio EP1304, EP553, EP492, EP493, EP1478, EP199, EP784
Marshall, David P479, **EP34**
Martin, Niamh EP363
Martin, Olwenn **OC8.3**
Martin, Sorina EP336
Martin, Yoann P285, OC6.5
Martín, Elena EP602
Martín Flores, Laura María EP1717
Martin Perez, Irene P402
Martín Rojas-Marcos, Patricia EP1125, EP151, P329
Martin Timon, Iciar EP1535
Martín Timón, Iciar **EP46**
Martinez, Guillermo RC2.3
Martinez Guasch, Laia EP44
Martínez Hartmann, Ana Rocío **EP995**, **EP841**, **EP382**
Martínez Montoro, José Ignacio EP405
Martinez Olmos, Miguel Angel EP669
Martínez-Barbera, Juan Pedro OC5.4
Martínez-Carrillo, María EP698
Martínez-Fuentes, Antonio Jesús P219, EP1102
Martínez-López, Ainara EP372
Martinez-Martin, Francisco Javier **P450**, EP1703, EP1833, **P497**, EP1742, EP1805, EP1776, EP1777, **EP1841**, EP1835, EP1707, EP1773, EP1706, P498
Martinez-Martinez, Ana EP1805
Martínez-Martínez, Ángela EP405
Martinez-Saez, Elena P307
Martínez-Urbistondo, Diego EP372
Martinho, Mariana EP457
Martiniuc, Diana EP950, **EP1491**, EP159
Martín-Nieto, Alicia EP1677
Martino, Marianna P253
Martinotti, Alice EP1186
Martins, Ana Cláudia EP1220, EP267, EP69, EP351
Martins, Patrícia EP1450
Martins, Teresa EP1501
Martins Fernandes, Andreia EP1501, EP1027
Martins Ferreira, Mafalda EP291
Martins Gama, João EP944
Martiradonna, Maurizio **EP1224**
Martorell Ferrer, Isabel EP630
Martos VanDussen, Juan Victor EP467
Martyn, Christina EP38
Marušić, Romana EP1680
Marville, Sabrina EP1439
Marzullo, Paolo EP1138, EP1215
Mascarenhas, Mário Rui P366
MASCUÑANA CALLE, JUAN ANTONIO EP582
Maseroli, Elisa EP1347
Masi, Davide EP966, **EP429**, **EP501**
Masi, Laura P97
Masjkur, Jimmy P30, EP55
Masliah-Planchon, Julien P285
Masood, Beenish EP1799
Masopust, Vaclav EP1113, EP1122
MASRI, HIBA EP896
Masri Iraqi, Hiba **P316**
Mastorakos, George P179, EP1365, P324, P343, P360, EP1733
MASTORAKOS, GEORGIOS P207
Matei, Anca EP1641, EP262
Matei, Anca EP354, EP996, EP1491, EP1292, EP1337, EP159
Matej, Radoslav P419
Matejkova Behanova, Magdalena EP350, **P81**
Mateniadou, Maria EP560, EP670, EP1365
Materazzi, Gabriele EP227, P383, EP226
Matesevac, Lisa P142
Mateus, Heidi EP1804
Mateu-Salat, Manel P83
Mathad, Nijaguna EP1153
Matheou, Andreas EP441
Matheou, Mike EP1181, EP1313
Mathew, Arun **OC10.4**, **EP260**
Mathews, Shebina Liz **EP89**, EP986, EP1216, **EP1427**, **EP774**
Mathiopoulou, Maria **EP1612**
Mathiopoulou, Maria EP177
Matijaca, Ana **EP1526**
Matijaca, Hana EP1526
Matikainen, Niina P20, **P35**, EP61
Matlim Ozel, Tugba P394
Matos, Catarina EP286
Matos dos Santos, Jessica Denielle OC11.5, EP424
Matrejek, Anna P3
Matrejek, Anna EP79
Matrone, Antonio **41**, OC1.5, P383, RC7.6
Matsumoto, Kazuhisa P53
Matsuura, Bunzo **EP684**
Mattinzoli, Deborah OC11.6
Mattogno, Pier Paolo EP1055, EP1060, EP1146, P298, EP1151, EP1057, EP1139, EP1069
Matukaitienė, Radvilė EP1175, EP4
Matusiak, Aleksandra EP1162
Maués de Oliveira, Ana Carolina EP137
Mauger, Morgane EP1860, **P17**, P458
Maurer, Julian EP1108
Maurer, Lukas P284
Mavromati, Maria OC3.4
May, Christine EP933, P437, EP109, EP949, EP1181, EP1313, EP45
Mayar, Emily **EP1194**, **EP73**
Mayilova, Aygun EP1605
Mayo, Rebeca EP372
Mazarakis, Demosthenes EP1541
Mazeda, Maria Luís EP1816
Mazii, Svitlana EP617
Mazzarella, Ciro P298
Mazzeo, Pierluigi RC9.4
Mazzeo, Pierluigi **EP1086**, **P56**, EP1094
Mazzeo, Pierluigi P289
Mazzeo, Pierluigi EP190
Mazzilli, Rossella EP1224
Mazziotti, Gherardo EP1048, P466
Mc Dermott, Niamh P283, P259
Mc Donald, Darran EP10, EP38
Mc Donald, Darran **P283**, **P259**
McBride, Pat P23
McCormack, Michelle EP419
McCormack, Shana P255, P256
Mccormick, Peter P468
McCredie, Riada P332
Mcdonald, Anne P361
McDonnell, Tara P151, EP1348
Mcdonnell, Tara P283, P259
Mcelvaney, Joseph P228
McEnroe, Olive EP10, EP38
McGarry, Catherine EP419
McGown, Patrick OC4.2, P322
McGuinness, Luke P74

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

McIntyre, Adam D. EP1843
McMullan, Paul P416
McNally, Stephen P283, P259
Me Lin Ie, Jéssica **EP137**
Me Me Ko, Aye **EP1051**
Mechorish, Roni P429
Medeiros, Regina EP325
Medenica, Sanja **EP1084**
Medici, Marco P432
Mediero Benítez, Marta EP372, EP487
Medina Puma, Luz Marina EP1054, EP990
Meeran, Karim OC9.4, EP363, P427
Meftah, Azzelarab EP1437
Megia, Ana EP44
Mehic, Dino P43
Mehlich, Dawid EP1137
Mehmet, Brien **EP1349**
Mehmood, Asif EP1848
Mehringer, Pauline P241
Mehringer, Pauline P239
Mehta, Suyog EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Meillet, Lucie EP1002
Meinhardt, Matthias EP1790
Meizoso-Pita, Olalla EP46, EP1535
Mekkattu, Shalini **OC3.3**
Mela, Aggeliki EP1438
Melamed, Philippa **P301**, **OC5.3**
Mele, Chiara EP1138, EP1215
Melgar Manzanilla, Virgilio EP1804
Melidou, Eirini EP1704, EP1855, EP1796
Melis, Alessia P58, EP1352
Melkonyan, Arthur EP544
Melnichenko, Galina P215, P451
Melnichenko, Galina EP1675
Melo, Enaldo OC5.5, P457
Melo Santos, Anne Raissa OC11.5, **EP424**
Melson, Eka P151
Melson, Eka **EP1348**
Melvin, Audrey EP456
Memi, Eleni EP1262, EP25
Mena Ribas, Elena EP1191
Menafra, Davide P12
Mendes, Catarina EP1326, EP525
Mendia, Amaia EP978
Mendieta, Gabriel **EP376**
Mendonça, Fernando **P77**
Mendoza Pimentel, Cynthia OC12.5
Menéndez-Torre, Edelmiro Luis EP1677
Meng, Fanrui EP1671
Meng, Lingqiong P86
Menghini, Deny EP559, EP465
Mengozzi, Giulio P58, EP1352, EP1030, EP497
Mengucci, Carlo EP98
Menino, João EP494
Menon, Ravi EP1865
Menon, Saieehwaran EP1607
MENTZELOPOULOU, PARASKEVI P192, P445
Menu, Louisa P234
Meomartino, Letizia EP189
Meomartino, Letizia **EP1455**
Merai, Adam P191
Mercanile, Giada P391, **EP936**, EP1314
Merchante Alfaro, Agustín Ángel EP1480
Mercier, Frédéric EP283
Merke, Deborah EP36, P21
Merlos-Navarro, Silvia EP253
Mert, Meral EP1070
Mert, Meral P110
Mert, Meral EP1092, EP121
Mertens, Jonathan **P134**
Merza, Zayd EP1494
Mesa Suárez, Laura EP1304, EP553, EP492, EP493
Mesinovic, Jakub EP269, EP303
Meskos, Achilleas EP1541
Mesonero Alonso, Marta EP1306
Messina, Erika **EP95**, **RC12.5**
Mestiri, Mariam EP608
Metelcová, Tereza EP398, EP414, P165
Methlie, Paal P38
Metso, Saara EP3
Mettraux, Valerie EP638
Metwally, Mostafa EP1908
Metz, Matthaeus EP1017
Meyer, Anja EP1759
Meyer, Anke P470
Meyer, Gesine **P345**
Meyer, Nina **P494**
Mezosi, Emese **42**, P428, EP1025
Mgaloblishvili, Tamaz EP908
Mgaloblishvili, Tamaz EP1524
Mhaouty-Kodja, Sakina **43**
Michael, Hudecek OC7.3
Michael, Therese EP1573
Michaelidou, Maria RC5.2
Michalak, Renata EP1162
Michalak, Renata EP1547
Michalaki, Marina EP1476
Michalakis, Konstantinos **P207**
Michalopoulou, Olympia EP1219, EP891
Michalopoulou, Theodora **EP44**
Michalska, Dana **EP352**, EP243, EP273
Michelet, Marie EP1002
Michelucci, Angela EP226, EP216
Michetti, Alessio EP1179
Michitaka, Kojiro EP684
Michnova, Ludmila P224
Michoula, Aspasia EP378
Micic, Dusan EP779
Mićić, Bojana EP563
Mickovski, Ivana **EP207**, **EP693**, **EP824**, EP200
Midlovets, Kostiantyn RC2.1
Miettunen, Paivi EP224
Mifsud, Simon EP209, **EP78**, **EP225**
Miglinas, Marius RC8.1
Migliorelli, Federico EP821
Miguel, Valeria de OC7.2
Mihai, Daniel P299
Mihai, Radu EP109
Mihailovic, Zoran EP1748
Mihailovs, Timurs EP518
Mihatsch, Patrick P11
MIhneva, Vesela EP600
Mihuta, Monica Simina EP1515
Mikolajczak, Renata P211
Mikulak, Marta EP57
Milanese, Marco P509
Milanovic, Sanja EP1177
Milardi, Domenico EP1060, EP1151, P367
Milat, Frances EP269, EP303
Miłek-Krupa, Justyna EP1591
Milenkovic, Bogdan P344
Milenkovic, Tatjana EP1895
Miles, Stephanie **EP949**, EP564
Milesi, Alessandra P501
Miletic, Marija EP172
Milewicz, Andrzej P343, P360
Milewicz, Andrzej P324
Milewska, Gabriela EP468, RC4.5
Milewska- Kobos, Ewa EP377
Milewski, Robert EP468
Milicevic, Mihailo P297
Milinkovic, Iva P120
Milioto, Angelo **P484**, **P485**
Miljic, Dragana EP1464, P297
Millan-Martin, Alberto EP698
Miller, Bradley P228
Miller, Jennifer P255, P256, RC2.5, P142
Milligan, Anne **EP1705**
Millou, Christina **EP257**
Millou, Christina EP1756
Mills, Edouard G P349, OC4.1, EP217, P351, OC4.2, P322
Milne, Andrew EP217
Milnes, Di P252
Milošević, Miodrag EP1748
Milosheska, Radmila EP207, EP693, EP824, **EP200**
Milutinović, Vuk EP426
Min, Thinzar EP1573
Minaldi, Elisa **RC7.6**
Minaldi, Elisa OC1.5, P383
Minamoto, Yuki EP1294
Minasyan, Mari **EP114**, **EP1083**, EP932, P247, EP1093, P246, EP1814
Miniewska, Katarzyna EP1721
Minnetti, Marianna EP966
Minnie, Elouise EP157
Mirabelli, Maria **P159**, **OC2.1**
Mirabelli, Riccardo EP1182
Miranda, Antonio P151
MIRICA, ALEXANDRA **EP93**
Mirica, Alexandra EP129
Mirón, Benito EP698
Mirosevic, Gorana EP313, EP511
Mirsepanj, Romina P73, P84
Mirtsou, Nikoletta EP1541
Mirzaei, Hadis **RC12.6**
Mishra, Ipsita **EP1023**, **EP1410**, **P152**
Misra, Akanksha **EP1312**
Missbrenner, Cornelia EP1348
Mitro, Peter EP91
Mitropoulou, Marina EP654
Mitrovic, Dragana P67
Mitrushi, Arben EP1631
Mitsumasa, Kishimoto EP224
Miyake, Teruki EP684
Mlaco, Lamija EP1856
Mladenović, Violeta **EP1422**
Mladenovska, Ivana EP368
Mlawa, Amanda EP940
Mlawa, Gideon EP976, EP658, **EP1281**, EP1300, EP937, EP940
Mlekus Kozamernik, Katarina **P76**
Młodożeniec, Aleksandra **EP1463**
Młodożeniec, Piotr EP1463
Mnif, Mouna EP608
Mocellini, Francesca EP1186
Modica, Roberta OC7.4
Modica, Roberta RC6.2
Mogno, Carlo P289
Mogno, Carlo EP233
Mogno, Carlo EP282

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Mogos, Iustina Cosmina EP214
Mohamed, Abubaker RC6.4
Mohamed, Zainaba P293
Mohamed Said, Said EP924
Mohammed, Azmi EP1838, **EP1732**, **EP1242**
Mohammed, Mohammed EP1791
Mohammed, Mohammed EP1799
Mohanta, Dr. Bibhuti Bhusan EP1638
Mohd Ali, Masliza Hanuni EP1555
Mohd Noor, Najmi EP456
Mok, Ji-Oh EP437, **EP438**
Mokan, Marian P363
Mokáň, Marián EP1121
Mokhort, Alena EP1646
Mokhort, Tatiana **EP530**, EP1031
Mokhort, Tatsiana **EP1646**, **EP620**, **EP334**
Mokrysheva, Natalia EP1675, EP1544, EP256, P215, P451
Moldavski, Ofer P361
Moldoveanu, Dan EP283
Molinaro, Eleonora OC1.5, P383, RC7.6
Molinero-Marcos, Inmaculada P450, **EP1703**, EP1833, P497, EP1742, EP1805, **EP1776**, EP1777, EP1841, EP1835, **EP1707**, EP1773, EP1706, P498
Mollard, Patrice **44**
Møller, Jens-Jakob OC4.3, EP1316
Molnár, István EP1507, P389
Molnár, Zsolt EP985
Moloney, Niamh **EP581**
Mona, Rekik EP1627, EP787
Monashnenko, Olha **EP704**, **P197**
Moneta, Claudia RC8.3
Mongolu, Shiva EP1728, EP1279
Monjardino, Teresa RC4.6
Monnot, Alexandra **P403**
Monoranu, Camelia OC3.1
Monsalve, Claudia EP1804
Monsanto, Alice EP989, EP291, EP974, **EP1168**, EP206, EP611, EP1120
Montanelli, Lucia EP150
MONTASTIER, Emilie EP1002
Montefiori, Simona EP1352
Monteiro, Ana RC5.3, RC4.6
Monteiro, Ana Margarida EP286
Monteiro, Sílvia EP696, EP494
Montesano, Giulia P58
Montibus, Bertille RC6.1
Monticone, Silvia P452
Monzani, Maria Laura EP1066, EP1130
Moog, Sophie OC7.2
Moon, Jae Hoon P373
Moore, Mary P283, P259
Moqeem, Uroosa EP1854
Mora, Mireia P83, EP1205
Mora, Stefano P72, P97
Morabito, Letteria Anna OC8.5, P112
Morales, Evelyn P436
Morales Pérez, Francisco EP1717
Morales-García, Diéter EP405
Morales-Ruiz, Manuel P195
Morán López, Jesús Manuel EP1717
Mora-Ortiz, Marina RC2.3
Mora-Romero, Bella P346
Moraru, Medeea P382
Moravec, Tomas EP1141
Moreau, Benjamin P17, EP1002
Moreira, Ana Paula EP944
Morelli, Nicola P358
Morelli, Valentina EP27, EP51
Morello, Giulia EP1019
Moreno, Carolina EP291, EP974
Moreno, Cristina P79, OC10.3
Moreno, Telma P77
Moreno-Moreno, Paloma EP1185
Moreno-Moreno, Paloma EP1102
Moreno-Ruiz, Inmaculada EP46, EP1535, P116
Morera, Julia P272
Morgado, Ana EP1816
Morgan, Fiona P340
Morgante, Cesare EP1001
Morillas Jiménez, Virginia EP420
Morillo Macias, Virginia Patricia EP1480
Morino, Katsutaro EP1104
Morino, Mario P154
Morita, Satoru EP37
Morman, Rachel P340
Morrell, Alexander P495
Morrone, Stefania EP429
Mosbah, Helena EP1002
Moscatiello, Simona EP459, EP512
Mosconi, Cristina RC6.4, P2
Moser, Kathrin RC5.5, EP1049
Moser, Othmar EP518
Moskva, Khrystyna EP646
Mossman, Jean EP464
Motolese, Erika EP347, EP1451, EP1179
Motsiou, Dimitra EP1592, EP123, EP1394, EP685, EP1241
Motta, Giovanna RC9.6
Motta, Irene EP1044
MOUCHTOURIS, PANAGIOTIS EP519
Mourão Rodrigues, Eduarda EP286
MOURE RODRIGUEZ, MARIA DOLORES P267
Mourougavelou, Vishnou EP1700
MOUSTAKI, MELPOMENI` EP891
Moutsatsou, Paraskevi EP25
Moyano-Sánchez, Ana María EP630
Mpatzakis, Panagiotis EP1116
Mrkáčková, Karolína EP263
Mruzek, Hanna EP1416
Mucha, Argjent EP368
Mudaliar, Rajshekhar P449
Mueller, Ronja EP15
Mueller, Sven C. EP1344
Muir, Christopher RC4.2
Mukaetova-Ladinska, Elizabeta EP1388
Mukherjee, Poulomi EP752
Mulatero, Paolo P452
Mullan, Karen P416
Müller, Hermann P255
Müller, Hermann L P293, P256
Müller, Michelle EP991, EP1126, **P275**
Müller-Pfefferkorn, Ralph P10
Mulligan, Kathleen P23, P68
Mumlev, Arthur EP1159
Mumusoglu, Sezcan P321
Mun, Hyewon **EP748**
Mungari, Roberta P286, EP1014, P278, EP1044
Mungari, Roberta EP957
Muniyappa, Suresha EP1243, P99
Muniz, Mariana EP478
Muñiz Sevilla, Paula P329
Muñoz, Concepción EP630
Munoz-Garach, Araceli EP826, EP890, EP550
Muñoz-Torres, Manuel EP253
Munter, Gabriel EP102, P397
Muradov, Nizami EP1605
Muradyan, Irina EP544, EP1411
Murakami, Masanori P53
Muresan, Andrei EP318, P230, EP919
Murphy, Kate EP581
Murray, Robert D P266, RC3.4, P274
Murugesu, Rakithan OC3.3
Muryzina, Iryna **EP104**
Musa, Abdelmajid EP1485
Musallam, Manal EP667, **EP142**, **EP653**, **EP576**, **EP432**
Musat, Madalina EP23, EP619
Musat, Madalina Daniela Lucia EP318
Musial, Karol EP79
Musiałkiewicz, Jan EP912
Musleh, Mohammud P427
Musolino, Antonio **EP51**
Musso, Elena EP189
Mutlu, Ümmü P279, P291, EP53, **P460**, EP258
Muzurovic, Emir EP146
Mykhalchyshyn, Galyna EP1650
Mykhalchyshyn, Galyna EP866
Mykytyk, Miroslava EP1012
MYLONAS, PANAGIOTIS P445
Mytareli, Chrysoula EP25
Na, Hee Young P373
Nacea, Claudia EP771
Nacea, Claudia EP122, EP1897, EP1887
Nacea, Claudia Alexandra EP1522
Nacu, Miruna-Viorela **EP336**
Nádasdi, Bernadett **P341**, **EP1370**
Naeem, Ammara EP1720
Näf Cortes, Silvia EP44
Nafees, Samraiz EP1279, EP1490
Nagarajah, kalyani **EP1731**, **EP1389**
Nagata, Yuki EP1129
Nagy, Endre P389
Naimi, Foued EP408
Nair, Bindhu EP1674
NAIT CHALLAL, Rania **P55**
Nakaguchi, Hironobu EP684
Nakaidze, Nana EP1244
Nakamura, Toshifumi P53
Nakasatien, Soontaree EP745, EP1572
Nakis, Alexandros EP1363
Nalluri, Bhanu EP1780
Nana, Aia **EP1679**
Nandakumar, Subhiksha EP1676
Nanni, Simona OC12.1
Nannipieri, Francesco RC1.2
Naomi, Fresht EP1791, EP1700
Napier, Catherine RC9.5
Napolitano, Giorgio P431
Nar, Asli EP292, EP1481, P173
Narayanan, Ram Prakash **EP1376**, EP441
Narongchartsopon, Supichaya EP1199
Narula, Kavita OC9.4
Naruse, Mitsuhide P53
Nascimbeni, Fabio EP575
Naseer, Aisha EP933, EP45
Nasirov, Nijat P279
Nasirova, Khurshida EP1309, EP1662, EP1645
Naskręcka, Monika P290, EP612
Nassar, Karin P339
Nastasa, Teodora **EP1641**, EP262
Nastase, Valeria Nicoleta **EP1115**

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Nasuruddin, Alia Nasriana EP758
Natalia, Porcereanu **EP1813**
Natesh, Pratibha EP1756, EP76
Natorska, Joanna P376
Natsuki, Yuka EP1129
Navardauskaite, Ruta **EP1379**, **EP439**
Navarra, Raffaele P334
Navarro, Jorge EP1022, EP1011, EP1167, EP1124, EP1158, P263
Navarro-Hoyas, Clara EP1124
Navas-Moreno, Cristina EP405
Naves Díaz, Manuel EP259
Navmenova, Yana EP530
Navodnik Preložnik, Maja **P149**
Nawabi, Jawed P284
Nawaz, Maimoona **EP1222**
Ndjengue Mindang, Elisabeth Louise **P238**
Ndrio, Altin P77
Nechifor, Mihai P491
Nedeljkovic Beleslin, Biljana EP172, EP1651
Nedeska Minova, Natasha EP647
Neggers, Sebastian P305, OC5.1, P69, P228, EP994
Negri, Mariarosaria EP400, EP470, **P169**, P29
Nehme, Nathalia Medeiros P235
Neirijnck, Yasmine OC9.1
NEMUTLU, Emirhan P463
Nenkov, Rumen EP1708
Neporada, Veronika **EP1862**, **EP1821**
Nesi, Gabriella P464
Nešković, Nenad EP1680
Nestares, Teresa EP698
Netea-Maier, Romana Teodora P95
Netsach Pe'er, Naama P191
Netuka, David EP1113, EP1122
Netzer, Doron P91
Nevalainen, Pasi P20, P35, **EP61**
Neves, Celestino EP494
Neves, João EP696, P77, P414, EP494
Newell-Price, John OC3.4, P306, RC9.5
Newman, Stanton P23, P68
Ng, Aaron P406
Ng, Chrislyn **EP269**, **EP303**
Ng, Shi Ling OC6.3
Nguyen, Dung EP399
Nguyen, Hanh EP222
Nguyen, Julie EP317
Nguyen, Thu P494
Nhili, Mohamed **EP101**, **EP128**
Ní Ghallchóir, Meadhbh EP419
Nicholas, Richard P427
Nickel, Alexander RC11.1
Niclewicz, Julia Ventura EP1750
Nicolaides, Nicolas P471
Nicolanti, Francesca EP1182
Nicolazzi, Ludmila **P1**
Niculescu, Dan EP68
Niculescu, Dan Alexandru **EP214**, EP917
Nicuta, Viorica EP977, EP1149, P299
Niddam Sanchez, Raquel EP420, P227
Niedziela, Emilia **EP1591**
Nielsen, Eigil H P249
Niemira, Magdalena EP468
Nieuwdorp, Max EP563
Niewiadomska, Alina P240, EP1629
Nikaj, Andi **EP1081**, EP991, EP1064
Nikolic, Valentina EP668
Nikolic Djurovic, Marina **EP1464**, P297, P120
Nikolopoulou, Anastasia EP1546, EP1568
Nikookam, Khash EP686, **EP768**, **EP677**
NIKOPASCHOU, MARTHA P471
Nistor, Alexandra EP966
Nistor, Theodora **EP68**
Nita, Roxana EP68
Nitoi, Luciana Carmen EP1562
Niu, Dau-Ming **P379**
Niyazoglu, Mutlu P52, P33
Niyazoğlu, Mutlu EP1034, EP1201, EP1133, EP24, EP270, EP1163, RC3.6
Niziolek, Helena **P43**, **EP54**, **EP131**, P455, EP50
Njamen, Dieudonne P238
Nobbenhuis, Inge **P294**
Nocete Aragón, Ignacio **EP1730**
Nocito, Matteo EP1315
Noelting, Svenja OC7.2, EP1108
Nogieć, Anna EP954, P3, P262
Nogueira, Cláudia EP1123
Nogueira, Filipa EP731
Nogueira, Isabel **EP1308**
Nogueiras, Rubén OC4.4
Nomikou, Maria EP589
Nonclercq, Denis P234
Nonnato, Antonello EP1352
Noronha, Carolina EP1027
Nosal, Marcin **EP1622**, **P218**, **EP1643**
Noschese, Giacomo P286
Notte, Antonella P303
Nouira, Sawsen EP75, EP1499
Novac, Roxana **P232**, **EP87**
Novais Araújo, Alexandra EP238
Novak, Zdenek EP1453
Novo, Ana Margarida EP1285
Nowacka-Woszuk, Joanna P248
Nowak, Elisabeth **45**, **RC5.5**, EP1075, OC5.5, OC3.2, **EP1049**, EP33, EP29, RC8.4, EP1036
Nowak, Urszula **EP1324**
Nowis, Dominika EP1137, EP1103
Nowotny, Hanna F. OC3.2, OC9.6, P45
Nozato, Yoichi P53
Nozza, Emma RC7.5
Ntalaperas, Kostantinos RC10.1
Ntali, Georgia P166
Ntali, Georgia EP519, EP139, EP115, EP1387, EP1265, RC10.3
Ntikoudi, Anastasia EP889, EP819
Nunes, Isabel Serra EP483
Nunes de Camargo, Felipe OC11.5, EP424
Nunes Silva, João EP1220, EP267, EP69, EP351
Núñez-Morales, Ángela EP405
Núñez-Santos, Miguel Ángel EP1213, EP951
Nuti, Francesca OC8.2, OC8.5
Nyirő, Gábor OC6.4
Nyunt, Aye **EP1223**
Nyunt, Sandhi P349, OC4.1, P351, P322
Nyunt, Sandhi **OC4.2**, **P427**, **P325**
O Connor, Lucia EP602
O' Sullivan, Siobhan **EP811**
O'Brien, Ciara EP419
Oakey, Rebecca OC7.6, RC6.1
Oana Stefania, Stanca EP1258
Oberholzer, José EP1108
Obermayer-Pietsch, Barbara EP1348
Obradovic, Milan EP1560
O'Brien, Donncha P283, P259
Obtel, Nicolas RC10.2
Obuobie, Emmanuel Kofi EP1731
Ocak, Banu **EP1569**, **EP1642**
Ocampo Cortes, Diego Fernando EP1898
Ocaña-Wilhelmi, Luís EP405
Ochman, Paweł P221
Ochoa-Vera, Miguel EP1465, EP1511
O'Connell, Jeremy OC2.2, EP739, P172
O'Connell, Liam P283, P259
Oczko-Wojciechowska, Malgorzata OC7.1
Odabaş, Hatice EP943
Odalovic, Sara **EP444**, P67, EP149
Odermatt, Lolita **EP638**
Oduro-Donkor, Dominic EP254
Oestlund, Imken P151
Oettle, Matthias **RC9.1**, **EP97**
Oeztuerk, Gizem EP15
Ogłodek, Ewa P218
Ognjanovic, Sanja EP1311, EP900, **EP43**, P344
Ognjenović, Anja EP426
Oguz, Arzu EP292
Oguz, Seda Hanife P317
Oh, Mansuk **P443**
Ohlsson, Claes RC2.3, EP1907
Ojeda-Pérez, Betsaida EP1077
Ojeda-Sanchez, Lisette EP1833, EP1841
Ok Kurt, Ayşe Merve P460
Okamoto, Ryuji P53
Okamura, Shintaro P53
Okçu Heper, Aylin EP1042
Okeyo, Janetricks P261
Okita, Tomonori P174
Okita, Tomonori P185
Okosieme, Onyebuchi RC1.6, P449
Okroj, Dominika P62
Øksnes, Marianne P38
Okutan, Sema **P22**
Olafsson, Isleifur EP49
Olate, Laura EP1804
Oleaga, Amelia P79, OC10.3
Olejarz, Michał **P49**
Oleksyk, Olga EP1012
Oliva, Alessandro P367
Oliveira, Arthur EP1047
Oliveira, Carla R. P. OC5.5, P457
Oliveira, Joana EP947
Oliveira, Joana EP1123
Oliveira, João EP525
Oliveira, Margarida EP1458
Oliveira, Maria João EP1326, EP525
Oliveira, Mariana RC5.3
Ollero, M Dolores P267
Ollier, William EP441
Ollila, Helena P357
Ollila, Meri-Maija OC4.3, **P350**
Olmos, Roberto EP30
Olsen, Anne Helene EP1063
Ölsner, Laura OC3.1
Olsson, Aleksandra OC8.1
Olsson, Daniel S P296
Olsson, Tommy P26
Olsson Bontell, Thomas P296
Olujimi, Folakemi P322
Olveira, Casilda EP253
Olveira, Gabriel EP253
Omar, Chrysanthi-Tzenin EP1116
Omer, Tahir **EP1095**, EP1180
Omeri, Ledia EP170
Ominsky, Mike OC10.2
Oms, Sandra EP821

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Onay, Hüseyin OC11.2
Onchis, Darian EP920
Ondruskova, Dominika **EP1269**, **EP1264**
Onesimu, Ezra Leander OC6.6, P27
Ongaro, Luisina EP1076
Oniani, Mariami P228
Onofrei, Adina EP122
Onofrei, Adina-Ioana **EP771**, EP1897, EP1887, EP1522
Opalic Palibrk, Milica EP1311, EP900, EP43, P344
Opalinska, Marta **P211**, EP242, P32
Opalinska, Marta P226, EP79
Or Koca, Arzu EP1100
Oral, Elif OC11.2
Orce, Stella EP1073
O'Reilly, Michael W. EP10, EP38, P151, EP125, P283, P259, EP1348
Orellana-Jaen, Andrea EP698
Orešič, Matej EP497
Orešič, Matej **46**
Oriol Ocejo, Patricia **EP562**
Orjonikidze, Mariam **EP1249**, **EP141**, EP1295, EP174
Orłowska-Florek, Renata EP1463
OROIS, AIDA EP1205
Orois, Aida **P83**
Örs, Ali EP1815
Orskaya, Handan Hanım EP585
Ortega, Emilio EP821
Ortega-Bellido, María P219, EP951
Ortiga-Carvalho, Tania Maria EP1308
Ortiz, Angel Michael EP435
Oscarson, Mikael RC11.6
O'Seaghdha, Conall EP10, EP38
Osher, Esther EP1183
Osher, Etty EP1107
Osinga, Joris RC1.1
Osman, Sumaya **P339**
Ostrowska, Magdalena P51
Otsuka, Fumio EP1063
Oulad Ahmed, Bothayna RC11.4
Ould Rouis, Taha OC12.4
Ouřadová, Anna EP263
Ouvrard-Pascaud, Antoine P31
Owen, Lisa EP65
Owens, Dimitra EP1363
OZ GUL, Ozen EP1774
Ozanne, Susan EP1400
Ozbek, Mustafa EP1745
Özbek, Mehmet Nuri OC11.2
Ozcan, Ömer **EP64**
Özçelik, Serhat P314, EP943, P504, P486
Ozdemir, Huseyin Baran P500
Ozek, Fatma Zulal EP1070
Ozen, Hasan EP1384
Ozen, Samim OC11.2
Özen, Nefise EP1100
Ozer, Samed P442
Ozeryansky, Larisa EP1611
Özgü, Can EP1774
Ozgur, Su EP1189, EP1204
Ozisik, Hatice **EP1189**, **EP1204**
Ozkan, Hayriye Gulsah EP1079, EP1070
Ozkan, Uygar P385
Ozkanbas, Necmettin EP935
özkara akkuş, feride P204
Ozkaya, Hande Mefkure EP1231
Özoğlu, Meryem P314, EP943, P486
Ozon, Alev EP1384
Ozono, Keiichi OC10.1
Özsu, Elif OC11.2
Öztunalı, Çiğdem EP1068
Ozturk, Feyza Yener RC5.4
Ozturk Unsal, İlknur EP1457, P489
Pabian, Gabriela EP79
Pacak, Karel **47**, OC7.2, EP1108
Pacakova, Slavka EP447
Pačesová, Petra EP1453
Pach, Dorota EP242
Pachucki, Janusz EP906
Packowska, Anna P306
Pacocha, Monika EP212
Paczkowska, Anna P503
Paczkowska, Katarzyna **EP651**
Padmanabhan, Mukund P36
Padovano Sorrentino, Francesco EP1069
Padrta, Tomáš EP1113
Paetow, Ulrich P305
Pagano, Loredana EP1455, EP189
Pagano, Paola EP1069
Pagin, Elena RC9.4
Paglia, Francesca **EP1130**, EP1066, P97
Pagnano, Angela EP246
Pagotto, Uberto EP459, EP394, P104, OC1.6, EP80, OC4.6, P323, P80, EP512, EP98, P2
Pailodze, Mariam EP355
Pailodze, Mariam **EP1443**, **EP1250**
Pailodze, Nino EP1250
Painter, Rebecca EP503
Paja, Miguel P267
Paja, Miguel **P79**, **OC10.3**
Pakosz, Marcin P240, EP1629
Pal, Aparna EP1181, EP1313
Palak, Ewelina EP468, RC4.5
Palanza, Paola OC8.2
Palavinkina, Ksenia EP1646
Palazzi, Sara P303
Palermo, Andrea **OC10.2**, OC10.1, OC12.4, P72, P97
Palha, Ana EP1449
Palioura, Eleni **EP1255**, **EP1335**
Pallapati, Anusha P361
Palm, Camilla Viola **P327**, **RC11.3**, P371, EP1360
Palma, August **P254**, **EP56**
PALMA, ISABEL EP1326
palmieri, serena OC7.2, P96, RC7.5, EP27, RC6.2
Palumbo, Chiara EP1055
Palumbo, Chiara EP1146
Palyga, Iwona EP1591
Palys, Karolina EP1416
Pambinezhut, Fathima EP1583, EP319
Pamporaki, Christina **EP100**, **P42**, P10, EP1790, P45, P19, P30, EP55
Pamporaki, Christina P445
Pan, Bailin EP1328
Pan, Chenhao P82
Pan, Xiaoxi EP1035
Pan, Xin EP31
Panagaki, Maria EP918, EP927
Panagiotopoulou, Andromachi EP139, **EP115**, **EP19**
Panagiotou, Athanasios EP332
Panasiuk, Anatol EP468
Panceraitė, Lina **EP4**
Pancini, Lisa EP1117
Panczak, Aleš EP273
Panda, Smritimayee **EP1091**, **EP215**
Pandelieva, Maria **EP1820**
Pandey, Amit **RC12.3**, **EP1760**
Pandit, Sucheta EP689, EP639, EP403, EP509, EP565, EP640
Pandozzi, Carla EP966
Pané, Adriana EP1096
Pang, Yingxian **EP59**
Panizo Fra, Javier EP1304, EP553, **EP492**, **EP493**, EP1478, EP199, EP784
Pankiv, Volodymyr EP404
Panseri, Nicole EP1173
Pantelia, Kalliopi EP519, EP591, EP237, EP139, EP115, EP1387, EP952, EP19
Paoli, Donatella P12
Paolucci, Giordano P24
Papadakis, Georgios OC3.4, RC10.6
Papadakis, Georgios P1
Papadakis, Nicos P100
Papadima, Christina EP918, **EP927**
Papadimitriou, Christos EP1733
Papadimitriou, Dimitrios **EP378**, **P179**, P343, P360
Papadimitriou, Dimitrios P445
PAPADOGIAS, DIMITRIOS P445
Papadopoulos, Charalampos EP1459, EP1859, EP1766
Papadopoulou, Anna EP231, EP239
Papadopoulou, Anna EP1365
Papadopoulou, Anna-Maria EP1594
Papadopoulou, Debbie EP363
Papadopoulou, Efthymia P182
Papadopoulou, Katerina EP1438
Papadopoulou, Nektaria RC10.1
Papadopoulou-Marketou, Nektaria EP239, P196, P213
Papakokkinou, Eleni P280, RC9.2
Papalexis, Petros EP1045, **EP1496**, EP25, P141
Papalou, Olga EP145, EP591
Papanastasiou, Labrini EP113, **EP192**, EP1594, EP1082, **EP1879**
Papanastasiou, Polyanthi P208, EP850, P182
Papanikola, Nektaria EP1363
Papanikolaou, Eleni EP39, EP1230, EP306, P90
Papapanagiotou, Angeliki P25
Paparodis, Rodis P192, P179, **P445**, P324, P343, P360
Papastergiou, George EP1594
Papathanassiou, Katerina EP729
Pape-Köhler, Carolina EP1479
Papini, Anna Maria OC8.2, OC8.5
Papotti, Mauro OC6.1
Papoulidis, Ioannis EP1877
Pappa, Dimitra EP597, EP852, P170
Pappa, Kalliopi EP654
Pappachan, Joseph EP182
Pappu, Sai Subrahmanyam **EP1780**, **EP1198**
Paragh, Gyorgy P389
Paragliola, Rosa Maria EP1451
Paranzini Miguita, Ana EP529
Parasiliti Caprino, Mirko OC7.2, P58, RC9.6, RC6.2, **EP497**
Paraskeva, Vasiliki EP850, P182
Parati, Gianfranco EP51
Paravani, Piero **EP1182**
Parazzoli, Chiara P27, EP51

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Pardi, Elena EP227, EP226, EP216
Parenti, Martina EP106
Pariente, Benjamin P452
Parizek, Antonin EP445
Park, Eon Chung EP1747
park, hajin **EP545**
Park, Hyeong-Kyu **EP411**
PARK, IE BYUNG **EP645**
Park, Jae Hyun EP1701
Park, Ji Yong EP1597, EP1670
Park, Jieun EP385
Park, Jong Suk **EP374**
Park, Joonseon P409
Park, Jung Hwan EP754
Park, Kye-Yeung EP754
Park, Min Jeong P44, P34, **P57**
Park, Na-Rae EP210
Park, Paul EP1106
Park, Se Hee P407, **P405**
Park, Seung Shin **P44**, P34, P57
Park, So Yeon P373
Park, Soyeon P44
Park, Soyeon P57
Park, Suzy **P507**
Park, Tae Sun EP1673
Parker, Chloe P353
Parkin, Nicola EP125
Parpala, Sanni P350
Parr, Nicholas EP260
Parra Barona, Juan Manuel EP1717
Parra-Ramírez, Paola **EP1125**, EP151
Parsa, Ashkan EP956
Parsons, Sue P254
Partyński, Bartosz EP954
Paschalidi, Charikleia EP192, **EP1594**, EP1082
Paschou, Stavroula A. **EP479**, **EP654**, EP1219, EP891
Pascu, Bogdan EP1358, EP1423, EP1615, EP730
Pascual, Alberto P346
Pascual-Corrales, Eider **EP275**
Pashkovska, Nataliia EP551, **EP542**
Pashkovska, Natalija EP664
Pashkunova, Sylvia EP600
Pasińska, Magdalena P252
Paskeviciene, Deimante **EP466**
Pasmant, Eric RC10.2
Pasquali, Daniela P334, P97
Passarelli, Marisa EP137
Passauer, Jens P30, EP55
Passos, Dolores EP69, EP351
Passos, Dolores EP1220, EP267
Pasteur, Ndikuriyo Herve OC7.5
Pastore, Angela RC3.3
Pastrana, Juan Carlos EP372
Pataco, Andreia EP325
Patel, Aaran P349, OC4.1, P351, OC4.2, P322, P325
Patel, Anjali EP1368
Patel, Bijal P351, OC4.2, P322, P325
Patel, Haridarshan EP1474
Patel, Leena EP34
Patel, Nitesh EP596, EP636, EP788
Patel, Priyankaa EP1164
Patelli, Ilaria P271
Paterlini, Silvia OC8.2
Pathak, Niranjan EP596, EP636, EP788
Pathak, Niranjan EP689, EP639, EP403, EP509, EP565, EP640
Pathmanathan, Sega EP2
Patil, Anish RC1.6, P449
Patil, Dipak EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Patil, Sandesh EP596, EP636, EP788
Patnaik, Lavina **EP396**
Patra, Shinjan EP502
Patrianakou Xanthakou, Eleni P445
Paul, Alexander **OC3.1**
Paul, Sayanti EP502
Paulino, André EP731
Paun, Diana EP771, EP122, EP1897, EP1887, EP1522
Pausch, Christine P269
Pavel, Elena-Maria EP1277, EP196
Pavlevska, Elena EP368
Pavlou, Eleftherios P25
Pavlovič Bačkorová, Barbora **EP91**
Pawlak, Tadeusz EP103
Paximadakis, Emmanouil P208
Payer, Juraj P114, EP701
Pearce, Elizabeth N. P416
Pearce, Mark RC5.2
Péč, Martin EP1121
Pecani, Marin **EP1635**, **EP683**
Pecci, Valeria OC12.1
Pecori Giraldi, Francesca P258
Pedral S. D. Leite, Luciana EP1047, P457
Pedro, Jorge P77, EP1450
Pedroli, Aurora OC11.6, P330
Pedrolli, Francesca P123, **EP1019**, P154, **P509**
Pedroncelli, Alberto M. **P266**, RC3.4, P274
Pędziwiatr, Michał P15
Peeters, Patricia EP12
Peeters, Robin RC1.1, OC8.6
Pegka, Sofia EP891
Pehlivan, Esma EP140
Pehlivan, Murat EP1755
Peirano, Loris P271
Peiró-Marqués, Francisca María EP1022, EP1011, EP1167, EP1124, EP1158, P263
Peischer, Lea EP1108
Peitzsch, Mirko EP100, P10
Peitzsch, Mirko P19, P30, EP55, P452
Peixe, Carolina EP731
Peixe, Carolina EP1449
Pejkov, Risto EP200
Pekic Djurdjevic, Sandra EP1464, **P297**, P120
Pekkolay, Zafer OC11.2
Pekmezci, Aslihan P33
Pekmezci, Aslihan **EP24**
pelaez, nazaret EP630
Pelineagra, Oriana EP1570
Pelineagră, Oriana EP1039, EP1105, EP1248
Pellegata, Natalia EP911
Pellegrini, Giulia P444
Pellegrino, Micaela EP219
Pellikaan, Karlijn P260
Pelosi, Annalisa OC8.2
Pelsma, Iris EP1067
Peltsverger, Maya Y. **EP281**
Pengo, Martino EP51
Penitenti, Julia P464
Pennisi, Grazia EP497
Pennlund, Anna P296
Pepe, Georgia EP1723
Pepe, Giorgia OC8.5
Pepe, Giorgia P112
Pepe, Jessica P96
Peppa, Melpomeni P207
Peppa, Melpomeni EP479
Perdomo, Carolina M. EP372, **EP602**
Perea Cortés, Jaime EP1145
Pereira, Alberto M. P250, EP973
Pereira, Beatriz R EP1220, EP267, **EP69**, **EP351**
Pereira, Francisco P457
Pereira, Ines P414, EP494
Pereira, Josué EP1123
Pereira, Leopoldina EP992
Pereira, Maria EP286
Pereira, Maria Teresa EP1027
Pereira Gregorio, Hugo EP1195
Peretianu, Dan **EP268**
Pérez, Paula EP1304, EP553, EP492, EP1478, EP199, EP784
Perez Algorta, Guillermo P146
Perez Bustillo, Alicia EP1306
Pérez Daga, José Antonio EP420
Perez Damasco, Paulo EP1171, **EP1746**
Pérez de Arenaza Pozo, Victor EP562
Pérez de Azpeitia, Leire P79, OC10.3
Perez Garcia, Leire **EP244**, **EP1789**
Perez Lopez, Paloma EP1195
Pérez López, Carlos EP1125
Pérez Machín, Paula EP493
Pérez Reyes, Pilar EP390, EP630
Perez-Chacon, Gema P346
Perez-García, Maria del Pino P497, EP1707
Pérez-Gómez, Jesús P210
Perez-Gonzalez, Beatriz P143
Pérez-Ricardo, Dania EP613
Perez-Rivero, Jennifer Maria EP1703, P498
Perlemoine, Karine RC9.3, P55, OC6.5
Perogamvros, Ilias P445
Perotti, Chiara P509
Perri, Carmela EP936, EP1314
Perri, Carmela **P391**
Perrone, Alessandro EP98
Perrone, Serafina OC8.5, P112
Perrotta, Adolfo Marco P97
Perry, Julie RC2.5
Persani, Luca EP1127, EP51, EP1347, P501
Pertaia, Lia EP1604
Pesant, Marie-Hélène RC11.2
Peshkova, Tamar EP1537, EP832
Pesic, Milica EP668
Pesonen, Paula OC4.3
Peters, Michaele P151
Petersenn, Erik RC8.4, **RC8.2**, EP97
Petersenn, Stephan OC3.4
Petignot, Sandrine EP1482
Petkova, Valentina P192, P445
Petraikin, Alexey EP1080
Petrák, Ondrej EP70, **48**
Petrakis, Ioannis P100, P94
Petrangeli, Elisa EP429
Petrescu, Catalina EP1897, EP1887
Petreski, Hristijan EP1895
Petria, Iulia EP1014, P315
Petričević, Fran EP1526
Petričević, Simona EP1748
Petrossians, Patrick P252, P305
Petrossians, Patrick EP1482
Petrova, Eugenia EP307
Petrovska, Lileia **EP712**
Petrovska, Natasha **EP314**

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Petrovskyy, Roman EP712
Petrovskyy, Taras EP712
Petryk, Anna OC12.4
Petta, Salvatore EP497
Pétursdóttir, Iðunn Valgerður EP1061
Peverelli, Erika OC12.5, EP1173, **RC7.5**
Peyronnet, Benoit EP14, P17
Pfeiffer, Andreas P494
Pfob, Christian P85
Pham, Tung EP222
Philipp, Schuetz OC3.4, EP1064
Philippidou, Constantina EP1459, EP1859, EP1766
Phillips, Susan P255, P256
Phylactou, Maria P349, OC4.1, P351, OC4.2, P322
Pia, Anna Rosa EP219
Piacentini, Andrea RC3.3, P272, EP94
Piaggi, Paolo EP1296, P84
Piaggi, Paolo EP216
PIANOU, NIKOLETTA EP237
Piasecka, Marta **RC9.2**
Piazza, Anna P104, OC1.6, P80
Piccione, Alessandra P258
Pichler, Mirjam EP1033
Pickl, Winfried P455
Pico, Antonio **EP1022**, **EP1011**, EP1167, EP1124, EP1158, P263
Piekielko-Witkowska, Agnieszka EP1137, EP1103
Pierides, Michael EP65
Pierotti, Laura EP226, P84
Pierotti, Laura EP227, P96, **EP216**
Pierre, Deprez EP127
Pierrepont, Zachary EP1468
Pierret, Aureliane P349, OC4.1, OC4.2, P322
Pierret, Aureliane **P351**
Pietrareanu, Oana EP961, EP1190
Pigliaru, Francesca OC12.3, P97
Pignata, Luisa EP150
Pignata, Luisa P24
Pigni, Stella **EP590**, **EP1048**
Pihan-Le Bars, Florence EP1860
Pilecki, Grzegorz EP369
Pilecki, Zbigniew EP369
Piltan, Parham P385
Piltonen, Terhi OC4.3, P350, EP1906
Pimentel, Bruna EP1458
Pineda-Torra, Ines RC6.3, OC2.6
Pinhas-Hamiel, Orit **P128**
Pinhas-Hamiel, Orit **P163**
Pinhasov, Albert EP395, EP499, P191
Pinheiro, Jorge EP1123
Pinna, Laura RC1.2
Pinto, Beatriz P77
Pinto, Diogo EP1098
Pinto Ribeiro, Rita EP245, EP286
Pirags, Valdis EP518
Pirana, Veronica EP1352
Pirard, Catherine RC8.3
Pirga, Iulia Alexandra **EP1462**
Pirvu, Raluca **EP961**, **EP1190**
Pisarnturakit, Pongthep EP315
Pisarska-Adamczyk, Magdalena P15
Pisconti Machado, Giovanna Voigt EP1750
Piscopo, Mariangela P12
Pisimisi, Maria EP1612
Pisimisi, Maria **EP177**
Piskinpasa, Hamide EP1092, EP121, EP1079, EP935, P394, EP1070, P110
Pistori Floriano Gerardi, Melissa EP529
Pitea, Marco P96, P97
Pitino, Rosa EP1138
Pitino, Rosa EP1215
Pitocco, Dario P367
Pitteloud, Nelly P346, EP1439
Pittrow, David P269
Pivonello, Claudia **EP400**
Pivonello, Claudia EP470, P169, P29
Pivonello, Rosario EP400, EP470, P169, **OC9.5**, P253, P29, P12
Piwońska-Solska, Beata EP1093
Piyadigama, Indunil EP401
Pizza, Gianmarco EP80
Pizzolanti, Giuseppe P462
Pkhaladze, Elisabed EP328, **EP345**, EP365, EP1609
Plachý, Lukáš EP350
Plakhetko, Solomiia **EP879**
Planchon, charlotte P508
Planck, Tereza P89
Planque, Mélanie P210
Platonova, Nadezhda EP1675, P215, P451
Plaza-Clavero, Rosa EP259
Plesca, Simina **EP950**, EP1491
Pletsch-Borba, Laura P494
Plomgaard, Peter OC2.5
Płoski, Rafał EP1137
Płoskonka, Ewa EP197
Plotton, Ingrid EP1366
Plummer, Lacey EP1343
Pnueli, Lilach P301, OC5.3
Pocaterra, Giulia EP1127
Podgórska, Joanna EP63
Podlewski, Jacek EP242
Podstawka, Oskar P27
Pofi, Riccardo P12
Pogliaghi, Gabriele EP51, P501
Poglitsch, Marko OC6.2
Pohrt, Anne P494
Poiana, Catalina EP214, EP903, EP1115, EP1672, EP1062
Poiana, Catalina EP917, EP961, EP893, EP1251, EP1190, EP68, EP757
Poiana, Catalina EP1247
Poiană, Cătălina EP1683
Poiană, Cătălina EP241
Poitou, Christine EP1002
Pojatić, Đorđe EP1466
Pokrzywa, Agata EP906
Polak, Michel RC3.3
Polański, Zbigniew EP1354
Polansky, Amir P129
Polat, Şefika Burçak EP84
Polat Korkmaz, Ozge EP270
Poldervaart, Rosalie **P260**
Poliani, Luigi P223
Polichroniadi, Despina EP589
Policola, Caterina EP1179
Politi, Letterio P466
Polito, Francesca P311
Poljičanin, Tamara P156
Polovina, Snezana **EP779**, EP1074
Pommie, Christelle EP1035
Ponczek, Michał B. EP1590
Ponikwicka-Tyszko, Donata EP468, RC4.5
Ponte, Maria **EP325**
Pontecorvi, Alfredo EP1055, EP347, EP1146, P298, EP1151, EP1057, EP1139, EP1069, P367, EP960
Pontecorvi, Alfredo EP1032
Pontecorvi, Alfredo EP1060, OC12.1, EP1451
Pontecorvi, Alfredo EP1179
Pontes Cavalcante, Isadora P55
Ponzetto, Federico **P58**, **EP1352**, EP497
Pop, Elena EP1012
Popa, Oana EP1570
Popov, Dmitrii EP413
Popovac, Hrvoje P222, EP910
Popovic, Bojana EP1311, EP900, EP43, P344
Popovic, Ilinka EP1560
Popovic, Petra EP668
Popovic, Tade EP1586
Popovic, Vera P297
Popovic Pejicic, Snjezana EP803, EP1425
Popovic Peric, Tamara EP1246
Popow, Michal EP220, P465
Porcel-Pastrana, Francisco P219
Porpodis, Konstantinos P182
Pórpora, César EP495
Pors, Susanne P338, P372
Pörsti, Ilkka P20, P35, EP61
Porter, John RC9.5
Portilla, Rommel P395
Porto, Edoardo P288
Portu, Jon P79, OC10.3
Posea, Ioana Maria EP1460, EP23, EP7, **EP112**
Poshi, Klodi EP1053, EP1237, EP364
Possieri, Corrado OC12.1
Posso Salgado, Paulina EP1037
Postelnicu, Ioana EP1062
Potasso, Laura OC5.1, P292, **P273**, EP1126, P275
Potorac, Iulia EP1482
Pouliou, Apostolia EP1596
Poutachidis, Anastasios EP1116
Poutanen, Matti RC2.3, P350
Powell, Connor EP1748
Pozo, Juan EP1804
Pozo-Relaño, María Isabel **EP909**
Pozza, Carlotta P358, P444, P12
Prado-Moraña, Teresa P188
Prasad, Valluri EP689, EP639, EP403, EP509, EP565, EP640
Prats Custal, Ariadna EP44
Prats-Escribano, Antonio P219, **P210**
Prauzińska, Magdalena P248
Pravin, Paul EP1881, EP1772
Precali, Antonia EP635
Preda, Cristina EP248, EP996, EP1491, EP1292, EP1337, EP159
Preda, Cristina EP950
Preda, Martina EP634
Preda, Veronica EP823, EP634, EP697
Preda-Ivascu, Monalisa EP68
Prehn, Cornelia P452
Premawardhana, Lakdasa RC1.6, P449
Prencipe, Nunzia EP1029, P315, P278
Prencipe, Nunzia **EP1186**, EP1030
Preston, Christopher EP222
Prete, Alessandro **49**, OC6.6, P27, RC9.5, P8, RC7.1
Prete, Alessandro OC1.5, P383, RC7.6
Pretorius, Mikkel P75

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Prevot, Vincent P346
Prie, Miruna EP196
Príncipe, Rosa Maria EP1123, EP483, EP238
Prinzi, Antonio RC6.2
Prinzi, Natalie EP1117
Priou, Mélanie EP1860
Prochazka, Jan EP399
Procopio, Massimo P96, P97
Procopio, Matteo RC6.2
Procopiuc, Camelia EP1251
Prodam, Flavia EP400, EP590, **EP1138**, **EP1215**, EP1048
Prodanov, Tamara OC7.2
Profka, Eriselda OC11.6, P330
Proikaki, Stella EP1592, EP123, EP1394, EP685, EP1241
Pronin, Evgeny **EP1080**
Pronin, Vyacheslav EP1080
Propato, Arianna P506, P464
Prosheva Bajraktarova, Tatjana EP1895
Prosperi, Daniela EP1182
Protas, Nadiia EP417
Protas, Yurii **EP417**
Pruidze, Ana **EP328**, EP345, EP365, EP1609
Psaltopoulou, Theodora EP654
Psaltopoulou, Theodora EP479
Psoma, Ourania EP722
Ptak, Anna EP1354, P354
Puar, Troy H OC6.3
Puar, Troy Hai Kiat OC6.4
Puca, Dea EP854
Puca, Edmond EP854
Puca, Entela **EP854**
Pugliese, Flavia EP337
Puglisi, Soraya RC6.6, EP95, P253, RC12.5
Pui, Roxana EP1657, EP194, EP1263, **EP507**, **EP834**, EP1515
Puig-Domingo, Manel P307, EP1025
Pulawska, Kamila EP468, RC4.5
Puliani, Giulia OC7.4
Puma Duque, Marco **EP1037**
Puntil, Simona EP966
Puocci, Gennaro P29
Purschke, Tobias P145
Puscas, Teodora **EP1277**, **EP196**
Puscasu, Diana EP1894
Puscasu, Irina EP248, EP996, EP1337
Pushkarev, Volodymyr EP901
Pusl, Thomas P85
Puszkiel, Alicja RC9.3
Qamar, Shakil EP1
Qamar, Sulmaaz EP1865
Qayum, Ambreen P351
Qayyum, Khurram **EP2**, **EP1728**, **EP1729**, **EP1279**, EP1490
Qi, Yanmei EP295
Qiao, Nidan **RC3.2**
Quaglino, Pietro EP95
Quartararo, Giovanni P506
Quattrocchi, Carlo Cosimo EP1754
Quehenberger, Peter P43
Queirós, Joana EP696, P414, EP494, EP1450, P400
Queirós, Joana EP525
Queiroz, Maiara P148
Quek, Timothy **EP710**
Quesnoy, Alexandre P55
Quinkler, Marcus EP1049, P5, P45
Quinn, Mark OC7.6, **RC6.1**
QUINTANA, JHON EP1898
Quintero Rodríguez, Óliver EP1304, EP553, EP492, EP493, EP1478, EP199, EP784
Quirke, Jo RC9.5
Quítalo, Ana EP1188
Quítalo, Ana EP1267
Qureshi, Asjid EP198
Qureshi, Nadeem EP1413
Racanelli, Vito EP265, EP1754
Rachabattula, Hyma EP1803
Radács, Marianna EP985
Rada-Iglesias, Alvaro P252
Radenković, Saša EP668
Radian, Serban EP68
Radian, Serban EP1062
Radic, Lena EP1311, EP900, EP43, **P344**
Radić, Nevena EP779, EP1074
Radocha, Jakub EP1533
Radojkovic, Milan EP668
Radojković, Danijela **EP668**
Radomir, Lidia EP757
Radomislensky, Irina P128
Radovic, Natasa EP146
Radu, Beatrice EP1615
Radulescu, Vlad EP1460, **EP23**, P382, EP7, EP112, **EP1149**
Radzeviciene, Lina EP466
Rae, Mick P332, OC4.5
Raffin-Sanson, Marie-Laure P285
Rafi, Samama RC5.1
Rafique, Shemitha EP1470
Raftopoulos, Christian EP1046
Ragazzon, Bruno RC9.3, P55
Ragia, Dimitra EP1592, EP123, EP1394, EP685, EP1241
Ragnarsson, Oskar P276, RC9.2, P484, P485
Ragnarsson, Oskar P14
Ragno, Erica OC12.3
Rago, Teresa OC1.5
Ragonese, Marta P311
Rahim, Mariam Mohammad EP303
Rahimi, Oshrit EP499
Rahman, Nafis EP468, RC4.5
Rahman, Shadman **EP1581**, EP1606
Rai, Ashutosh EP1084, P453
Raica, Marius EP1115
RAINGEARD, Isabelle P304
Raizada, Nishant P131, EP396
Raja Azwan, Raja Nurazni EP758
Rajadhyaksha, Manoj OC12.4
Rajasivam, Rubern EP103
Rak, Agnieszka EP1405, EP1324, EP1322
Rakhimzhanova, Marzhan EP796
Rakitzi, Litsa EP1796
Rakitzi, Litsa EP1704, EP1855
Rak-Makowska, Beata **EP1137**, EP480, **EP1103**
Rakusa, Matej **EP348**
Ralph, David EP1377
Raluca, Furnica **EP127**
Ram, Raja P320
Ramadan, Anoud EP45
Ramadoss, Vijay **EP65**
Ramanan, Ahimalaipet V EP224
Rambla Aguilar, Laura EP1535, P116
Ramesh, Nair EP363
Ramirez, Maria EP82
Ramona, Dobre EP1672, EP241, EP1062
Ramos, Maria José EP525
Ramos Perez, Lorena P143
Ramundo, Francesco EP960
Ramundo, Giada P2
Ranathunga, Ishara **EP1583**, **EP319**
Randazzo, Brian EP1117, **P288**
Randell, Tabitha EP34
Randeva, Harpal S. EP1756, EP589, P138, EP1348
Rangel, Maria RC5.3
Rank, Andreas P85
Rantakari, Pia EP1421
Rao, Ranganatha EP254
Raoof, Naz EP1700
Rapagnetta, Giorgia P431
Rasal, Yogesh EP689, EP639, EP403, EP509, EP565, EP640
Rasheed, Erum P377
Rashid, Fauiza EP1736, EP1903
Raska Jr, Ivan EP273
Rasmussen, Åse Krogh EP60
Rasmussen, Jon EP1334, P265
Rasmussen, Jon **EP1058**
Råstam, Jacob P266, RC3.4, P274
Ratti, Antonia P509
Raunioniemi, Peppi EP1075
Ravanos, Konstantinos EP1877
Raveendran, Subhara **EP1157**
Ravel, Guillaume RC10.4
Raverot, Gerald P285, P270, RC12.4
Ravi, Samyukta EP1418
Ravikumar, Aparna **EP103**
Ravindran, Ravikumar EP211
Ravio, Taneli **50**
Ravn Bach, Sara EP1360
Ray, Nilanjana EP860
Razzaqe, Huma **EP474**
Rea, Maria EP559, EP465
Real Fernandez, Feliciana OC8.2
Rebrova, Yanina **EP488**, **RC2.1**, EP156
Recalchi, Serena EP429
Reddy, D Amulya **EP391**, **EP1041**
Reddy, Gowry EP317
Redondo, Carmo EP494
Reel, Parminder P452
Reel, Smarti P452
Rees, Aled **P340**, RC9.5, P435, OC9.5, EP125, **EP158**, EP1348
Rees, John P435
Refael, Tal OC5.3
Refardt, Julie Celine OC3.4, OC5.1, P69, EP994, EP1081, P292, P273, EP1126, EP1109, P203, P275
Reguero Callejas, María Eugenia EP275
Reid, Heather **P66**
Reimondo, Giuseppe EP95
Reinberg, Marie EP1540
Reincke, Martin EP100, RC5.5, OC6.4, EP1108, OC5.5, OC3.2, EP1049, P28, EP33, **EP94**, P42, EP29, RC8.4, P10, OC6.1, RC9.1, EP1036, RC8.2, P19, EP97, P452
Reinke, Rasmus OC12.2
Reis Guiomar, Joana EP1285, EP291, EP974
Reisch, Nicole RC9.5, EP1108, OC3.2, **EP36**, RC9.1, P5, P21, OC9.6, P45, EP97
Rejnmark, Lars OC10.2, OC10.1, P72
Rejnmark, Lars P98, OC12.4
Rekalı Şahin, Humeyra P279, P291

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Rekhviashvili, Maia EP1207
Rekik Majdoub, Nabila **EP1627**, **EP787**, **EP608**
Remde, Hanna OC7.2, P30, EP55
Remfry, Jessica RC6.6
Remón Ruiz, Pablo EP1145
Ren, Gaofei EP1035
Ren, Yan EP32
Renard, Célia EP1366
Renault, Lucie EP1366
Renda Livraghi, Daniele **P358**, EP1329
Repaci, Andrea OC1.6, P80
Resta, Maria EP1796
Reul, Astrid EP1108
Reusch, Jürgen EP1228
Reva, Darina **20**, **51**
Reyhan, Ekin P385
Reynaldo, Valeria EP1073
Rezq, Samar RC4.4
Rezvanisanijouybari, Parisa OC6.2
Rhee, Sang Youl **52**
Ribeiro, Cristina EP611
Ribeiro, Isabel EP1027
Ribeiro, Rita EP386, EP1589, EP632
Ribeiro, Vinicius **EP388**, EP371
Ribeiro De Oliveira Longo Schweizer, Júnia RC5.5, EP1049, P28, EP33, EP29, RC8.4, P457
Ricci Bitti, Silvia EP394
Riccobene, Federica **EP1562**
Richa, Carine P242
Richer dit Laflèche, Christophe **EP408**, **RC11.2**
Ricke, Jens P28, RC9.1, EP97
Riehle, Friederike OC5.2
Riester, Anna OC3.1
Rigamonti, Cristina EP590, EP1215
Rigana, Maria EP1255
Rigante, Mario EP1055, P298
Righi, Beatrice OC8.2
Rimkute, Agne EP20
Rinaldi, Mauro P123
Rios, Ana Cristina EP1098
Rios Vergara, Antonio P402
Risio, Alessandro **EP163**
Risovic, Ivona EP1441, EP1235
Risovic, Ivona EP1246, EP1177
Risson, Jean-Romain EP72
Ritter, Jacob EP1818
Ritzel, Katrin RC5.5, EP1049
Riveline, Jean-Pierre P458
Rivera, Wilfredo EP82
Rivera Ramirez, Juan Andres EP1684
Rizikou, Despoina EP889, **EP819**
Rizk, Marthe P55
Rizoulis, Andreas P192, P445
Rizzi, Alessandro P367
Rizzoti, Karine **53**, P346, OC5.3
Roa-Parra, Maria EP1465, **EP1511**
Robalo, Brigida RC5.3
Robalo, Brígida RC4.6
Robenshtok, Eyal P429
Roberts, Eiry OC9.5, P21
Roberts, Mary Scott OC10.4, OC10.1, P72
Robeva, Ralitsa **EP1386**, **EP1380**, P324, P343, P360
Robinson, Adam EP1119
Robledo, Mercedes EP1108, EP1790
Roca-García, Jesús RC6.3, OC2.6
Roca-Rodriguez, Maria del Mar EP995, EP841
Roccuzzo, Gabriele EP95
Rocha, Carla EP525
Rocha, Debora **P148**, EP393
Rocha, Gustavo EP457, EP992
Rocha, Jose EP731
Rocha, Thais P. EP1348
Rochira, Vincenzo EP1130, EP1066, EP62, P13, P97, EP1329
Rochira, Vincenzo P253
Rodari, Giulia **OC11.6**, **P330**
Roderick, Marion EP224
Rodien, Patrice P21
Rodionov, Gennady EP1749
Rodová, Marie EP1453, EP1521, P419, **P375**
Rodprasert, Wiwat **P357**
Rodrigo, Maite OC6.5, P83
Rodrigues, Dírcea EP974
Rodrigues, Dírcea EP1285, EP206
Rodrigues, Fernando EP1501
Rodrigues, Gustavo EP974, EP1168, EP206, **EP611**
Rodrigues, Ilda P77
Rodrigues, Leonor EP206, EP1120
Rodriguez, Ana Belen OC4.4
Rodríguez, Javiera EP1158
Rodríguez, María P195
Rodríguez, Veronica Engracia EP1735
Rodríguez Díaz, Cristina EP467
Rodriguez Elena, Gonzalez RC10.6
RODRIGUEZ FERNANDEZ, CARMEN EP1306
Rodriguez Fernandez, Selena EP1304, EP553, EP492, EP493, **EP1478**, **EP199**, **EP784**
Rodríguez González, Francisco EP467
Rodríguez Hernández, Orvelindo EP492
Rodríguez Mangas, Covandonga EP924
Rodríguez Morales, Jonay EP924
Rodríguez Sosa, Elena EP553, EP492, EP493
Rodríguez-Bedoya, Maria **EP1158**, P263
Rodriguez-Cruz, David EP1835
Rodríguez-García, María P195
Rodriguez-Martin, Andrea **OC4.4**
Rodriguez-Peralvarez, Manuel EP909, EP425
Rodríguez-Soto, Josune P79, OC10.3
Rodzoń-Norwicz, Małgorzata EP1463
Roethlisberger, Michel OC3.4
Rogowska, Jagoda Alicja EP1169
Rojas López, Tatiana **EP151**
Rojekar, Satish P361
Roland, Coras OC3.1
Roli, Laura EP62, P13
Rolighed, Lars P108, P98, OC12.2
Rolla, Malgorzata EP1192
Rolla, Roberta EP590
Roman, Alejandro EP1898
Romanet, Pauline P304
Roman-Gonzalez, Alejandro **EP1804**, **EP82**
Romani, Jennifer EP1750
Romanisio, Martina EP1138, EP1215
Romano, Alessandro **EP347**, EP1451, EP1179
Roman-Torres, Karisse EP526
Romberg, Christina **P203**
Romero, Damian **54**, **RC4.4**
Romero Merino, Paolo Augusto **EP1054**, **EP990**, **P395**
Romero-de la Rosa, Beatriz P346
Romero-Márquez, José Manuel EP609, EP443
Rømhild Davidsen, Jesper EP1360
Ronchi, Cristina L **OC6.6**, **P27**, RC6.6, OC12.5, RC6.4
Rontogianni, Phivi EP237, EP1265
Rosenblum, Marc EP1676
Rosendal, Christian P249, **EP1147**
Rosengren, Annika P484
Rosenkilde, Mette P328
Rosenzweig, Tovit **EP395**, **EP499**, **P191**
Rosiek, Violetta EP955, RC7.3
Rosińska, Magdalena EP1547
Roslan, Nurhanis Syazni EP758
Roslon, Marek EP1795
Roslyakova, Anna EP1675, **P215**
Ros-Mazurczyk, Malgorzata OC7.1
Ross, Ian **EP157**
Ross, Richard RC9.5
rossetti, rebecca EP501
Rossi, Gian Paolo P452
Rossi, Mattia EP189
Rossini, Alessandro P96
Rossini Murakami, Alexandre EP529
Rossmeisl, Martin EP399
Rosso, Chiara EP497
Rostomyan, Liliya P305
Rosu, Mihaela EP93, EP129
Roszczyk, Radoslaw EP183
Roszko, Kelly EP260
Roszkowska, Zuzanna EP906, EP1416, **EP183**, EP928
Rotaru-Wagner, Mara Patricia **EP1744**
Rotermund, Romand OC3.1
Roth, Christian L. P255, P256
Rotman-Pikielny, Pnina EP916
Rotolo, Laura **OC4.6**, **P323**
Rotondi, Silverio P97
Rotteglia, Cecilia OC8.2
Rougemont, Anne-Laure P1
Rouni, Georgia P471
Rouskas, Pavlos P208
Rouwette, Tom P293
Rowe, Charlotte **P68**
Rowe, Charlotte P66
Roxana Ioana, Dumitriu EP1115
Roy, Aparajita **EP52**
Roy, Ayan **EP502**
Roy, Diya EP1084
Roy Chaudhuri, Soumyabrata **EP752**
Rubin, Katrine OC4.3, EP1316
Rubin, Mishaela OC10.2, OC10.1
Rubinstein, German EP1049
Rubio Tenor, Angela **RC6.3**, OC2.6
Ruchala, Marek EP1056, EP402, EP561, EP1187, EP377, EP912, P49, EP868, P106
Rudaz, Serge EP80
Rudin, Deborah EP1081
Rudin, Deborah OC3.3, EP1064
Rudman, Yaron P268, RC3.5, EP1132
Rudman, Yaron P316
Rudnieva, Ilona **EP1618**, **EP1650**, P167, **EP866**
Ruf, Enam **EP1485**
Ruf-Zamojski, Frederique OC5.6
Ruggeri, Rosaria Maddalena OC7.4, P96, P97
Ruiz de Adana Navas, María Soledad EP420
Ruiz-Campos, Nerea EP405
Ruiz-Pino, Francisco P346, OC4.4
Ruka, Maren EP1278
Ruohonen, Suvi RC2.3
Ruotolo, Elena P97, P84
Ruseva, Zhenya **EP1040**, EP1708, **EP1301**
Rushatamukayanunt, Pradit EP315

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Russell, Georgina P38
Russo, Antonino **EP265**, **EP1754**
Russo, Flaminia EP1224
Russo, Matteo EP429
Russo, Valentina EP559, EP465
Rusu-Zota, Gabriela P491
Rutkowska, Aleksandra **OC8.1**
Ryan, Fiona EP34
Ryan, James EP581
Ryan, Laura P377
Ryba, Alice OC3.1
Rychlik, Ivan EP1404, P103, EP1408
Rydzanicz, Małgorzata EP1137
Rymuza, Julia EP1232
Ryu, Hyun Jin EP517
Ryu, Ohk-Hyun **P178**
Ryu, Vitaly P361
Ryznychuk, Mariana **EP1211**
Rzepecka, Agata **P93**
Rzepka, Ewelina P6, P262, EP1814
Sá, Juliana EP245, EP286
Saad, Ghada EP1156, EP1487, EP571
Saad, Ghada EP75, EP1499
Saad, Ghada EP835
SAAD, TOMER **EP896**
saafi, wiem EP1156
saafi, wiem EP75, EP1499, EP835
saafi, wiem EP1487, EP571
Saarela, Ulla EP1906
Saavedra, Ana EP1816
Saba, - **EP302**
Saba, Francesca RC1.2
Sabbadin, Chiara P56
Sabbadin, Chiara EP190
Sabio, Guadalupe P346
Sabirov, Askar EP724
Sabunciyan, Sarven EP499
Sackewicz, Agata P221
Sadovskaya, Viktoria **EP1719**
Saeed, Sawsan EP1350
Saeed BiAllah, El-Muhtadi EP109
Safdar, Sidra EP300
Saffari, Seyed Ehsan OC6.3
Sagan, Karol EP1024
Sagarribay, Amets EP1220
Sagimbayeva, Madina **EP287**
Sagone, Noemi P97
Ságová, Ivana **EP1121**, P363
Şah Ünal, Fatma Tuğçe P176
sahay, rakesh EP1780, EP1198
Sahbaz, Anisa **EP1856**
Sahin, Mustafa EP1542, EP1042
Sahin, Mustafa EP1154, P204
Sahin, Serdar EP1231
Sahin Kimyon, Ozge EP1092, EP121, EP1079, EP935, P394, EP1070, P110
Sahoo, Banshidhar EP689, EP639, EP403, EP509, EP565, EP640
sahoo, Bansidhar EP596, EP636, EP788
Saidova, Farida **EP1605**
Saiegh, Leonard EP1025
Saienko, Yanina EP488, RC2.1
Saienko, Yanina EP156
Sailer, Clara EP1081
Sakai, Yasuna P174, P185
Sakali, Anastasia-Konstantina EP597, EP852, EP5, EP1596, EP327
Sala, Elisa EP957, **P286**, EP1014, EP1044
Saladino, Andrea EP1152, P288
Salah, Marwa **EP1510**, **RC8.6**
Salama, Bahaa OC6.4
Salami, Halimah P339
Salcedo Allende, Maria Teresa P143
Salehi, Mahdi OC7.2
Salehi, Parisa P142
Salenave, Sylvie P242, P304
Sales, Daniele EP1678
Sales, Filipa EP1816
salhi, houda EP255
Salimkhanov, Rustam EP1544
Salko, Olga EP620
Salle, Laurence P458
Salman, Serpil EP1743
Saltiki, Katerina **EP1476**, P461
Salvador Peiro, Natalia EP1535
Salvatori, Roberto OC5.5, EP1047, P457
Samakidou, Georgia EP1541
Samara, Chrysoula EP192
Samaranayake, Dulani EP401
Samarasinghe, Dhiraj EP222
Samardzic, Vladimir EP1560
Samaritani, Virginia P104, P80, **P2**
Sambak, Patryk EP1322
Saminga, Nurshadia P228
Samiotaki, Martina P471
Samoš, Matej P363
Samoš, Matej EP1121
Sampaio, Francisco EP261
Samsel, Radosław P51
Sanchez, Diana EP1804
Sanchez, Maria EP1804
Sanchez, Yamila EP899
Sánchez, Elena EP487
Sánchez, Marta EP1835, EP1706
Sanchez Crespo Juarez, María EP582
Sanchez Garcia, Ana Maria P450, EP1742, EP1776, EP1777
Sanchez Gaya, Victor P252
Sánchez-Gallego Alonso, Macarena EP492, EP493, EP1478, EP199, EP784
Sanchez-Garrido Nogueras, Miguel Angel OC4.4
Sanchez-Hernandez, Rosa María EP1805
Sánchez-Iglesias, Sofía P188
Sanchez-Ortiga, Ruth EP1124
Sánchez-Prieto Castillo, María EP1630
Sandbu, Rune P75
Sandrine, Lemoine OC10.1, P72
Sanfuentes, Benjamín EP30
Sankar, Adhithya EP1222, EP993, EP1119
Sankaran, Lakshmi EP143
Sanmartín Sánchez, Alicia EP1191
Sansano, Elena EP1158
Sanson, Lidiana EP491
Sansoni, Veronica P73
Santamaria, Susana EP821
Santamaría, Alejandra P79, OC10.3
Santamaría-Quiles, Alicia RC6.3
Santamaría-Quiles, Alicia **OC2.6**
Santambrogio, Alice OC7.6
Santana, Barbara P457
Santana, Nathalie P457
Santana Soares, Beatriz OC3.4, EP1047
Santana-Ojeda, Borja P450, EP1703, **EP1833**, P497, EP1742, EP1805, EP1776, **EP1777**, EP1841, **EP1835**, EP1707, EP1773, EP1706, P498
Santi, Daniele RC4.1, P358, EP575
Santillan, Cintia EP1205
Santini, Ferruccio EP1296, EP106, EP1291, P312, P24
Santos, Ana P EP947
Santos, Beatriz EP1750
Santos, Caridad EP783
Santos, Elenilde G. P457
Santos, Jacinta EP1501
Santos, Maria Joana EP1589
Santos, Maria Joana EP286
Santos, Rita EP856
Santos, Sara EP947
Santos Vives, Alicia P280
Sanyal, Debmalya EP752
Sanz Pascual, María del Carmen EP275
Sapalidis, Konstantinos EP1855
Saracyn, Marek P211
Saraiva, Catarina EP1458
Saraiva, Joana EP974
Saraiva, Miguel EP1326
Saravinovska, Kristina EP444, P67, EP149, EP1351
Sardella, Chiara EP227, P96, EP226, EP216, P84
Sarer Yurekli, Banu EP1204, EP140
Sari, Ramazan EP1743
Sarı, Abdulkadir P204
Sarigianni, Maria EP1116
Sarmento-Cabral, André P219, P210
Sarmiento-Ramón, Juan EP1465, EP1511
Sarnecki, Michal **RC3.3**, EP94
Sarria Estrada, Silvana Isabel P307
Sartori, Chiara OC8.2
Sarwar, Humma P71
Sas, Karolina EP963
Sasai, Yumiko EP1294
Sasikanth, Thanikai **EP1756**
Sassi, Marina EP113, EP192, EP1594
Sasson, Liat **EP1240**
Satman, Ilhan EP1743
Satta, Andrea P84
Saudelli, Enrico EP459, P80
Saudelli, Enrico **EP512**
Saugar, Elaine **EP938**
Šauperl, Aleksandra P149
Savagner, Frederique RC10.2
Savarese, Gabriele P444
Savas, Furkan EP1711
Savelberg, Angelique **OC5.1**
Sävendahl, Lars P228
Savey, Véronique EP1002
Savic, Suzana EP1246
Savkovic, Sasha RC4.2
Savvidis, Christos EP1592, EP123, EP1394, EP685, EP1241
Sawicka-Gutaj, Nadia EP561, EP1187
Sayadi, Hanene **EP1632**
Saydam, Simge RC5.4, **EP1070**, **P110**
Sayer, John OC10.1
Sayers, Niamh P478
Sayfi, Suhrab P118
SAYGILI, Emre **RC6.6**, RC3.6, EP1131
Saygılı, Emre Sedar EP1346, P194
Sayım Aydoğan, Kübra **RC5.4**
Saylam, Barış P410
Sbardella, Emilia EP1026
Sbiera, Silviu OC7.3, OC3.1, OC12.5, OC6.1
Scacchi, Massimo P501

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Scaglione, Luca EP1030
Scala, Andrea EP966
Scaroni, Carla P253, EP1025
Scatolini, Maria P223, RC12.5
Scepanovic, Vuk P297
Schaaf, Ludwig EP973
Schally, Andrew V. EP1019, P509
Schauer, Marc Philipp **OC7.3**
Schedl, Andreas OC9.1
Scheller, Lukas EP463
Schellino, Roberta P509
Schembri, Jake **EP209**, EP225
Scherer, Martha P447
Scherer, Thomas EP54
Schernthaner-Reiter, Marie Helene EP54, EP50
Scheundel, Ronny EP15
Scheyer, Nicolas **P272**, EP1075
Schiffer, Lina **P151**
Schilbach, Katharina RC5.5, OC3.4, EP1108, OC5.5, P228, P269
Schillaci, Ilenia EP512
Şchiopu, Alina-Elena **EP1292**, **EP159**
Schipor, Sorina EP318
Schiteanu, Cosmina **EP234**
Schmid-Tannwald, Christine P28, EP33, EP29, RC9.1, EP97
Schmitt-Böhrer, Angelika P71
Schnabel, Dirk P269
Schnait, Franziska **EP50**
Schneider, Holger P452
Schommers, Aurélien **EP1482**
Schovanek, Jan P81
Schrader, Joerg EP911
Schreiber, Anna Lynn **P5**
Schrenk, Moritz RC9.1
Schrenk, Moritz **EP1036**
Schriber, Aleksandra EP317
Schuchmann, Luzi Sophie EP1907
Schulz, Stefan EP1077
Schulze, Manuel EP100, P10, P30, EP55
Schutte, Teun P293
Schwartz, Yair P305
Schwarz, Peter OC10.2
Schweizer, Júnia R.O.L. **OC5.5**
Sciarra, Francesca EP966, EP1026
Sciarroni, Elisabetta EP106, EP1291, P312
Scillitani, Alfredo P96, EP337, EP27, EP51
Scimia, Cecilia P255, P256
Scopa, Chiara OC8.2
Scordo, Marianna EP150
Scordo, Marianna P24
Scott, Mari-Anne EP554
Scott, William P151
Scott-Coombes, David P435
Scozia, Gabriele EP559, EP465
Scurati, Samuele P58
Scutari, Maria OC1.5
Sealfon, Stuart OC5.6
Secener, Ali Kerim OC12.5
Seçgin Demir, Ece **P314**, EP943, **P504**, P486
Šeda, Ondřej OC10.5, **P132**
Sedda, Francesca EP1709
Šedová, Lucie **OC10.5**, P132
Seegoolam, Mohammad Zaid **EP1493**
Seekjær, Mathilde OC12.2
Seelig, Eleonora OC11.3
Seetho, Ian P118
Sefraoui, Lamia P55
Segarra Balao, Ana **EP830**, **EP1630**, **EP851**
Segev, Adrian EP395
Segni, Maria P305
Ségrestin, Bérénice EP1002
Sehgal, Shivali EP1810
Seidensticker, Max P28
Seiffert, Jacqueline EP222
Seki, Yasufumi EP37
Selivanova, Lilia EP1080
Seljelid, Berit EP1136
Sells, Taylor EP1106
Selvatico, Gloria EP1455
Selvi Gunel, Nur EP1204
Seminara, Stephanie EP1343
Sen, Suparna EP395
Senanayake, Russell EP96, RC6.5
Şenay Özçalık, Merve **EP292**, **EP1481**, **P173**
Sendur, Halit EP41
Sendur, Suleyman Nahit P317, EP1239, P16, EP1111, P295, EP1384
Senel, Samet EP84
Senesi, Pamela EP1665
Seneviratne, Sumudu P228
Senger, Carolin P284
Senoymak, Mustafa Can P130
Senra, Catarina EP325
Seo, Min-Hee EP614
Seong, Moon-Woo RC2.4
Sepp, Krisztian **EP985**, EP1006
Sepulveda, Gian EP1106
Sequeira, Vasco P71, RC11.1
Serakinci, Nedime EP934
Serebro, Merav EP1107, P268
Seren, Nazlican EP1204
Serpa, Nelyana de Oliveira P235
Serra, Mercè EP1096
Serra Soler, Guillermo EP1191
Serrano, Joaquin EP1167, EP1124, P263
Serrano García, Francisco Javier EP390
Serrano-Jiménez, María **EP425**
Serrano-Lopez, Victor OC4.4
Sertons, Yaël **EP1344**
Serup, Matias RC11.3
Serzhenko, Sergey EP1540
Sesti, Franz EP966, P444, RC6.2
Settanni, Fabio P58, EP1352
Seufert, Jochen P266, P274
Severino, Mariana EP731
Sevillano-Collantes, Cristina EP46, EP1535, P116
Seweryniak, Piotr EP756
Seydaoğlu, Gulsah EP1815
Seyfried, Florian EP463
Sezerman, Osman Ugur P442
Sfakiotaki, Maria P100, P94
Sfikakis, Petros P25
Sha, Wei EP1019, P509
Shaba, Enxhi P311
Shabaan, Balqees OC6.6
Shafiq, Taimoor EP878
Shafqat, Muhammad murtaza EP925, EP300
Shah, Akash EP596, EP636, EP788
Shah, Dareen EP1368
Shah, Manish **P162**
Shah, Najeeb EP2, EP1729, EP1279, EP1490
Shah, Nalini P305
Shah, Shalin EP596, EP636, EP788
Shah, Shruti EP1170
Shah, Usman EP768
Shaharyar, Amal EP208
Shahat, Ghofran EP180
Shahbazyan, Satik **EP1411**
Shaheen, Fozia OC6.6, EP10, EP38, EP1348
Shahinas, Edenisa EP1053
Shahsuvarov, Oruc EP1605
Shaikh, M Guftar P228
Shaikh, Sibhghatulla EP692
Shakeel, Nehan **EP1**, EP419
Shalamanova, Liliana EP441
Shamansurova, Zulaykho EP1331, EP724, EP777
Shamansurova, Zulaykho EP777
Shamsaldeen, Mohammed EP42
Sharian, Karineh **EP544**
Sharif, Sireen EP406, RC2.2
Sharma, Angelica OC9.4
Sharma, Ankita P36
Sharma, Bhavna **EP1810**
Sharma, Jayant EP419, EP1848
Sharma, Maryada P453
Sharma, Prabhat EP596, EP636, EP788
Sharman, Philippa P23
Shazra, Mariyam **P37**
Shchubelka, Khristina EP1012
Shea, Heidi P142
Shehu Kolnikaj, Tea **EP1278**
Shelever, Sofiia EP1307
Shen, Yanting OC7.2
Shende, Prakash EP596, EP636, EP788
Sheng, Zhujun P459
Shepelkevich, Alla **P355**, **EP838**, **EP310**
Shepelkevich, Alla **EP1372**, **EP1373**
Shepelkevich, Catherine EP1372, EP1373
Shereen, Ezzat EP1684
Sheremetyeva, Elizaveta P351
Sherlock, Mark **55**, EP10, P283, P259
Sherlock, Mark EP38
Sherriffs, Anna OC4.5
Shervashidze, Tamar EP1537, EP832
Sherwin, Olivia RC5.6, OC5.6, OC7.6, OC3.6
Sherwin, Olivia **OC5.4**
Sheth, Grishma EP1418
Shetty, Apurva EP596, EP636, EP788
Shi, Bimin EP32
Shi, Luming OC6.3
Shiju, Sharon EP1674
Shil, Kishore P448
Shimon, Ilan P268, P316, EP1240, EP1132, EP896
Shimon, Ilan P429
Shimon, Ilan RC3.5
Shinkov, Alexander EP1380
Shinwarie, Zalanda P339
Shishkov, Savi EP1040
Shiyam Sundar, Lalith Kumar EP97
Sho, Hiroyuki P174, P185
Shochat, Tzipora P268, P316, EP1170
Shodikulova, Gulandom EP1749
Shoemaker, Ashley P255, P256, P142
Shonia, Natia EP353
Shore, Angharad EP1573
Short, Jacob **EP1909**
Shorten, Lucas P9
Shoshiashvili, Inga EP355
Shraga-Slutzky, Ilana P109
Shu, Aimee OC10.2

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Shu, David EP1008
Shuka, Anila EP1631
Shukla, Jitendra EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Shulhai, Anna-Mariia OC8.2, OC8.5, P112
Shykula, Solomiia **EP527**
Shyti, Erkena EP1514, EP1667
Siampanopoulou, Vasiliki EP1045, EP1496, EP1262, EP25, P141, EP1723
Siatra, Panagiota OC9.3, **OC9.1**
Sibilla, Michela EP1029, EP1186, **P315**, P278
Sibley, Christopher OC10.2
Sicilia, Ida OC1.6
Siddique, Huriya EP925, EP300
Siddiqui, Fatima **P107**
Sidelnyk, Nadiia **EP578**
Siderova, Mira EP1040, EP1301
Siderova, Mira EP1708
Siegelaar, Sarah EP92, EP503
Siegenthaler, Judith EP1064
Siemienowicz, Katarzyna P332, **OC4.5**
Siemiński, Mariusz EP939
Sigala, Sandra P223, RC7.5
Siggelkow, Heide **P72**
Sighakoli, Sameer EP1581, EP1606
Signore, Alberto EP1182
Sigthorsson, Gudmundur EP49
Sigurjónsdóttir, Helga EP49, **EP1061**
Siles-Guerrero, Víctor **EP609**, **EP826**, **EP884**, EP443, EP890, EP535, EP601, EP550
Siligato, Damiano EP1001, EP152
Silva, Angela P457
Silva, Beatriz P77
Silva, Bruna EP245
Silva, Bruna EP1816
Silva, Camilo EP602
Silva, Cláudio EP1450
Silva, Diana Alexandra Festas EP696, P77
Silva, João EP495
Silva, Leandro Augusto **EP1501**, **EP944**, **EP1285**
Silva Fernandez, Julia EP390
Silva Gadelho, Luís **EP457**
Silva Jordan, Raysha Shirley EP1054, EP990
Silverstein, Julie M. P266, P274, EP1676
Silvestre de Souza Trigueiro, Nicholas EP137
Sim, Min Seop RC2.4
Sim, Sing Yang EP73
Sim, Sing Yang EP1194
Simeakis, George P192, P445, **P426**
Simeoli, Chiara EP1075, EP470, P169, **P253**, P29
Simeoli, Chiara P12
Simjak, Patrik EP445
Šimková, Markéta EP86
Simó, Olga EP435
Simo Canonge, Rafael P143, EP435
Simon, Godwin EP658, EP937
Simón-Frapolli, Víctor **EP674**, **EP869**, **EP845**
Simoni, Manuela **56**, RC4.1, P358, EP575, P391, EP936, EP1314
Simoniene, Diana EP466, **EP853**
Šimonienė, Diana EP339
Simó-Servat, Andreu P267
Sims, Steven P361
SIMSIR, ILGIN EP1843
Simunkova, Katerina P38
Singayar, Carolina Shalini EP758
Singh, Apinderpreet EP1084, P453
Singh, Manish EP596, EP636, EP788
Singh, Sarishka **P423**, **EP1644**
Singh, Smita EP1810
Singhal, Vaibhav EP215
Sinha, Aakansha P113
Sinha, Aakansha EP746
Sinha, Akshat P339
Sinik, Marija EP1560
Sinka, Rita P341, EP1370
Sinni, Dimitra **EP649**, EP453
Siolos, Athanasios EP729
Siori, Dimitra P90
Siracusano, Giordana EP1001, P258, EP152, P311, EP1229
Siragusa, Giuseppe P462
Sirbegovic, Ilma EP1856
Sirbu, Anca EP336
Sirek, Aleksandra **P354**
Sirkova, Aneliya EP940, EP1854
Sisó, Marina EP1096
Sitarz, Katarzyna EP79, P32
Sitch, Alice J. RC7.1, EP1348
Sitkin, Ivan P451
Sjölin, Gabriel P89
Skakkebæk, Niels Erik P357
Skalicky, Petr EP1141
Skariah, Naina EP855
Skoczyńska, Anna **EP1590**
Skodova, Tereza **EP1165**, EP1141, EP86, P224, EP445
Skoglund, Thomas P276, P296
Skogseid, Britt RC6.5
Skordilis, Kassiani OC6.6, RC6.4
Skoric Polovina, Tanja P222, EP910
Skøttrup Christiansen, Louise EP1360
SKOUTAS, DIMITRIOS P207
Skouvaklidou, Elpida EP1508
Skov, Jakob **P384**, EP11
Skowrońska-Szcześniak, Anna **P465**
Škrlec, Ivana **EP1466**
Skrzypski, Marek P140
Skytte, Jacob Lercke P338, P372
Slashchuk, Konstantin EP1540
Sleiman, Patrick EP1106
Śliwka, Przemysław EP1452, P240, EP1629
Sloka, Natalia EP1192
Smaha, Juraj **EP701**
Smarandache, Romeo P382
Smeeton, Fiona EP1051
Smith, Alden EP1157
Smith, Diarmuid EP10
Smith, Ella EP1164
Smith, Jennifer EP526
Smith, Lyndsay OC10.4, EP260
Smith, Paul P151
Smith, Terry OC1.3
Smokovski, Ivica EP1611
Smoleń, Sylwester P240, EP1629
Snaterse, Guy EP1344
Snoep, Jacky P151
Soares, Ana Rita EP483
Soares, Pietra P77
Soares, Raquel P77
Sobanski, Vincent P9
Sobczuk, Joachim EP651
Sobirjonova, Oyshabonu **EP724**
Sobolewska, Joanna EP1238
Sobral, Ana Margarida **EP291**, **EP974**, EP1168, EP206, EP611, EP1120
Society for Endocrinology, UK, CAHASE2 investigators EP158
Söderling, Jonas EP11
Sohail, Hafiz EP1
Sohail, Hafiz Muhammad **EP419**
Sojat, Antoan Stefan EP444, P67
Šojat, Dunja EP793, EP794, EP1680
Sojka, Paweł **EP1162**
Sokmensuer, Cenk P16
Sokolova, Anastasiia **EP531**
Sokolova, Liubov EP901
sokolovska, jelizaveta EP518
Sokolowski, Grzegorz P3
Sola, Chiara **RC9.6**
Solak, Mirsala **P222**, EP910
Solanki, Sam RC5.1
Solari, Sandra EP30
Soldat Stankovic, Valentina EP803, **EP1425**, EP1246
Soledispa, Nicole EP1073
Soler-Humanes, Rocío EP405
Soliman, Ashraf EP546, EP987, EP667, EP142, P369, EP1214, EP653, EP1371, EP576, EP432, EP749
Soliman, Nada EP653, EP1371, EP749
Soll, Dominik P284, EP1818
Solmi:, Beatrice OC4.6, P323
Solnica, Bogdan P226
Solodovnikoff, Margarita P322
Solovey, Mariana P305, **EP1159**, **EP1902**
Somogyi, Anna **EP1507**, P389
Son, Heejun **RC2.4**
Son, Jang Won EP748
Son, Youngho EP418, EP427
Sonawane, Ashutosh EP689, EP639, EP403, EP509, EP565, EP640
Sonawane, Dr. Dipesh **EP596**, **EP636**, **EP788**
Sone, Masakatsu P53
Song, Han EP739, P172
Song, Mosea **EP1180**
Song, Sun Kyung EP1670
Song, Xiaoxiao **EP31**
Songsaeng, Dittapong EP315
Sonmez, Alper EP1743
Sonmezoglu Kutuk, Irem **P321**, **EP656**, EP1797, **P440**, P500, EP1886
Sonnet, Emmanuel **EP72**
Sonowal, Supriya **EP689**, **EP639**, **EP403**, EP509, EP565, EP640
Soonawalla, Zahir EP933
Sørensen, Amanda EP1058
Soria Becerra, Marina EP1630
Soria-Alcaide, Gonzalo P346
Sośnierz, Ewelina **P240**, **EP1629**
Sotiropoulos, Georgios EP1733
Sotiropoulou, Maria EP145
Soto, Alfonso RC11.4, **EP1145**, P267, EP1102, P180
Soto, Alfonso EP1185
Soto-Moreno, Alfonso EP1213, EP1161
Sottile, Johana EP1167, EP1124, EP1158, P263
Sottile, Johana EP1022, EP1011
Soukup, Jiří EP1122, EP1521, P419, P375
Soulé, D'jalma EP69
Sourij, Harald EP518
Sousa, Ana EP457

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Sousa, Ana Margarida EP992
Sousa, Isabel EP325
Souteiro, Pedro EP947
Sowa Staszczak, Anna P226
Sowińska-Przepiera, Elżbieta P503
Soyaltin, Utku Erdem P394
Söylemezoğlu, Figen P317
Soyluk Selcukbiricik, Ozlem EP53, P460
Soyluk Selcukbiricik, Ozlem P279, P291
Soyyiğit, Şadan EP726
Špačková, Veronika EP849
Špačková, Veronika **EP1533**
Spaggiari, Giorgia RC4.1, P358, **EP575**
Spagnuolo, Luca P303
Speksnijder, Esther M. EP92
Spencer-Segal, Joanna L. P266, RC3.4, P274
Sperduti, Samantha RC4.1, P391, EP936, EP1314
Spieler, Peter OC7.3
Spiteri, Martha **EP166**
Spitzweg, Christine EP1108
Spoltore, Maria Elena EP501
Spoudeas, Helen A. P293
Spoutil, Frantisek EP399
Spranger, Joachim P494
Sprengers, Misja EP503
Spritzer, Poli Mara **57**
Sprovera, Paula **EP1458**
Spyroglou, Ariadni EP1733
Spyropoulos, Panagiotis P445
Srakočić, Sanja EP426
Srb, Nika EP1466
Sridhar, Ananth OC10.4
Sridharan, Kalyani P305
Sriramachandran, Annie OC3.2
Srirangalingam, Umasuthan P8, EP36, **P21**
Srivastava, Manoj EP596, EP636, EP788
Stabile, Andrea OC7.3
Stacey, Emily EP85
Stachowska, Barbara EP21, EP1197, EP1323
Stafie, Ingrid-Ioana EP950, EP1491
Stalla, Günter EP1075, RC9.5
Stalla, Günter Karl P269
Stamou, Maria EP1343
Stan, Madalina-Bianca EP619
Stanciu, Andreea-Cristina **EP917**
Stanciu, Diana EP1277, EP196
Stanciu, Mihaela EP1277, EP196
Stancu, Cristina EP17, P382, **P230**, EP7
Stanczyk, Agnieszka EP1795
Stańczyk, Agnieszka EP480
Stanescu-Smocot, Anastasia Patricia EP1149
Stanic, Anja EP1441, EP1235
Stanimirovic, Aleksandar P297
Staniszewska-Mróz, Joanna EP197
Stankovic, Jelena P22
Stankovic, Sandra EP699, EP762
Stankovic, Tatjana EP699, EP762
Stankovic, Valentina P120
Stanoiu- Pinzariu, Oana EP1744
Stańska, Alicja **EP561**
Starovatskyi, Oleksandr P271
Stasiak, Bartłomiej EP1547
Stasiak, Magdalena **P347**, **EP1547**
Staszewski, Jacek EP756
Stathi, Maria Gabriella P166
Stathori, Galateia EP39, EP1230, EP139, EP115, P90
Statiri, Eleni EP108, EP1265
Stavridoi, Thomais P415
Stavrinidou, Marisia EP1340
Stawerska, Renata EP1452, EP212, P347
Stawerska, Renata P240, EP1629
Steckel, Lucas **EP1033**
Stedman, Mike RC1.6, P449
Steenblock, Charlotte OC9.3, OC7.6, OC9.1, P65
Stefanaki, Katerina EP479, **EP1219**, **EP891**
Stefanou, Dimitra P141
Stefańska, Agnieszka P226
Stein, Frank RC11.1
Steinhauer, Sonja OC12.5
Steinkogler, Annika RC5.5, EP1049
Steinmetz, Tali P129
Steiropoulos, Paschalis EP850
Stelmachowska-Banas, Maria EP1169
Stelmachowska-Banaś, Maria EP1143, EP1172
Stener-Victorin, Elisabet EP1907, EP1905, EP1906, EP1909
Stenvers, Dirk Jan P250, EP92
Stepanovic, Boban EP444, P67, **EP149**
Stephanie, Burger-Stritt P5
Stephanie, Espiard P237, RC12.4
Stephanou, Dimitroula EP1045
Stephenson, Alice **P479**
Stępień, Jakub EP1238
Stępień, Maciej EP63
Steplewski, Matthew EP1187
Stępniak, Jan **EP984**, EP1590
Stepura, Olena **EP617**
Stergianos, Stavros **EP11**
Stessel, Björn EP469
Štětkářová, Ivana EP1210
Stevchevska, Aleksandra **EP1361**, EP368
Stevens, Adam EP1759
Stigliano, Antonio OC6.5, P253
Stimson, Roland P332
Stochholm, Kirstine P244
Stoev, Lyuben EP1708
Stoev, Svetoslav EP1320
Stoeva, Iva EP1386, EP1380
Stoicea, Mihai Ciprian EP1520
Stojanovic, Marina EP149
Stojanovic, Marko EP1464, P297, **P120**
Stojanovic, Nemanja EP1300
Stojkovic, Mirjana **EP172**, **EP1651**
Stokar, Joshua **OC10.6**
Stokes, Gabrielle EP269, EP303
Stokes, Giangela **P353**
Stonyte, Aiste EP1467, EP1556
Storbeck, Karl P151, EP1359, EP1348
Stougiannos, Pavlos P208
Straka, Martin P114
Straka, Martin EP88
Stramazzo, Ilaria EP1315, RC1.4
Strasburger, Christian J. P269, P284, EP1818
Stratakis, Constantine P252, EP1476, P461
STRATIGOU, THEODORA EP453, EP591, EP237, EP952, EP19, RC10.3
Strauss, Leena RC2.3
Street, Maria **OC8.2**, **OC8.5**, **P112**
Streit, Jona EP1135
Strickland, Rhiannon EP85
Strinati, Vittoria EP501
Strmen, Timotej EP1905
Strong, Theresa P142
Strzelczyk, Janusz EP963, EP99
Strzelec, Martyna EP1192, EP1323
Stüfchen, Isabel RC5.5, OC5.5, EP1049, **P28**, EP33, EP29, **RC8.4**, RC9.1, RC8.2, EP97, P452
Stummer, Walter EP1059, EP1135
Sturgeon, Julia OC9.5, P21
Sturnia, Sara EP1138, EP1215
Stylianidou, Christianna P445
Stylianou, Konstantinos P100, P94
Stypinski, Daria P36, EP116
Su, Wan **OC3.5**, **OC9.2**, **P487**
Subrahmanian, Anushka **EP1368**
Subramanian, Prem OC1.3
Sucaliuc, Alina EP304, EP1013, EP250
Suchy, Wiktoria P247, **P246**, EP1814
Suchy, Wiktoria EP1083
Sudhakar, Murugan EP224
Sudzinova, Adriana P50
Suero Molina, Eric EP1059, EP1135
Sufaro, Yuval Zeev P268
Sugata, Jun EP1104, EP1184, **EP1088**
Sugimura, Yoshihisa **EP1129**, EP1200
Suh, Sunghwan **EP484**
Suhandynata, Raymond T. EP228, EP1374
Suharinizam, Nur Fatin Aqilah Binti EP1881
Suharinizam, Nur Fatin Aqilah Binti EP1772
Sukhtankar, Gitanjali Jaywant EP224
Sulaieva, Oksana P167
Sulcebe, Genc EP1514, EP1667
Suligowska, Agnieszka **EP1574**
Sulimowski, Gabrielle P234
Sultan, Kawthar EP1350
SULTANA, NUSRAT **P448**, **P473**
Suman, Medha **P276**
Sumanatilleke, manilka EP277, EP1221
Sumarac-Dumanovic, Mirjana EP779, **EP1074**
Sümegi, Dóra **EP1000**
Suminskaite, Dominyka EP853
Sumnik, Zdenek EP350
Sun, Zhuolun **EP6**
Sundin, Anders RC6.5
Sundquist, Kristina EP1479
Sundström-Poromaa, Inger OC4.3
Supe, Pravin EP596, EP689, EP636, EP788, EP639, EP403, EP509, EP565, EP640
Suranthiran Naidu, Thaalitha Naidu **EP815**, **EP1555**
Suslyk, Halyna EP1492
Sussel, Lori **58**
Sust, Mariano P280
Suturina, Larisa P320, EP637
Suyono, Seso Sulijaya **EP1398**
Suzuki, Atsushi EP1129
Svanevik, Marius P75
Svedberg, Agneta P266, RC3.4
Svobodová, Tereza EP398, **EP414**, P165
Svojtková, Michaela EP86, **EP445**
Swee, Du Soon **EP133**
Swee, Du Soon OC6.3
Sweeney, Kieron P283, P259
Świątkowska-Stodulska, Renata OC7.2, OC6.4, OC6.5, P93, P309
Świątkowska-Stodulska, Renata P39, P62
Świątkowska-Stodulska, Renata EP939
Świerkot, Maria EP197
Switzer, Aaron EP435, OC11.1
Sygula, Aleksandra OC7.1, EP905
Sylvetsky, Noa EP102, P397
Syrenicz, Anhelli EP1024

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Syrris, Christoforos EP1153
Szalat, Auryan OC10.6
Szamatowicz, Michal RC4.5
Szántó, Erika EP1507
Szczepanek - Parulska, Ewelina P106
Szczepanek-Parulska, Ewelina EP377, P49
Szczesniak, Dorota EP1192
Szeredás, Bálint OC6.4
Szewczyk, Sebastian **EP220**
Szmigielska, Maria P388, **P425**
Sztefko, Krystyna EP79
Szubstarska, Patrycja P211
Szucio, Weronika RC4.5
Szücs, Nikolette OC6.4
Szumińska, Małgorzata P226
Szydłowski, Jarosław P248
Szyluk, Karol EP369
Szypenbejl, Jacek EP939
T' SJOEN, Guy EP1316
Tabacchi, Elena OC1.6
Tabar, Viviane EP1676
Tabarin, Antoine P272, P508
Tabassum, Humera **EP317**, **P436**, **EP1418**
Tabuchi, Yukiko P174, P185
Tack, Lloyd P228
Tadic Latinovic, Ljiljana EP1586
Tadross, John RC6.5
Taebnia, Nayere EP1905
Tafani, Marco EP429
Tagger-Green, Nirit P121
Tagliafico, Alberto P271
Tahapary, Dicky EP1419
Tahara, Shigeyuki EP1063
Tahl, Serge P470
Taieb, ACH EP75
Taifas, Diana **EP1251**
Taimah, Manal **EP449**, **P146**
Takacs, Istvan OC12.4
Takahashi, Katsutoshi P53
Takahashi, Yutaka P53
Takano, Noriyoshi EP37
Takebe, Saya **EP37**
Takizawa, Hiroki EP1129
Tal, Galit EP1317
Tal, Noa P268
Tal, Orna EP741, EP486, EP742
Talaibekova, Sezim P194
Taleb, Raghda EP579
Talevska, Ana **EP1611**
Talkowski, Michael EP1343
Tallini, Giovanni OC1.6
Tam, Abbas Ali EP84
Tam, Trevor EP1260
Tamaeva, Safi EP1080
Tamagno, Elena EP1019
Tamatea, Jade **EP1610**
Tamburello, Mariangela P223
Tamouridis, Stefanos EP597, EP1596, P170
Tan, Colin Jingxian OC6.3
Tan, Hao Wei EP1493
Tan, Huiwen **RC2.6**, EP1090
Tan, Kathryn Choon-Beng EP1488, P378, EP8
Tan, Michael Chien Sheng OC6.3
Tan, Rachel Si Jing EP1095
Tan, Tricia P351, OC4.2, P322, P325, **EP430**
Tan, Wai Kit Alvin OC6.3
Tan, Yi Ting OC6.3
Tan Öksüz, Sinem Başak **EP1542**, **EP1042**
Tanaka, Tomohiro P255, P256
Tanday, Raj EP768, EP677
Tandeter, Howard EP1497
Tandl, Veronika EP1348
Tang, Jie P195
Tang, Rongsong EP633
Tankova, Tsvetalina EP1820
Tantoh Ndinteh, Derek P238
Tapa, Denise EP1644, P254
Tarabasanu-Mihaila, Ioana-Elena EP1679
Tarallo, Cinzia EP1818
Tarapongpun, Tanakorn EP315
Tarbaeva, Natalya EP1675
Tarbaeva, Natalya P215
Tarcau, Otilia-Andreea EP1491
Tariel, François P17
Tarigan, Tri EP1419
Tarko, Klajdi EP1278
Tarnowska, Julia P39
Tartaglione, Linda P367
Tartaglione, Tommaso EP1146
Taş, Funda Feryal OC11.2
Tasci, Ilker EP1743
Taskiran, Bengur **EP143**
Tastekin, Mustafa Berkay **P317**, **EP1111**, **P295**
Tatarczuch, Aleksandra **EP1354**
Tatarida Palla, Maria Chrysoula **EP39**, **EP1230**, **EP1541**, EP306, P90
Taubaldiyeva, Zhannat EP293
Taufik, Bara **EP198**, **P118**
Taujan, Georgiana EP93, **EP129**
Taulbjerg Kristensen, Tine P327, EP1360, EP1364
Tauni, Rahat EP1552
Taura, Daisuke P53
Tausanovic, Katarina EP149
Tavares, Isabel EP1450
Tavares, Patrícia EP457
Tavares Da Silva, Beatriz EP989, EP1027, **EP1326**, **EP525**
Tavoni, Antonio P312
Taxová Braunerová, Radka EP398, **P165**
Tay, Chau Thien P320, EP637
Tay, Wei Lin OC6.3
Taylor, Angela OC6.6, EP10, EP38, P151, RC7.1, EP1348
Taylor, Peter RC1.6, P449
Tazhigulova, Zhaniya EP287
Tchelidze, Nazi **EP1752**
Tchorzewska-Skrobich, Magdalena P290
Tébar Caballero, Mariano P402
Tebben, Peter OC10.1, P72
Tęcza, Krystyna EP1463
Tedoradze, Nino **EP1565**
Tee, Hwee Ching EP577
Teede, Helena **P320**, EP637
Teh, James EP224
Tehrani, Fahimeh P320, EP637
Tei, Randi P22
Teixeira, Vera EP1098
Tek, Semih P52, P33
Tekin, Selin P317, EP1239, EP1111, P295, EP1384
Tekin Uzman, Rukiye Dilara EP1201, **EP1133**
TEKOU, KONSTANTINA P426
Telci Caklili, Ozge **EP1743**
Teli, Vaishali EP1532
Tellier, Genevieve **P105**
Telo, Sofiela EP610
Temizturk, Mina Gulfem EP1842
Tena-Sempere, Manuel RC2.3, P346, OC4.4
Tencerova, Michaela **EP399**
Tentolouris, Nikolaos EP560, EP670
Tentolouris, Nikolaos EP25
Tenuta, Marta P358, **P444**, P12
Teo, Ada OC6.3
Teodoriu, Laura EP159
Teoli, Jordan EP1366
Teong, Xiao Tong EP558
Tepnadze, Nikoloz EP908, **EP1524**
Terenzi, Umberto EP280
Terlutter, Tim **OC3.2**
Terzea, Dana EP1520, EP318
Terzea, Dana Cristina EP917
Terzolo, Massimo EP95, RC12.5
Tessler, Fraklin P401
Testa, Stefano **EP1117**
Tetradze, Lika EP908
Teumer, Alexander P432
Tevzadze, Mariam EP328, EP345
Thabet, Aisha EP579
Thakker, Rajesh RC10.2
Thandi, Jagraj **EP1199**
Thankam, Sunil EP1611
Thankamony, Ajay EP34
Thant, Aye Aye **P113**
Thant, Aye Aye EP746
Theiler-Schwetz, Verena RC9.5
Theillac, Bernard P227
Theochari, Maria EP1733
Theocharis, Angelos P166, EP115, EP1387
Theodoropoulou, Marily RC5.5, EP1049, RC8.2
Theodorou, Angeliki **EP1676**
THEWJITCHAROEN, YOTSAPON **EP745**, **EP1572**, **EP1659**
Thierry, Susanne OC11.3
Thomassen, Mads EP1364
Thomeret, Louis **RC9.3**
Thompson, Amie EP302
Thomsen, Annika Runegaard P338, P372
Thuillier, Philippe EP72
Tiago Guimarães, João P77
Tiberg, Fredrik P266, RC3.4, P274
Tiberio, Guido P223
Tichomirowa, Maria **P447**
Tigas, Stelios **EP722**, EP729
Tikos, Georgios EP1508
Tilici, Dana EP771, EP1522
Tilici, Dana EP122, EP1897, EP1887
Tillio, Paolo Amedeo EP590
Timmers, Henricus Johannes Louis Maria P452
Timmers, Tessa P250
Timmons, Joseph EP1705
Timón, Blanca EP562
Timper, Katharina EP638
Tinahones, Francisco J EP405
Tinahones Madueño, Francisco José EP869, EP845
Tinazli, Ali EP657
Tini, Sabrina EP400, EP590
Tiosano, Dov EP1317
Tiracorrendo, Matteo EP1182
Tirosh, Amit P305
Tirukonda, Prasanna Sivanath OC6.3
Tiryaki, Mehmet P314
Tisserand, Gautier OC7.2

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Tivers, Michael EP85
Tizianel, Irene P56, EP1094, **RC9.4**
Tizianel, Irene P289
Tizianel, Irene EP190
Tjandrawinata, Raymond Rubianto EP1398
Tkacz, Edyta **P226**
Toboła, Agata P51
Tobon, Catalina EP82
Todorova, Biljana EP1895
Todurov, Ivan EP617
Tofail, Tania P473
Tofé Povedano, Santiago EP1191, EP1480
Toffoli, Barbara EP491
Tokarczyk, Kamila EP963
Tőke, Judit OC6.4
Tolosa, Melissa Joyanne **EP627**
Tomas, Nerea EP44
Tomás Pérez, Alejandro EP1730
Tomasello, Laura P462
Tomašević, Jelena EP1748
Tomas-Garcia, Maria EP698
Tomé García, Mónica EP1305
Tomkins, Maria **EP10**, **EP38**
Tomkins, Maria P283, P259
Tomlinson, Jeremy EP676, EP125
Tomlinson, Jeremy W EP1383
Tonacchera, Massimo EP150, P24
Tong, Aaron OC6.3
Tong, Anli EP32
Tong, Anli OC7.2
Tonge, Joseph EP34
Toole, Barry J. EP228, EP1374
Topaloglu, Oya EP1711, P410, EP84, EP1484, EP726, EP641, EP249, EP1015
Toporowska-Siwiak, Aleksandra EP1172
Toppari, Jorma P357
Torazza, Carola P509
Torchio, Marianna EP95, RC12.5
Tordjman, Karen **EP1107**
Toren, Michal EP1317
Torregrosa, Eugenia EP1158
Torregrosa-Quesada, María Eugenia EP1011, EP1167, EP1124
Torregrossa, Liborio EP226
Torregrossa, Liborio EP216, P84
Torregrossa, Liborio OC1.5, P383
Torrejón, Sara EP1096
Torres, Manon **EP1402**
Torres, Marco Onofrio P97
Torres Degayon, Silvia RC11.4, P180
Torres-Barea, Isabel EP382
Torres-Granados, Carmen OC4.4
Torstensson, Sara EP1907
Toruner, Fusun EP41, EP656, EP1797, P440, EP1886
Toshevska Stefanoska, Marija **EP368**
Tosin, Anna EP1017, P43, EP54, EP131
Tosin, Anna **P455**
Toti, Florian EP1278, EP1787
Totomirova, Tzvetelina EP600, **EP732**
Touchot, Nicolas EP464, P256
Tourigny, David S. OC3.1, OC6.6
Tournis, Symeon P102, EP239, RC10.3
Toutounchi, Sadegh EP63
Tovkai, Oleksandr EP404
Toz, Hasan EP1070
Tozman, Murat EP140, EP1843
Trabado, Severine P242, P304
Traboulsi, Eva EP1122
Trachana, Varvara P461
Tran, Hieu T N **OC6.3**
Trattnig, Siegfried EP54, EP131
Traynor, Carol EP10, EP38
Treasure, Peter RC9.5
Trebicka, Jonel EP1059, EP1135
Trejo-Lopez, Jorge EP1144
Treppiedi, Donatella EP1173
Tretyak, Olena EP404
Trevisi, Gianluca P298
Treviso, Juan Carlos EP1073
Tribotti, Laura EP80, EP512
Tribovane, Denil EP1098
Trifanescu, Raluca EP1062
Trimpou, Penelope P14
Trinh, Anne EP303
Trinh, Beckey OC2.5
Triphob, Anchisa **EP315**
Tritos, Nicholas P261
Trivellin, Giampaolo **P252**, P305
Triviño Yannuzzi, Vanessa EP1535
Trofimiuk-Muldner, Malgorzata EP954, P3
Troshina, Ekaterina EP1675, P215
Troshina, Ekaterina P451
Trukhin, Alexey EP1540
Tryfon, Stavros P182
Tsagarakis, Stylianos P38
Tsai, Cheng-Yu RC1.3, **P412**
TSAI, Chih-Wei EP621
Tsai, Wan-Chi EP945
Tsalkitzi, Afroditi EP889
Tsalkitzi, Afroditi EP819
Tsanaxidou, Stella EP139, EP115
Tsantarlioti, Olga EP39, EP1541
Tsaroucha, Maria P445
Tsaryk, Iryna **EP551**, EP542
Tschaidse, Lea OC9.6
Tsekmekidou, Xanthippi EP1855
Tsekouras, Athanasios P445
Tselebis, Athanasios EP1241
Tselepi, Charikleia EP729
Tseng, Ching-Hua **EP179**
Tseniklidi, Ermioni P445
Tsentidis, Charalampos EP108, EP1265, EP1438
TSIAMA, VASILIKI EP1592, EP123, EP1394, EP685, EP1241
Tsikopoulos, Konstantinos EP217
Tsioumas, Georgios **P208**
Tsirogianni, Alexandra P166
TSIRONA, SOFIA P445
Tsirou, Georgia EP1045, EP1496, EP1262, EP25, **P141**
T'Sjoen, Guy EP1344, P327, EP1360
Tsolakidou, Anastasia EP1265
tsoli, marina EP927
Tsoli, Marina RC10.1, P213
TSOLI, MARINA **EP918**
Tsopouzidou, Despoina EP1045, EP1496, EP1262, EP25, P141
Tsourouflis, Gerasimos EP1568
Tsoutsouki, Jovanna **P349**, **OC4.1**
Tsoutsouki, Jovanna P351, OC4.2, P322, P325
Tsumura, Tetsuro EP1200
Tsvetov, Gloria EP473
Tsvetov, Gloria P91, P109
Tsvetov, Gloria P316
Tucci, Lorenzo OC6.6, P27, **RC6.4**, EP98, P2
Tudik, Peter **P363**
Tudorache, Maria EP1460, EP1149
Tueros, Brigida P395
Tufan, Ceren EP1346, **EP1131**
Tufekci, Damla RC12.2
Tuğcu, Murat EP1569
Tuladhar, Radhika EP1280, EP205, EP1428
Tuleja, Anna Barbara **OC7.1**
Tuliantseva, Yelyzaveta EP1767
Tumanian, Hovhannes EP1275
Tumkur Prasad, Nithin **EP1769**, **EP1863**
Tun, Zin P423, EP1644
Tunç Topuz, Büşra EP1346, P194, EP1131
Tuntaş, Ahmet Furkan EP1298
Turan, Nedim EP943
Turan, Senol EP1231
Turan Erdogan, Beril **EP1711**
Turashvili, Nino **EP1626**
Turhan Iyidir, Ozlem EP292, P385, EP1481, P173
Turino Silva, José Francisco OC11.5
Turner, Helen **59**, P437
Turner, Jeremy OC10.1, OC12.4
Turner, Laurent EP558
Turowska, Magdalena **P388**, P425
Turunen, Tanja EP1905, **EP1906**
Tutar, Yusuf P502
Tuzcu, Göksel P390
Twig, Gilad P128, P163
Tyssen, Johanna EP1479
Tzagkaraki, Evmorfia EP1476, P461
Tzamouri, Stavroula EP145
Tzanela, Marinella P166
Tzanela, Marinella EP145, EP649, EP519, **EP453**, **EP591**, EP237, **EP139**, EP115, EP1387, EP952, EP19
Tzifa, Garyfallia P445
Tzimagiorgis, Georgios P207
Tzoraki, Maria **EP1869**, **EP1872**, **EP1723**
Tzoulakitze, Christina EP1116
Tzoulis, Ploutarchos P445
Ubeda Dilme, Maria EP1191
Ubranek, Margrit P353
Ucan, Bekir EP1457, EP1745
Uceda-@Rodriguez, Esperanza RC2.3
Uceda-Rodriguez, Esperanza OC4.4
Uchkunkhonova, Shakhzoda **EP1331**
Udholm, Nichlas **OC12.2**
Udholm, Sebastian OC12.2
Udumyan, Ruzan P89
Ugalde, Aitziber P79, OC10.3
Ugleholdt, Randi EP60
Ugur, Kader **EP1298**
Ujhelyi, Bernadett EP1507
Ukena, Jenny OC10.2
Ukrainets, Kateryna **EP664**
Ukrainets, Oleh EP664
Ukrainets, Oleksii EP1159
Uktveris, Rimantas EP1379
Ulas, Ezgi EP1189, EP1204
Ulaş, Ezgi EP140
Ünal Kocabaş, Gökçen EP1204, **EP140**, **EP1843**
Undas, Anetta P376
Undas, Kamila **P376**
Ungureanu, Maria-Christina EP262, EP1292
Ünsal, Mustafa Gökhan P390
Unubol, Mustafa P390

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Unver Ozkahraman, Aysel P52
Unver Ozkahraman, Aysel EP1034, **EP1201**, EP1133, **EP1163**
Upton, Thomas P38
Urbani, Andrea EP1060, EP1151
Urbani, Claudio EP1296, EP106, EP1291, P312, **P24**
Urbankova, Helena EP88
Urbano Ferreira, Helena EP494
Urbanovych, Alina EP578, EP879, EP1473, **EP814**, EP527, EP1446, P158
Urbina Solano, Sandra EP1713
Urbonas, Mykolas RC8.1
Uroš, Ana EP511
Urtula, Anton Angelo **EP1436**
Urusova, Liliya P215
Urwyler, Sandrine A. EP1081, P294, EP1064, P203
Uslar, Thomas **EP30**, **P19**
Uth, Michael P447
Utkus, Algirdas RC8.1
Uygur, Meliha Melin **P467**, **RC12.2**, **EP1724**
Uygur, Özgür P467
Uzun, Metehan P194
Uzun, Nagihan EP1745
Uzun Karaüzüm, Selin **OC11.2**
V. Nagy, Endre EP1507
Vacek, Petr EP1113
Vaclavikova, Eliska EP1453, EP1521, P419, P375
Vaczlavik, Anna P55, EP138, RC12.4
Vaduva, Patricia RC9.3
Vaduva, Patricia EP1860, EP14, P17, OC6.5
Vaduva, Patricia **RC12.4**, **P458**
Vaglica, Fabiola P462
Vágvölgyi, Anna EP1370
Vágvölgyi, Anna P341
Vai, Silvia P97
Vaidya, Anand EP30
Vaillant, Charly P272
Vajkoczy, Peter P284
Valaiyapathi, Rajalakshmi EP430
Valakos, Dimitris P461
Valassi, Elena EP1083, EP1025
valayatham, vijiya mala EP1607
VALCU, RAZVAN P232
Valente, Miguel EP69
Valentino, Giammarco P334
Valeri, Federico P298
Valeri, Federico EP1151
Valeri, Federico EP1060
Valerio, Laura RC7.6
Valk, Gerlof D. **60**, **EP973**
Valkusz, Zsuzsanna EP1006, EP1563
Valladares, Carlos P395
Vallejo Herrera, Maria Jose **EP971**, EP1286
Vallejo Herrera, Veronica EP971, EP1286
Valsamidis, John EP1116
Valvis, Nicolaos P445
Vamvakidis, Kyriakos P426
van de Giessen, Elsmarieke P250
van de Ven, Annenienke EP1075, EP64
Van Den Berg, Sjoerd RC1.1
Van den Berghe, Greet EP469
van den Broek, Medard EP973
van der Groef, Romy OC5.1, **P69**, EP994
van der Hoeven, Loren **P250**
van Duursen, Majorie **61**
van Hall, Gerrit OC2.5
van Herwaarden, Antonius P95, EP64
Van Oyen, Dunja EP1017
van Santen, Hanneke **62**, **P255**, **P293**, **P256**
van Trigt, Victoria EP1067
Van Uum, Stan EP1684
Van Velsen, Evert P69, OC10.1, P72
van Zaanen, Els P69
Vanderwegen, Eline **EP469**
Vandeva-Kalvacheva, Silvia EP1380
Vandi, Giulia P104, P80
Vanhorebeek, Ilse EP469
vankayalapati, Praveena **EP363**
Vankemmel, Romain P4
Vaňková, Markéta **EP398**, P161, EP414, P165
Vantaggiato, Lorenza P311
Vantyghem, Marie Christine P200, P237
Vantyghem, Marie-Christine RC12.4
Vanuga, Peter EP1269, EP1264, P114, EP88
Vaquero-Barrios, José Manuel EP253
Vara Luiz, Henrique EP1188, EP1098
Varadhan, Laks EP234
Varaldo, Emanuele EP1029, OC3.4, EP1186, **P292**, P315, P278
Varaldo, Emanuele EP1030
Varausová, Anežka **EP86**, P224
Varbanets, Daria **EP156**
Varela, Ana P77, P414, EP1450
Varghese, Elizabeth EP1756
Varghese, Jeena OC7.2
Variji, Athena EP558
Varlamov, Elena EP1075
Varnavas, Petros P445
Varo, Nerea EP602
Varughese, George EP234
Vashakidze, Vitali EP328, EP345, **EP1609**
Vashakidze, Vitali EP365
Vashakmadze, Natia **EP1825**, EP1752
Vasileiou, Vasiliki EP654
Vasileiou, Vasiliki RC10.3
Vasilikos, Vasilios P208
Vasiljevic, Alexandre P270
Vassallo, Josanne EP166
Vassiliadi, Dimitra RC7.1
Vassiliadi, Dimitra Argyro EP145, P38, EP649, EP1733
Vatier, Camille EP1796
Vatseba, Tamara **EP901**
Vatsellas, Giannis P461
Vaychulis, Irina A. **EP1178**, **EP40**
Vayolipoyil, Sarath EP103
Vaysse, Frederic RC10.2
Vaz Lopes, Marta EP261, EP1534, EP856, EP1449
Vazquez, Maria RC2.3
Vazquez Martinez, Clotilde EP562
Vazquez Segoviano, Miriam RC5.6, **OC5.6**, OC7.6, OC3.6, OC5.4
Vcelak, Josef EP1453, EP352, EP398, EP1141, P161, EP86, EP350, EP243, EP1521, P419, P375, EP414, EP1210, **P381**, P81, P165
Včelák, Josef OC10.5
Vedelek, Viktor P341, EP1370
Veen, Roland RC7.1
Veerasamy, Kevin **EP456**, **P377**
Veerasomboonsin, Veekij EP1572, EP1659
Veerni, Rathna B. P37
Veerus, Liisa EP1368
Vega, Sebastian P395
Vega-Beyhart, Arturo **EP1205**
Vegas-Aguilar, Isabel Mª EP869
Vejrazkova, Daniela **P161**, EP414, EP445
Vékony, Bálint **OC6.4**
Vela Florensa, Gerogina EP582
Velardi, Valerio EP491
Velasco, Gloria EP487
Velasco Torres, Myrian EP613
Veldhuijzen van Zanten, Sophie EP994
Velesiotis, Christos EP25
Veličković, Nataša EP563
Velíková, Marta EP1210
Velkoska Nakova, Valentina EP876, EP647
Velo, Suada EP610
Velojić Golubović, Milena EP668
Velusamy, Anand EP96, P8
Velychko, Valentyna EP1821, **EP1767**
Venegas, Eva EP1185
Venegas Moreno, Eva **RC11.4**, EP1145, EP1102, **P180**
Venegas-Moreno, Eva EP1161
Venetis, Christos EP1340
Veneto, Laura EP1215
Venetsanaki, Vasiliki EP942
Veniou, Eirini EP1541
Ventura, Mara EP1168
Ventura, Paolo EP575
Vepkhishvili, Giorgi EP174
Verbalis, Joseph OC5.2
Verbeek, Willem EP1067
Verdelet, Tristan P242
Verdelli, Chiara P73
Verdoux, Marie P304
Vered, Shiraz P163
Vereshchynska, Andriana EP814
Vergani, Edoardo P367
Verissimo, David EP1220, EP267, EP69, EP351
Verkauskiene, Rasa EP20, EP466
Vermeersch, Pieter EP228, EP1374
Verrico, Monica RC6.2
Verroken, Charlotte EP224
Verstandig, Anthony EP102
Vervalcke, Jeroen EP1344
Ververi, Athina P415
Vestergaard, Peter EP1147
Vesterinen, Tiina EP61
Vesterinen, Tiina P35
Vetrani, Claudia EP400
Vetter, Diana EP1108
Vettorazzi, Sabine EP15
Vezzoli, Giuseppe P97
Vezzoli, Valeria P501
Vicari, Alessandra EP1055
Vicennati, Valentina OC1.6, P2
Vicennati, Valentina EP98
Vicente, Almudena P307
Vidal, Oscar P83
Vidal-Ostos De Lara, Fernando **P227**
Vidovic, Mile EP177
Vidović Iviš, Sonja EP426
Vieira, Inês EP974
Vieira, João EP731
Vieira, Sónia P77
Vignali, Filippo EP62, **P13**
Vignozzi, Linda EP1347
Viitala, Kreeta P357
Vila, Greisa EP1017, EP54, EP131, EP50

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Vilarrasa, N OC11.1
Vilas-Boas, Eloisa P148, EP393
Villa, Chiara P285
Villalba Armario, Paula P402
Villalobos Leon, María Laura P227
Villar Taibo, Rocio P267
Villar Taibo, Rocio EP669
Villar-Gouy, Keila R. OC5.5, P457
Vinagre, Irene EP821
Vinales, Karyne EP317, P436, EP1418
Vincent, Anna OC12.2
Vincent, Royce P342, P352
Vincenzi, Ludovica EP1026
Vinegrad, Nuphar **EP1531**
Viñes Raczkowski, Meritxell EP1480
Vinhais, Joana **EP1220**, **EP267**, EP69, EP351
Vinograd, Adi P128, P163
Vinograd, Ofir EP486, EP742
Vinogradova, Yana EP1413
Vintilă, Teodora **EP248**, EP996, EP1337
Violetis, Odysseas EP1733
Violon, Florian RC9.3, OC6.5
Virani, Mehul EP596, EP636, EP788
Virili, Camilla EP1315, **RC1.4**
Virtanen, Antti P35, EP61
Virtanen, Helena P357
Visotskii, Denis EP413
Vitale, Laura **EP1665**
Vitali, Diana P228
Vitellius, Géraldine EP1002
Vitku, Jana EP1165, EP1141, EP86, **P224**, EP445
Viukari, Marianna **P20**
Viukari, Marianna P35, EP61
Vivanco, Stefanni P395
Vizcaya, David P74
Vlachopapadopoulou, Elpis EP1869, EP1872, EP231, EP1723
Vlachopoulos, Charalambos P208
Vlachou, Eugenia **EP889**, EP819
Vlad, Mihaela Maria EP1039, EP1105, EP1248, EP1570, **EP289**, **EP1148**
Vlad, Repede P232
Vladoiu, Suzana EP318
Vladoiu, Suzana P230
Vlasakova, Renata EP273
Vlastos, Antonios P207
Vlavcheska, Hristina **EP1895**
Vlcek, Petr EP1521, P375
Vlček, Petr P419
Vodanović, Ivana Dora EP635
Vodola, Emanuele Pierpaolo EP1151
Vogeser, Michael EP228, EP1374
Vogiatzi, Maria P21
Vogt, Everton P148
Vogt, Éverton **EP393**
Vohra, Kushaa EP1252
Voicu, Gabriela EP307
Voinea, Iulia-Alexandra **EP307**
Vojnović Milutinović, Danijela **EP563**
Volkanovska Ilijevska, Cvetanka EP314, EP876, **EP647**
Völkel, Wolfgang RC8.4
Volkova, Anna EP521
Vollmer, Shobitha **P137**
Voltan, Giacomo EP282, RC9.4, P253
Voltan, Giacomo EP1086, **P289**, **EP233**
Voltan, Giacomo EP190
Völter, Friederike RC5.5, OC5.5, EP1049, P28, EP33, EP29, RC8.4
Vorona, Elena EP1059, EP1135
Vorotnikova, Svetlana EP256
Vosátková, Michala EP1141, EP86, EP1210
Vozza, Elisabetta EP400
Vrachnis, Dionysios EP5, EP1596, EP327
Vratarić, Miloš EP563
Vrbacky, Marek EP399
Vrbikova, Jana EP86
Vrecl Fazarinc, Milka P328
Vroonen, Laurent EP1482
Vryonidou, Andromahi EP1255, EP1335, P324, P343, P360, RC10.3
Vučenović, Nikolina P222
Vudu, Lorina EP1813
Vugt, Siebren P250
Vujacic, Natasa **EP187**
Vujnovic, Jana EP444, P67
Vujosevic, Dunja EP1351
Vujosevic, Snezana EP146
Vujovic, Jelena P67
Vujovic, Svetlana EP444, P67
Vukšić Polić, Melita EP1680
Vyhnalova, Katerina EP1453, EP1521, **P419**, P375
Vyllioti, Aikaterini Themis P59
Vysotskaya, Kseniya **EP1675**, **EP413**, **EP521**, P215
Wabitsch, Martin P255, P256, P151
Wada, Norio P53
Wagenfeld, Andrea P151
Wagner, Pia OC3.2
Wagrodzki, Michal EP964
Wais, Paulina P290
Walczyk, Agnieszka EP1591
Walecki, Jerzy EP1218
Wallin, Göran P89
Walsh, Ciaran **EP1854**
Walti, Carla EP1064
Wan Hamzah, Wan Mohd Hafez EP1555
Wan Jaafar, Wan Daizyreena EP815
Wändell, Per EP1479
Wandurraga-Sánchez, Edwin EP1465, EP1511
Wang, Chih-Yuan EP1601
Wang, Fulin EP983
Wang, Haining EP1671, **P365**
Wang, Huaiying **EP1090**
Wang, Jingpin EP633
Wang, Katharina EP1108
Wang, Rui **P495**
WANG, SUWEI P261
Wang, Wanzhou EP983
Wang, Wei EP1035
Wang, Weiqing P48
Wang, Xiangbing **EP295**, **P86**
Wang, Xiaoli EP1035
Wang, Xiaoli **P36**, **EP116**
Wang, Xinzhu EP1328
Wang, Yong OC7.5
Wang, Yongjian EP1035
Wang, Yuan P332
Wang, Zhenxun OC1.3
Wangpaichitr, Medhi EP1019, P509
Wanothayaroj, Ekgaluck EP1659
Wardlaw, Sharon L. EP1676
Wardley, Poppy RC5.1
Wargelius, Hanna-Linn RC6.5
Warren, Mark OC10.1, P72
Warringa, Leonie **RC1.1**
Wasif, Pearl EP1350
Wąsik, Norbert EP1187
Wasniewska, Malgorzata OC8.5, P112
Wąsowski, Dariusz EP906
Wass, John EP157
Wasserman, Halley P72
Waszkiewicz-Hanke, Małgorzata P51
Watada, Hirotaka EP1129
Watanabe, Daisuke EP37
Watanabe, Mikiko EP868, EP429, EP501
Watanabe, Minemori P53
Watson, Jo P340
Watti, Jezdancher **EP1602**
Watts, Akemys EP821
Weaver, Jamie RC5.2
Weaver, Katie EP228
Webb, Susan P280
Weber, Timm P145
Wee, Hui Chia P434
Węgrzyn, Karolina P226
Węgrzyn, Karolina **P32**
Wehmeier, Michael P145
Wei, Jia **OC6.1**
Wei, Shaoqing **EP983**
Weigensberg, Marc EP1317
Weiner, Dana P128
Weiß, Brigitte P494
Weissman Rosenfeld, Mayalee EP499
Welin, Staffan RC6.5
Welp, Ann-Christin OC9.6
Welt, Corrine P353
Wermers, Robert OC10.1
Wernicke, Charlotte P494
Wester, Sara OC1.3
White, Steve EP441
Whitehead, Simon EP143
Whitelaw, Ben EP52
Whyte, Martin EP441
Wichlińska, Małgorzata EP212
Wickramarachchi, Ashani **EP1383**
Wiebke, Schlötelburg P11
Wieczorkiewicz, Tomasz EP1238
Wiederkehr, Katja EP1157
Wiegand, Felix **EP423**
Wiegering, Verena **63**
Wiejak, Anna Maria EP1790
Wieke, Jakob P85
Wiener, Yifat EP147
Wier, Dustin EP1374
Wijenayake, Umesha **EP933**, **EP109**
Wildemberg, Luiz E EP1185
Wildemberg, Luiz Eduardo EP989
Willenberg, Holger S. P5
Williams, Graham Richard **64**
Williams, Tracy P42, OC6.1, RC9.1, P19
Williams, Tracy Ann EP6, EP59, P28, RC8.4, RC8.2, EP97
Willis, Thea OC5.4
Wilmer, Alexander EP469
Wilson, Harry EP160
Wilton, Anthony P105
Winder, Catherine P277, EP1164
Winson Gnanathayalan, Shahini **EP277**, **EP1221**, **EP361**
Winter, Elizabeth M. **EP224**
Winterfeld, Ursula **65**

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Winzeler, Bettina OC3.4, EP1081
Wisnu, Wismandari EP1419
Witek, Kornel **EP1238**
Witek, Przemysław EP1160, EP928
Witek, Przemysław EP1238
Withers, Dominic OC5.4
Witkowska, Ewelina EP212
Witowska, Agnieszka P106
Wittemans, Laura P151
Wittert, Gary EP558
Wizner, Jakub **EP1322**
Wlodarczyk, Irmina RC9.5
Włodarski, Paweł EP1137
Woelfle, Joachim P269
Wojciechowicz, Tatiana P140
Wojciechowska-Durczyńska, Katarzyna EP1452, EP57
Wojewódzka-Mirocha, Marta P221
Wolczynski, Slawomir EP468, RC4.5
Wolf, Jan P396
Wolf, Peter **EP1017**, P43, EP54, EP131, P455
Wollman, Ayala EP395, EP499
Wong, Carlos P82
Wong, Hui Chin EP577
Wong, Kang Min OC6.3
Wong, Kelly Hiu Ching **EP8**
WONG, Man Chi EP621
WONG, Yin San Florence EP621
Woodside, Jayne V P416
Wouters, Els EP12
Woźniak, Beata EP77
Wray, Susan EP1909
Wrighton, Sebastian P455
Wróblewska, Maja **EP939**
Wrotkowska, Elżbieta EP912
Wu, Hong EP490
Wu, Junyi EP682
Wu, Wan-Chen EP1271, **P216**
Wu, Xueyan EP1782
Wu, Yang EP36
Wu, Yi-Tzu P177
Wyciślik, Magdalena EP905
Wydra, Arnika EP1169
Wyniger, Lorena OC11.3
Wyns, Christine EP1908
Xekouki, Paraskevi P100, P94
Xhabija, Nereida EP854
Xhardo Hysenbelli, Elona **EP610**
Xia, Mona EP430
Xiao, Haipeng OC2.3
Xie, Weinan **P459**
Xie, Zuoling EP32
Xiong, Xi P82
Xu, Changliu OC2.3
Xu, Lei EP116
Xu, Liangzhi P320, EP637
Xu, Meng Jie OC6.6, P27
Xu, Ruijuan P495, **P468**
Xydakis, Antonios P445
Yadav, Priyanka EP689, EP639, EP403, EP509, EP565, EP640
Yadav, Sapana EP1280, EP205, EP1428
Yadav, Subhash EP1638, EP1091
Yagüe, Isabel EP487
Yakubu, Jibira RC12.3, EP1760
Yalcin, Mehmet Muhittin EP41, EP1886
Yalcin, Mehmet Muhittin EP656, P440
Yalçın, Seda Nur P130
Yamagami, Keiko EP1294
Yamamoto, Tunehiko P174
Yamashita, Yui EP1294
YAN, KA SHING **EP621**
Yanachkova, Vesselina **EP1320**
Yanes Cardozo, Licy RC4.4
Yang, Annie OC2.2
Yang, Chao EP983
Yang, Chia-Feng P379
Yang, Fan P63, **EP32**
Yang, Hyewon P57
Yang, Jia EP1328
Yang, Jun EP100, P42, P10, P19, P30, EP55
Yang, Jun EP1035
Yang, Kun **EP633**
Yang, Mengliu EP370
Yang, Rui P365
Yano, Shoji EP1317
Yao, Yong OC3.5
Yapijakis, Christos EP306
Yarar, Coşkun EP1068
Yardımcı, Aytul EP24
Yarkandi, Shahad EP58
Yárnoz, Patricia EP602
Yassin, Mohamed P369, EP1214
Yasuda, Tetsuyuki P174, P185
YAU, Kent Ho-chung P228
Yau, Mabel OC9.5
Yau, Thomas EP1606
Yavropoulou, Maria **P25**, EP560, EP670, EP231, EP1365, **RC10.3**
Yazman, Volkan P467
Ye, Lei P48
Ye, Zhang OC3.5
Yee, Szemen OC6.3
Yehuda, Moshe P429
Yenidunya Yalin, Gulsah **P279**, **P291**, EP53, **EP585**, P460
Yenilmez Tunoğlu, Ezgi Nurdan P502
Yeo, Pei Shan **EP284**
Yerokhovych, Viktoriia EP1650, **EP714**
Yerokhovych, Viktoriia P167, EP866
Yetişken, Merve P390
Yeung, Arthur P349, OC4.1, P351, OC4.2, P322, P325
Yi, Danielle OC2.2
Yi, Dongwon P168
YI, Hyon-Seung **OC1.4**
Yi, Ka Hee P373
Yigit, Mehmet EP140
Yigit, Mehmet EP1189, EP1204
Yildirim Sozmen, Eser EP1204
Yildiz, Bulent P320, EP637
Yildiz, Bulent P321, P463
Yilmaz, Ayse EP1711
Yılmaz, Ezgi **EP1829**
Yılmaz, Müge P314, **EP943**, P504, **P486**
Yılmaz, Murat EP1523
Yilmaz Ozguven, Muveddet Banu EP1163
Yin, Win Lei **EP1573**
Ylänen, Antero P20, P35
Ylänen, Antero EP61
Ylli, Agron EP1053, EP170, EP1237
Ylli, Dorina EP1053, EP170
Ylli, Dorina EP610, EP1514, EP1667, EP364
Ylli, Zamira EP1514, EP1667
Yoel, Uri EP1531, **OC1.1**
Yogendranathan, Nilukshana EP1811, EP1851, EP1836, EP1803
Yokota, Kenichi P53
Yoldi, Guillermo P346
Yoneda, Takashi P53
Yonem, Arif P130
Yong, Sy Liang EP1607
Yoo, Seung Eun P373
Yoo, Soon-Jib EP748
Yoon, JeeHee EP1597, **EP476**, EP1670
Yordanova, Desislava EP1386, EP1380
Yörük Durmaz, Fatma EP1100
Yorulmaz, Göknur EP1523
Yorulmaz Kaya, Refika P440
Yoshida, Jun EP1200
You, Hongzhao P493
YOUNG, Hai Ka Betty EP621
Young, Jacques P242, P304, OC9.5, P21
Young, Megan P349, OC4.1, P351, OC4.2, P322, P325
Young, Morag EP558
Young, William OC7.2
Yousaf, Saira P423, EP1644
Yousef, Hanadie OC2.2, EP739, P172
Yousseif, Ahmed EP1791
Yoveva, Milena **EP976**
Yu, Hyeong Won P373
Yu, Min Heui P405
Yu, Sung Hoon **EP754**
Yu, Ted OC2.2
Yu Ling Tan, Grace EP1199
Yuan, Elvin Lim OC6.3
Yuan, Guojun P255
Yucel, Puren EP1212
Yuen, Kevin CJ **66**, OC5.5, P228, P294
Yuen, Tony **P361**
Yun, HYEOK JUN EP1701
YUN, Soo Jin **EP379**
Yun, Suk Bong EP1670
Yurdacan Sahin, Muge P110
Yurenia, Alena EP838, EP1031, EP1372, EP1373
Yusifova, Fidan **EP1886**
Yuskiv, Marianna **EP1473**
Yusuff, Shafiq P423
Yuzvenko, Tetiana EP404
Yuzvenko, Violetta **EP404**
Zablah, Jenny P395
Zabuliene, Lina **EP685**, **EP1241**
Zabuliene, Lina **RC8.1**
Zacharaki, Panagiota EP479, EP1219
Zachariassen, Line **P338**, **P372**
Zacharin, Margaret P305
Zádori, János P341, EP1370
Zádori, Petra Lilla EP1370
Zafirovic, Sonja EP1560
Zafra Jiménez, Ramón EP1191
Zaharia, Claudiu EP1277, EP196
Zaidi, Mone P361
ZAINA, ADNAN **RC1.5**, **EP1176**
Zajickova, Katerina EP352, EP350, **EP243**
Zajkowska, Klaudia **P221**
Zakauskiene, Urte RC8.1
Zaki, Beenish **EP1318**
Zak-Skryskiewicz, Zuzanna EP1160
Zalewska, Ewa P62
Zaliska, Ivanna **EP1664**
Zalloua, Pierre EP811
Zamberlam, Gustavo EP1076

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026

Zamfir, Carmen Lacramioara P491
Zampogna, Marta P97
Zamponi, Virginia OC7.4, EP1224
Zanatta, Lorenzo P464
Zanella, Adriana EP1678
Zanella, Simone EP265
Zara, Flavia EP1115
Zarifis, Dimitrios EP850
Zarkasi, Zaiem P113
Zarkasi, Zaiem **EP746**
Zarkovic, Milos EP1651
Zarkovic, Milos EP172
Zatelli, Maria Chiara OC7.4
Zavala, Eder P38
Zavalniuk, Oleksandra EP1618
Zavatta, Guido P104, OC4.6, P323, P80
Zavattaro, Marco EP1455
Zavrashvili, Nino EP1624, EP1249, EP141, EP1295, EP173
Zaw, Theingi EP1223
Zawadzka, Karolina **P6**, **P15**
Zawadzka, Katarzyna EP651
Zayer, Leen EP1674
Zdravković, Darko EP1748
Zdrojewska, Małgorzata P62
Zdrojowy-Welna, Aleksandra **EP21**, EP1197
Zdrojowy-Wełna, Aleksandra EP1192, EP1323
Zecha, Christine P11
Zeeshan, Amna P243, EP1584
Zeiter, Deborah P150
Zekerie, Sevim EP1040
Zele-Alvarez, Lucia Belen EP1805
Zelinka, Tomáš EP70
Zema, Giulia P2
Zembrzuska, Sonia P39, P62
Zembska, Agnieszka EP1192, EP1323, EP651
Zendran, Iga EP1192
Zendran-Zahorska, Iga EP21
Zeng, Luyi EP1535, P116
Zeng, Muling P195
Zeng, Qingyue RC2.6
Zengin, Ayse EP303
Zennaro, Maria-Christina P31, OC6.2, P452
Zepiridis, Leonidas EP1340
Zerva, Dimitra EP113, P59
Zessides, Christos EP722, EP729
Zeyda, Maximilian EP54
Zeyda, Maximilian EP131
Zeyghami, Ali **P480**
Zgliczyński, Wojciech EP1169, EP77, P51
Zgliczyński, Wojciech EP1172
Zgliczyński, Wojciech EP1143
Zgoda, Izabella **EP1750**
Zhai, Jing P346
Zhang, Di OC9.2
Zhang, Feifei EP983
Zhang, Jie EP32
Zhang, Liang **OC7.2**, RC6.5
Zhang, Luxia EP983
Zhang, Rui **P493**, **EP1782**
Zhang, Songyun EP1035
Zhang, Ting RC4.2
Zhang, Wei P63
Zhang, Wenyu **P10**
Zhang, Xueyi P78
Zhang, Yuhao EP31
Zhang, Zheng OC9.2
Zhang, Ziwei EP32
Zhao, Carol OC10.2
Zhao, Huaying (Helen) EP458
Zhao, Lijun EP558
Zhao, Qiang EP1205
Zhao, Xiaomiao P320, EP637
Zhao, Xiyan P459
Zhao, Yao RC3.2
ZHAO, Yifan **P153**
Zhao, Yongdong EP224
Zherdova, Nadiia EP1307, EP617
Zhou, Xiang EP1076
Zhou, Xiang P487
Zhou, Yue OC7.2
Zhu, Dalong EP32
Zhu, Huijuan EP1035, P487
Zhu, Julie OC6.3
Zhu, Ling EP133
Ziakas, Antonios P208
Ziani, Alaee P339
ZIANNI, DIMITRA P192, P445
Zibar Tomsic, Karin EP320, EP146, P280, EP910, EP635
Zibar Tomšić, Karin P222
Židó, Michal EP1210
Zidrou, Maria P102
Ziegler, Christian G. EP1790
Zielinski, Grzegorz EP1137, EP1093, EP1103
Zieliński, Damian EP963
Zikan, Vit EP350, **EP273**
Zikan, Vit OC10.1
Zikopoulou, Maria EP1855, EP1796
Žilaitienė, Birutė EP1175, EP20, EP4, EP999
Žilaitienė, Birutė EP339
Zimmermann, Petra EP1108, RC9.1, EP97
Zinych, Veronika EP714
Ziogas, Dimitrios EP1045, P141
Zips, Daniel P284
ZIRILLI, LUCIA EP62, P13
Zisimopoulou, Eleana **EP1459**, EP1859, EP1766
Zitzmann, Kathrin EP1108
Zivaljevic, Vladan EP149
Zivanov, Marta P280
Zivanovic, Dusan EP779, EP1074
zivkovic, marija EP314, EP876, EP647
Zlatkovic, Jovana EP668
Zmierczak, Hans-Georg EP224
Zogala, David EP243
Zografos, Giorgos EP192, P59, EP1879
Zohrabyan, Naira EP544, EP1888
Zona, Gianluigi EP1024
Zopp, Stephanie RC5.5, OC3.2, EP1049
Zorai, Eya EP75
Zoric, Goran EP187
zorzano, marta OC11.1
Zotou, Maria EP649
Zottarelli, Lisa EP1611
Zou, Dajin EP490
Zouaghi, Yassine P346
Zsuzsanna, Reti **P490**
Zubillaga, Mikaela EP46, EP1535
Zuhur, Sayid EP1829
Żuk-Łapan, Aleksandra EP1404, EP1218, P103, EP1408
Zulfiqar, Arooj EP1584
Zuñiga, Juzzy Tatiana EP1735
Zuolo, Michele EP265
Zurera Gomez, Carmen **EP630**
Zybek-Kocik, Ariadna P106
Žygienė, Gintare EP1790
Zygmunt, Arkadiusz **EP1452**, P347, EP1547
Zygmunt, Arkadiusz **EP212**
Zygmunt, Arkadiusz P240, EP1629
Żyłka, Agnieszka **P411**
Zytner, Palina P71, P239, EP500, RC11.1, EP423, P241

Downloaded from academic.oup.com/ejendo/issue/195/Supplement_1 by guest on 05 September 2026